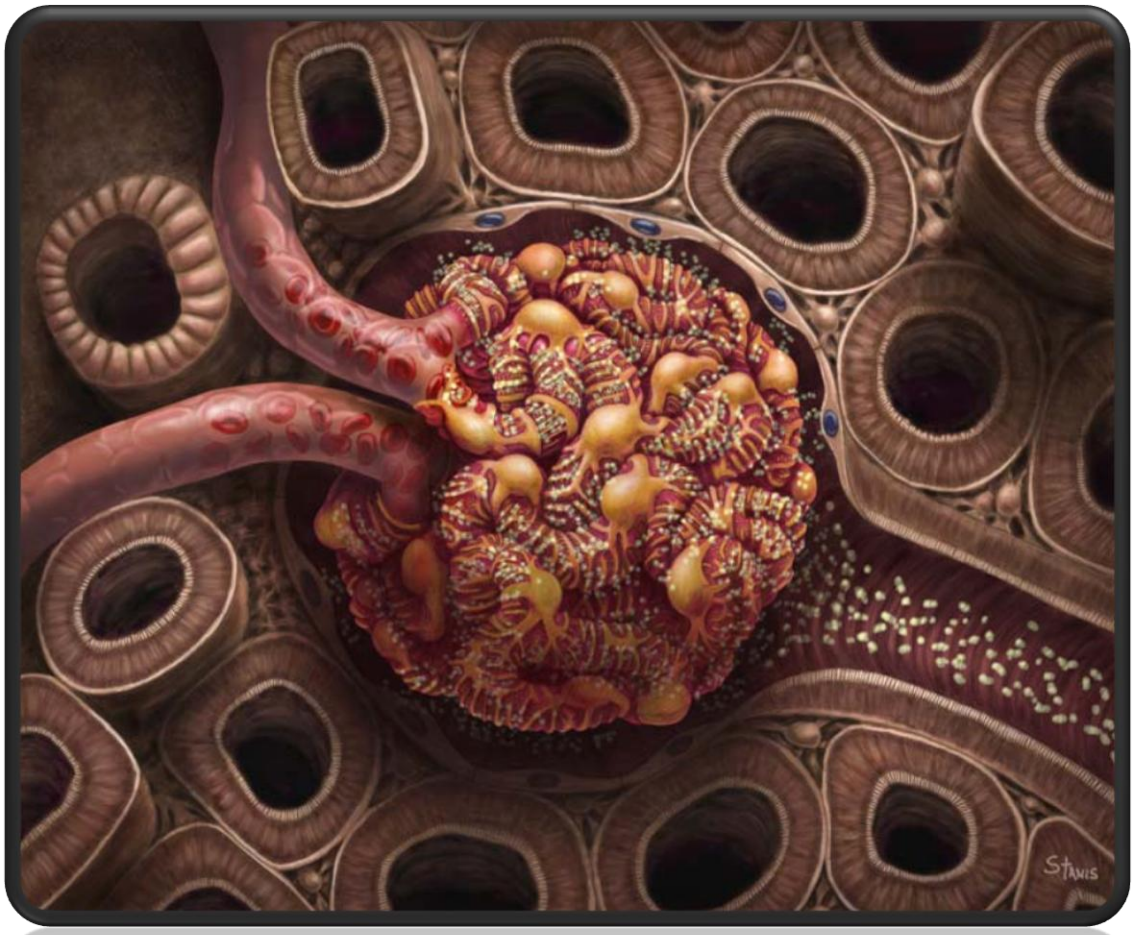
Physiology Team 431



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Tubular Secretion

Objectives:

At the end of this lecture student should be able to describe:

- Urea reabsorption
- Mechanism of Tubular secretion of K & H

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
- CO_2 diffuses into the cell + H_2O $\rightarrow H_2CO_3$
- H_2CO_3 $\rightarrow H^+$ + HCO_3
- HCO_3 is reabsorped by simple diffusion
- H^+ is secreted in exchange for Na^+

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 cotransported with Na
- Rate of absorption is under the control of PTH & V

Urea reabsorption

- **Plasma urea concentration =15-40mg /100ml**
- **End product of protein metabolism**
- **40-50% of filtered urea reabsorbed**

– **Reabsorbed by Passive diffusion following Na and 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

Tubular secretion:

- Secretion is opposite to reabsorption (from blood to lumen)
- Secretion only adds to the filtered substance

• From peritubular blood through peritubular space into renal tubular cell to tubular lumen

• Secretion:

Passive: (no carrier)

NH3=ammonia , salicylic acid

HAS A LIMIT

Active:

Tubular maximum (tm):
Creatinine & PAH

No tubular maximum:
K & H

K & H have the same carrier

Potassium is completely filtered & both reabsorbed & secreted

Potassium:

- 90% of filtered K is reabsorbed in PCT (proximal convoluted tubule).

- K is secreted in DCT (distal convoluted tubule) in exchange for Na and under the control of Aldosterone hormone.

the secretion of K can be tuned in DCT but constant at PCT.

Only if K is high in the blood, it will be secreted.

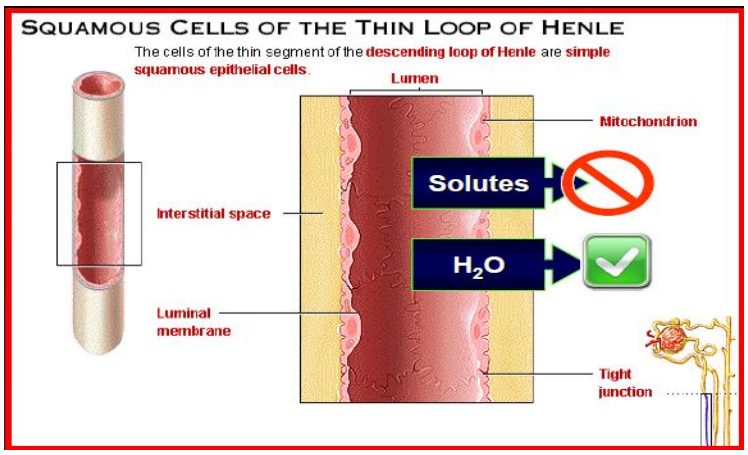
Remember: increase or decrease in K is dangerous to the heart

Hydrogen:

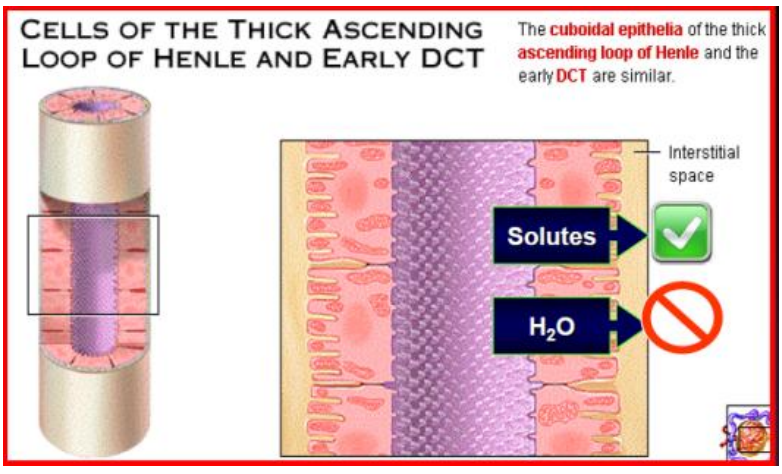
Excretion exchange for Na

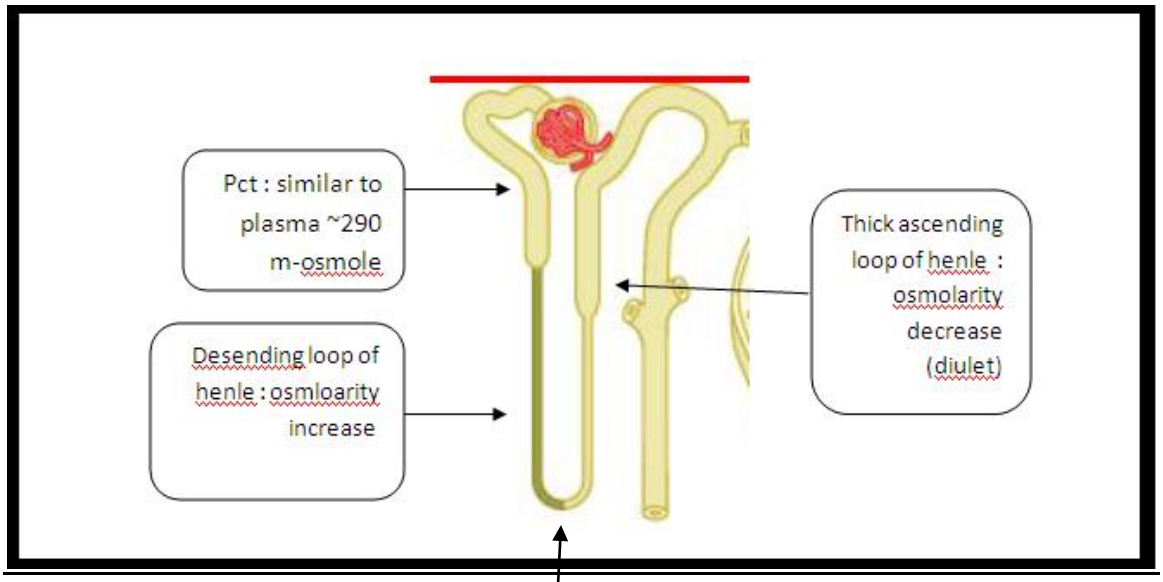
Osmolarity depend on solutes and water (if increase solutes osmolarity increase and when solutes decrease osmloarity decrease but for water when you increase osmolarity decrease and when water decrease osmolariy increase) so in case of PCT the osmolarity is the same as the osmolarity of plasma because both of water and solutes reabsorbed in equal portion which called isotonic , but in case of distal tubule you reabsorbed water so u decrease the water lead to increase osmolarity .

Descending limp of loop of henle (thin segment) : unlike PCT they have few mitochondria and flattened cells . only preamble in water reabsorbed not for solutes reabsorbed . the osmalirtay of the filtrate will increase because water reabsorbed and solutes remain And osmolarity reach 1200 m-osm. at the tip of loop of henle (osmolarity depend on solutes , when more solutes more osmolarity , less solutes less osmolarity)



Thick ascending loop of henle and early distal tubule , they shown together because functionally are similar . allow only reabsorbed of solutes but impermeable for water .. so once the filtrate ascend the osmolarity will decrease so it call the dilute segment because it make the osomlarity low (when you increase osmolarity you create a concentrate urine , but when you decrease osmolarity you create dilute urine).

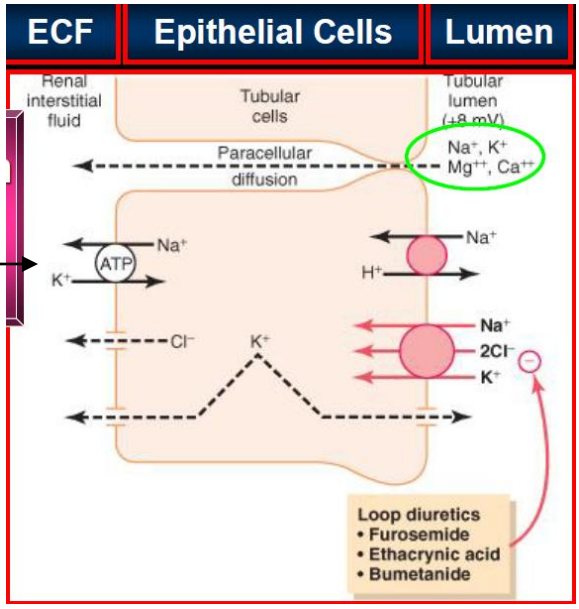




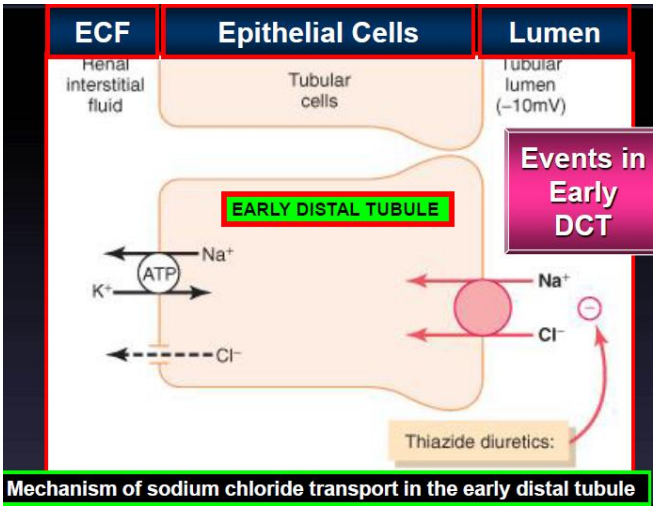
Events in thick loop of henle , many solutes reabsorb such NA , K , CL, ca mg but water not reabsorbed and thers is H secretion (means also acidification of urine occur in this segment)
Cotransporter of na , 2cl , k secondary active transporter (reabsorbed 4 ions in one time and this transporter present in luminal membrane)
Group of diuretic drugs (loop diuretics) block this channel , so solutes will not be absorbed and solutes will attract water , consequently you will pass lots of urine with a lot of solutes .

Ca and Mg enter the interstitial fluid via paracellular pathway

Na K ATP pump and it located in basolateral membrane to maintain electronegativity inside the cell .



Early DCT is similar to ascending loop of henle because Na reabsorbed while water not . it is also a duilet segment . there is an important transporter Na Cl transporter which present in luminal membrane(absorbed Na and also Cl) There is thiazide diuretics which block this transporter .



Mechanism of sodium chloride transport in the early distal tubule

Late dct and and early collecting tubule (these the hormone responsive part) that means the hormons can act at this segments such as ADH (anti diuretic hormone it is reabsorbed a lot of water and the person make minimal urine) . so if there is no ADH the absorption of water will not occur and the person will pass a lots of urine .
In this late Dcl and early collecting tubule have 2 types of cells principal cells (Na absorption and ADH related water reabsorbing) and intercalated cells(acid secretion and hco3 transport)
There is two hormone u have to know aldoserone (which primarily response to solutes reabsorbing) and adh (water reabsorbing) and both of them act on principal cells .

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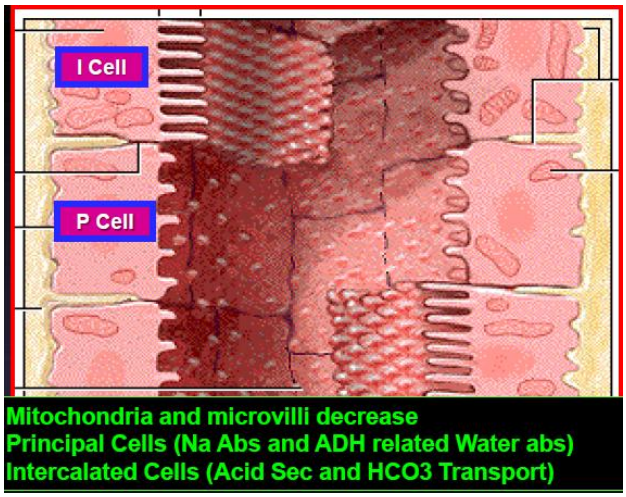
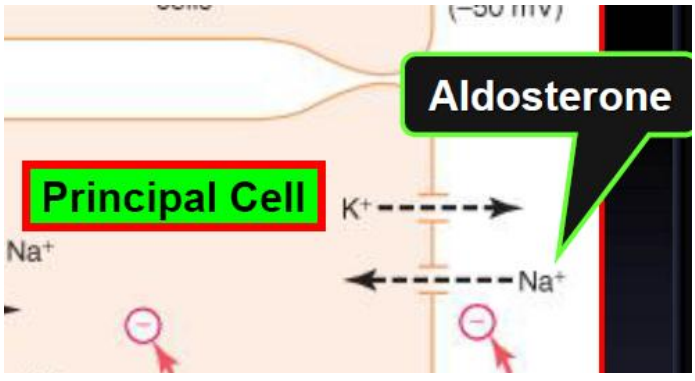


Mitochondria and microvilli decrease
Principal Cells (Na Abs and ADH related Water abs)
Intercalated Cells (Acid Sec and HCO3 Transport)

There is some channel know as epithelial sodium channel this channel will open only in response to aldosterone otherwise it remain close so once it open it will reabsorbed lots of sodium and k lost
So , the effect of hyperaldosteronism (which means lots of Na reabsorbed and lots k secretion) will be hypernatremia in blood and hypokalemia in blood .



Medullary collecting duct is mainly composed of principal cells. addition thing happen in this duct which reabsorbed of urea . which is the only waste product that reabsorbed and urea participate in urine concentration which about 50 % of concentration of urine done by urea .

Adh secreted in response two changes on the body if you have high osmolarity or low ECF volume such in case of dehydration (when your body loss lots of water so ADH secreted cause reabsorb of water to maintain ECF volume)
. ADH secreted by pituitary gland and the target cell For ADH is principal cell and the channel which found in the cell and ADH act on it called aquiaporins (water channed hiding inside the cytoplasm) when ADH come will do translocation of these channel Lead to move it from cytoplasm to cell surface so , the water now can be reabsorbed because the channel now in the surface and ADH can work at it and cause water reabsorbing) .
Target of ADH late DCT cortical collecting tubule and medullary collecting tubule

proximal convoluted tubule (PCT) :

- Water and solutes are equally reabsorbed in PCT, that's why the isotonic solution from glomeruli remains isotonic.

Proximal tubular cells very active cells , that are reabsorbed around 60 % presence of glomerular filtrate . (about 60 % of amount of fitration are reabsorbed again in blood by PCT)

Loop Of Henle:

Will not be discussed (controversial)

Descending (thin) | Thin Ascending | Thick Ascending

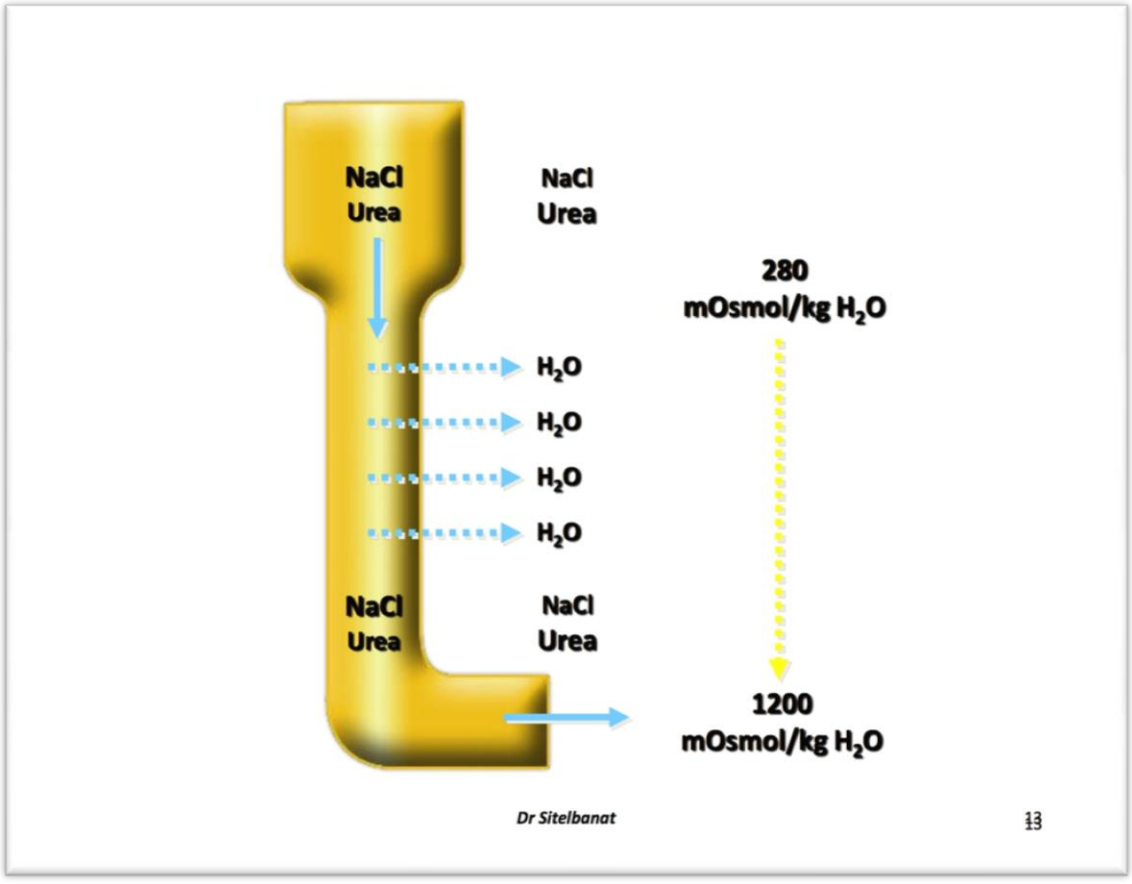
- Simple squamous epithelium

• Permeable to water but not for solute absorption

• 20% of filtered water is reabsorbed

• Osmolality of filtrate increases from 290 to 1200 mOsm/l at the tip of the loop (reaches maximum)

• The increasing osmolality is due to only water reabsorption, ↑NaCl and ↑ Urea concentration in filtrate

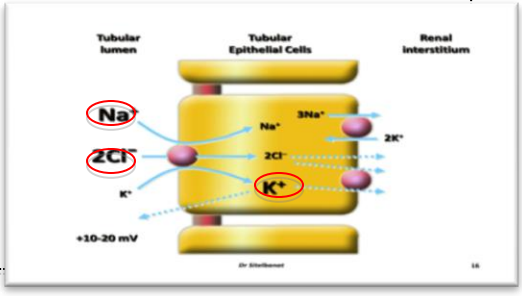


Thick ascending limb=diluted segment:

- Simple cuboidal epithelium
- 2/3 of loop of henle
- Water impermeable
- 1Na/1K/2Cl reabsorption by cotransport (luminar= in the lumen) and deposited in medullary tissue.
- Na/K ATPase in basolateral membrane
- Filtrate diluted due to solute reabsorption not water
- Osmolaritydropfrom1200to200mosm/l
- very sensitive to diuretic drugs (Furosamide). These diuretics block Na+-K+- $2Cl^-$ cotransporter, so:
  - Decreased NaCl reabsorption
  - Isotonic fluid delivered to distal tubule instead of a hypotonic fluid . (Normally it's hypotonic in the thick ascending)
  - Increased fluid excretion – "diuresis"

These drugs are called : "Loop" diuretics

K is very small so it can leak in any direction



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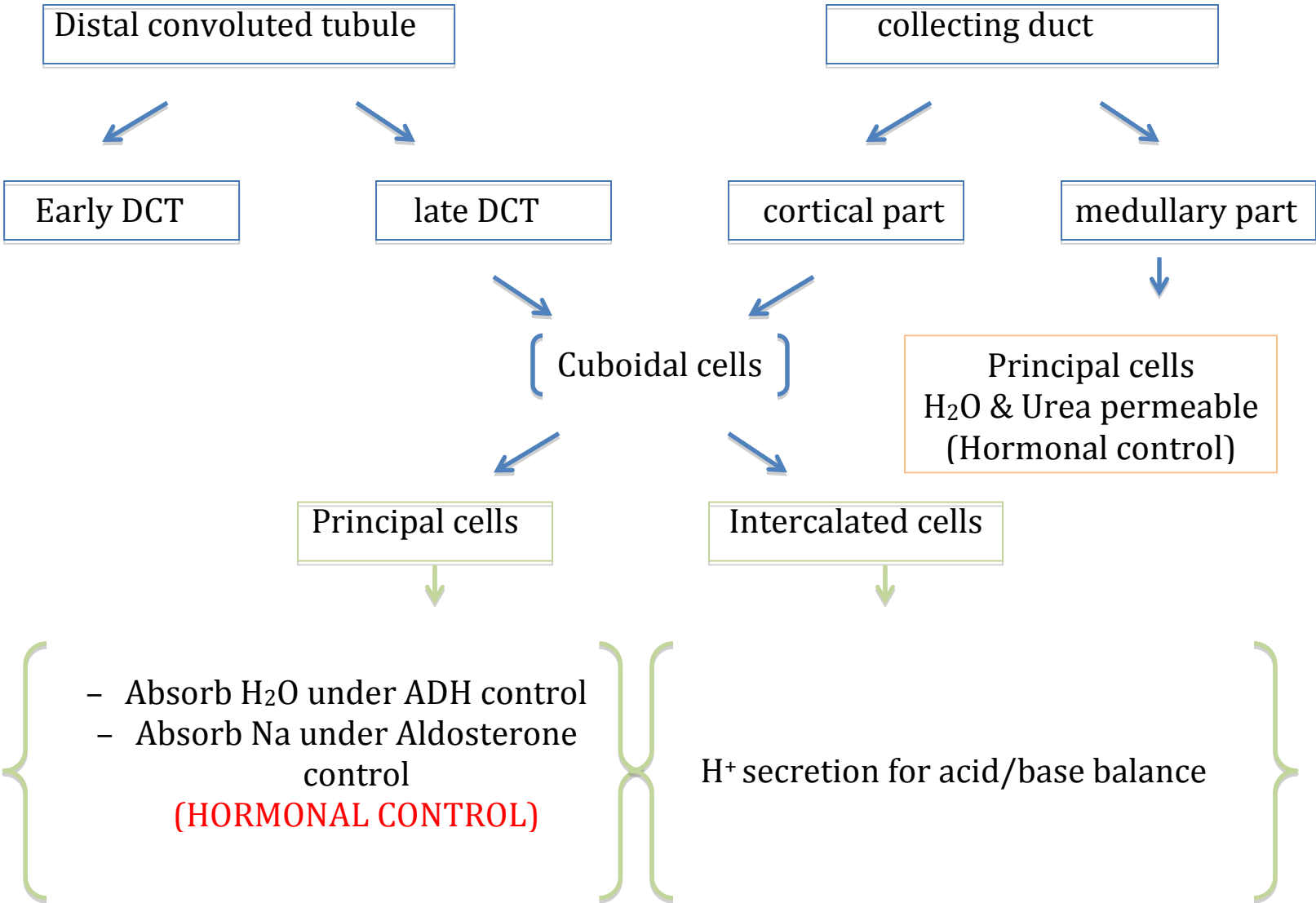

Distal convoluted tubule
collecting duct
Early DCT
late DCT
cortical part
medullary part
Cuboidal cells
Principal cells
H2O & Urea permeable
(Hormonal control)
Principal cells
Intercalated cells
– Absorb H2O under ADH control
– Absorb Na under Aldosterone control
(HORMONAL CONTROL)
H+ secretion for acid/base balance

Late DCT & Collecting Duct

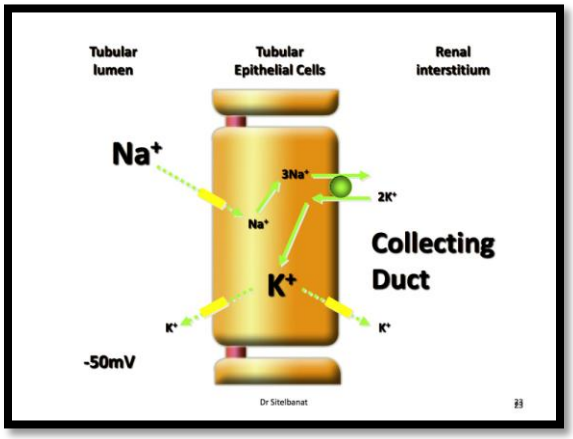
- 19% of filtered H2O is reabsorbed
- 9% of filtered Na+ is reabsorbed in exchange of K+ or H+

} Hormonal control

- Cl^- is freely reabsorbed

Collecting duct

- Water permeable under ADH
- Urea is reabsorbed in the presence of ADH
- Na reabsorbed in exchange for K under the influence of aldosterone



Urea Recirculation:

- Urea is completely filtered

• 50% of 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. So the kidney interstitium would be hyperosmolar to be able to reabsorb H_2O.

• ADH increases urea permeability of medullary collecting tubule, because ADH makes water permeable in the collecting duct so it drags urea with it.

Osmolality of the filtrate along the nephron

Osmolality of filtrate in PCT:

– similar to plasma ~290 m-osmole

- Due to reabsorption of equal portion of solute & water.
- –

Osmolality of filtrate in Desc. loop:

– graded increase in osmolality from 300 m-osm. to maximum of 1200 m-osm. at the tip of loop – Due to only water reabsorption

Osmolality of filtrate in Asc. Loop:

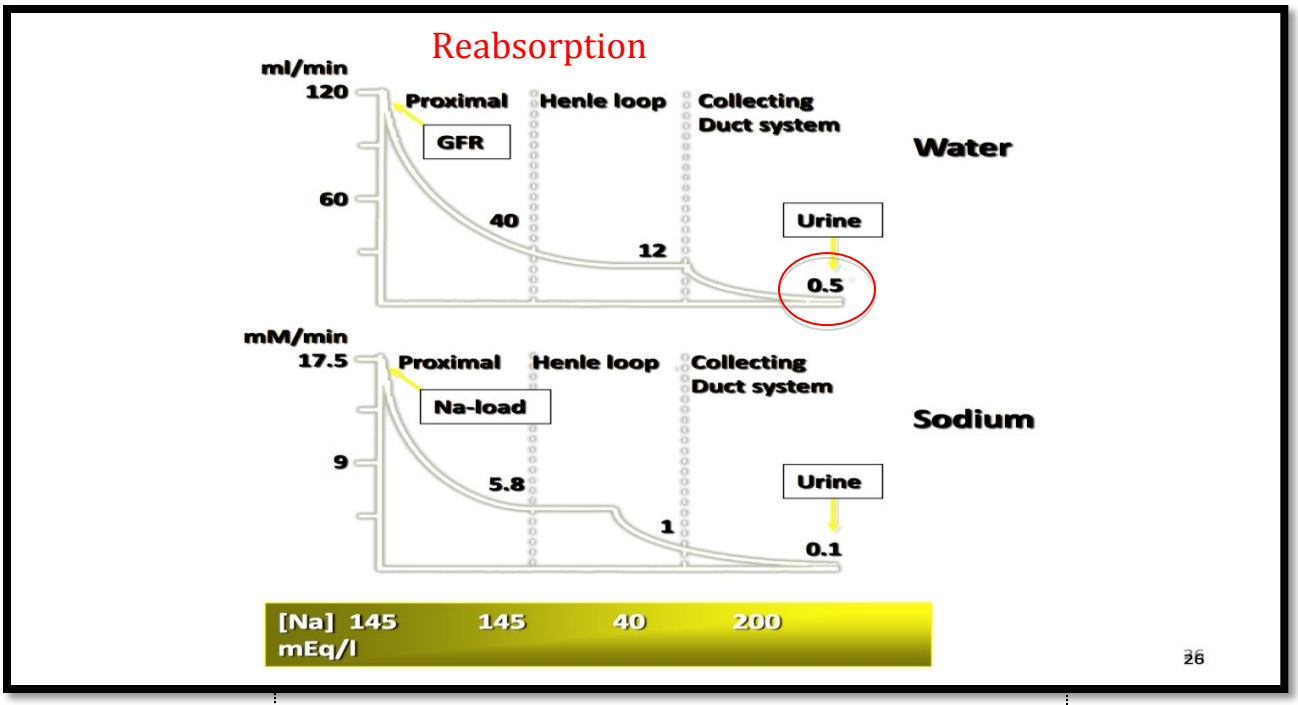
– graded decrease in osmolality 1200-150 – Due to only solute reabsorption.

Osmolality of filtrate in Collecting Duct:

– Osmolality depend on ADH

– Increase in ADH will increase water reabsorption, concentrate urine =1200 m-osm

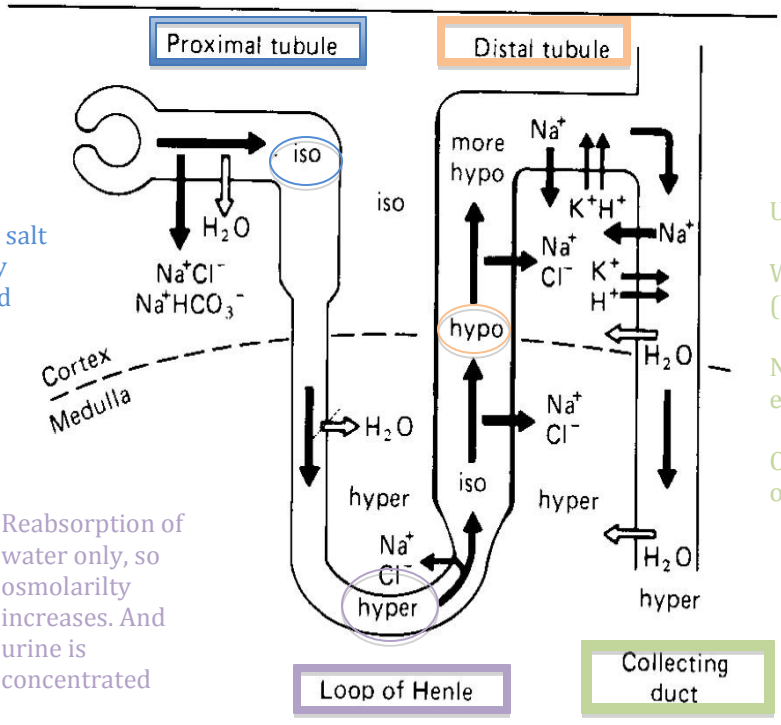
– No ADH , no water reabsorption , so dilute urine =50mosm



Urine output is normally 0.5 ml/min

Osmolality of the filtrate along the nephron

Reabsorption of salt only, so osmolarity decreases. And urine is diluted



Water and salt are equally reabsorbed

Urea is reabsorbed,

Water is reabsorbed (by ADH),

Na is reabsorbed in exchange for k^+ & H^+

Osmolality depends on ADH.

Reabsorption of water only, so osmolarilty increases. And urine is concentrated

Summery

- Secretion is either passive or active.
- Active secretion might be limited such as creatinine & Para-aminohipuric acid.
- K & H have the same transporter, and are secreted in exchange for Na
- In PCT water and salt are equally reabsorbed → iso-osmo. Urine
- In desc. loop only water is absorbed → hyper-osm & conc. Urine
- In asc. loop only Na,k,2Cl, are reabsorbed → hypo-osm & diluted urine.
- Late DCT and cortical duct have almost the same function, H_2O & Na are absorbed under hormonal control.
- Urea is reabsorbed partially at PCT, then reabsorbed also in medullary duct (under the control of ADH) into the kidney's interstitium
- The interstitium must be hyperosmolar in order to absorb water
- The body must have its supply of water daily

Questions

Q.1- why does hyperkalemia cause acidosis?

a. Because when K is high in the body, it will be secreted in exchange for Na, so H^+ is accumulated in the body (since the carrier is busy with K).

Q.2- what is the characteristic of urine in the distal tubule?
a. iso-osmotic
b.hypo-osmotic
c.hyper-osmotic

Q.3- what is the maximum osmolality of urine?
a. 290 m-osm
b. 1200 m-osm
c. 150 m-osm

Q.4- what is the cell responsible for acid/base balance?
a. intercalated
b. principal
c. podocyte

answers: b,b,a