Last lectures we defined clearance , we talked

about clearance of substance that are secreted, reabsorbed, filtered , not reabsorbed , not secreted , "clearance of inulin" , and clearance of this substance "inulin" is a measure of GFR . And clearance of substance that is completely secreted is a measure of renal plasma flow .

Then we started talking about tubular reabsorption , and the first thing we started talking about is **the proximal tubule** .

**In the proximal tubule** :

-the reabsorbtion **is obligatory (facultative reabsorption)** , and the reabsorption there is **isotonic reabsorption** . As if you have one cup of tea , two thirds of this cup of tea is reabsorbed ,,still everything> the concentration of the filtrate almost for everything is the same, osmolarity is the same (same concentration of filtrates) .

-Isotonic fluid has osmolarity that is around **300mOsmole** "this number is so important and you have to remember it , we're going to refer to it to determine hypo/hyper osmolar fluid and so on" .

-in the proximal convoluted tubule , there is reabsorbtion of Na+, Cl-, K+, bicarbonate, water, glucose and amino acids.

-amino acids and glucose are absorbed completely by secondary active transport , so at the end of proximal tubule , there shouldn't be glucose and amino acids **NORMALLY** . but it may appear if there is a disease " e.g . diabetes (diabetes mellitus , nephrogenic diabetes )"

RECALL : that if glucose exceeds the Tmax (tubular maximum) , the extra filtered will appear in the urine , because any reabsorption or transport mechanism that has a carrier , it also has a binding sites , if these binding sites are fully occupied (saturated) , we can't exceed that value.

-there are some secretions in the proximal tubule , we will talk about them when we come to acid-base balance , because these secretions are very important in regulating PH .

-**SLIDE 31** : Changes in concentration in proximal tubule.

if you want to follow the conc. Of certain ions/substances from the beginning till the end of proximal tubule .

* 1 is the normal concentration in the plasma 1:1 "tubular fluid/plasma fluid" , so here [glomerular filtrate ] is the same as plasma **EXCEPT** for proteins, if you follow this; follow the osmolarity as an example: since it is isotonic reabsorbtion the osmolarity does not change "300".
* notice that the osmolarity & [ NaCl] doesn't change .
* [glucose] & [amino acids] at the end of proximal tubule the concentration of them will become zero **"because they are fully reabsorbed ".**
* certain substances that are reabsorbed more than it's concentration in the plasma , e.g bicarbonate , and this because of acids base regulation "hydrogen secretion" , and you will remember this when we talk about Ph regulation of acid-base balance.
* creatinine and urea are almost secreted in the proximal tubule , creatinine is not reabsorbed it is secreted to some extent . "if you remember that when we talked about clearance of ceratinine is slightly more than GFR , but we can still use it as indication of GFR measurement **(endogenous substance**) . SO sometimes we use creatinine instead of inulin if inulin might cause allergy or infection to the patient .

**Now , we reached loop of Henle :**

* Loop of Henle has two parts :

1**-Thin descending part "**showing at the upper part of **slide 33" :**

* permeable to water , and impermeable to electrolytes .
* If it is permeable to water we expect that when water is reabsorbed , osmolarity in this part will increase , mean that we reached the end of proximal tubule with 300mOsmole "isotonic" , then it will become 315,400,600mOsmole !!
* at the tip of the loop of Henle , osmolarity will be the highest especially in the **juxtamedullary nephrone** ! [in juxtamedullary nephrons the osmolarity at the tip of loop of henle is around 1200mOsmole , which is the maximum , but it may reach 1400 in some people with longer loop of Henle] .

**2-ascending loop of Henle** :

* it has thin and thick ascending parts .
* The **thick** ascending loop of Henle is impermeable to water , it has active transport mechanism for Na, Cl, K co transport and for some other ions like Ca , bicarbonate ,Mg. So here , the osmolarity starts to decrease , and this is especially evident in juxtamedullary nephrons , the osmolarity goes down until it come less and less than 300 in the thick ascending part of loop of Henle ,, there is a lot of active transport of Na, Cl, k, (more than that in the proximal tubule) , that’s why it will become less than 300 , it may reach 100 or 70 … whatever .

\*\*this part of loop of Henle "thick part" + first part of the distal tubule is called diluting segments of loop of Henle or diluting segment of tubules .

\*By the end of loop of Henle "descending and ascending" around 25% of the fluid has been reabsorped.

\*10% of water and sodium chloride has been left to the distal tubule.

These 10% are regulated by hormones.

Water reabsorption is regulated by ADH.

If there is ADH then there is extra water reabsorption

If there is NO ADH then the 10% ( 18 liters) is going to go out.

So if a person doesn’t have ADH he will have diabetes insipidus.

Diabetes insipidus: relative deficiency in ADH

-----------------------------------------------------------------------------------------

180 liter is going to filtered everyday –10%=18 liter

So that person is going to produce 18 liters of urine per day.

Normal person produce 1 – 1.5 liters per day (the doctor said 2 liters is normal too))

The first 90% is absorbed no matter if there is ADH or not but the 10% is regulated by hormones

>>so if a person doesn’t have ADH he produce 18 liters of urine per day >>The **treatment**: We give the patient ADH.

25% of filtered water is reabsorbed in the proximal tubule, in the loop of Henle(Re-absorption and storage of chloride, secretion of hydrogen)is Not permeable to water, it is permeable to electrolytes; that’s why the osmolarity increases.

Osmolarity here is almost 100 mOsm; that’s why we call the diluting segment of the nephrone.

For producing diluted urine we eliminate the ADH.

In the thick ascending loop, there’s an active transport Na- Cl- K "active pump", There’s H+ secretion.

* **Slide 34**:

Gradient for Na is done by the Na/K pump. Here there’s Cl, K channels that they pass through it passively( So K goes out). Re-absorption is done in the peritubular capillary by the starling forces.

Here we can give a drug that blocks the K- Cl- Na co-transport, leading to no re-absorption of Na, K or Cl. Na and Cl They will stay in the tubule, trapping water with them so the urine output is quite high. These are what **diuretics** do, specifically “loop diuretics” because they work on the loop of henle. The most common diuretic is Furosemide; Furosemide is the lazic ,it blocks Na-K co transport,,, other examples: Ethacrynic acid and Bumetanide.

* **Slide 35:**

The **early distal loop** of Henle, Na-K pump is found in almost all tubules, but here we also have Na-Cl co-transport, an active transport in the early distal loop of Henle. Also, this may be blocked by diuretics. “Thoside diuretics""

Early distal tubule functionally similar to thick not permeable to water we call it diluting segment which is active reabsorbing to Na, Cl, K contains the macula densa that we talked about in regulation of glomerular filtration "between the efferent and afferent arteriole".

* **Slide 37:**

So early, late and collecting ducts>>

* Early distal tubules NOT permeable to water, NOT very permeable to urea.
* 5%of filtered NaCl is reabsorbed. The re-absorption in the distal tubule is usually controlled usually by hormones like:

***Aldosterone*** which promotes re-absorption of Na and Cl, and secretion of K exchange

At the late distal loop of Henle we have principle cells which are the cells of the tubule and also intercalated cells which are important in acid-base balance, important in secretion of H in exchange for Na or K re-absorpti -In late distal loop of henle

* **Slides 38,39,40:**

there are principal cells of tubules (cortical cells) and in between them there are what we called intercalated cells. .

Intercalated cells are important in acid-base balance , they are important in secretion of hydrogen in exchange for sodium or in exchange for potassium reabsorption .

* late distal loop is where ADH work

- so intercalated cells is the area where hydrogen is secreted.

-in diluting segment we said the osmolarity is very low .

- in principal cells there is secretion of potassium in exchange with sodium under the control of aldosterone.

so if you want to give a diuretic that competitively inhibits aldosterone-(Spironolactone OR Eplerenone ) these are called **Aldosteronre antagonists**, they antagonize aldosterone , these diuretics are sometimes very important because they don’t produce hypokalemia "low potassium", usually other diuretics when you take them a lot of fluid is going to pass through with sodium and potassium so this person is going to have hypokalemia (loss of potassium), AND any small loss in potassium will produce a lot of changes because potassium concentration was in extracellular about (5 mmol) if it becomes 4 or 3 it is too much on the heart .

- Another diuretic which is **Aldosteron inhibitor** will inhibit sodium reabsorption in exchange with potassium , so potassium will stay so these diuretics are called **potassium sparing diuretics** (they don’t change the potassium concentration ) so sometimes you refer to these diuretics when you don’t want to play too much potassium .

-there are other **blockers** that block the channels ; aldosterone that blocks the sodium –potassium pump in the distal tubule and cortical collecting duct .

**Diuretics that block the sodium channels** like ; Amiloride & Triamerence .

Amiloride & Triamerence have different sites of action, they work on the channel where sodium is reabsorbed in exchange potassium.

If you blocked the sodium-potassium pump there will be no gradient for sodium (sodium will not be reabsorbed and potassium will not be secreted).

-Ameloride might change the potassium but not to that extend because it work on the sodium pump.

The intercalated cell which contain H pump that secret H actively and there is potassium hydrogen exchange mechanism or counter transport mechanism (H pump found in stomach)in some people who have gastric ulcer they should take hydrogen pump blockers.

ADH mainly found in intercalated and collecting duct which open the water channel so the water moves according to osmolarity gradient .

**Transport characteristics of medullary collecting ducts:**

* (+ADH)H2O reabsorbtion :ADH control water reabsorbtion which is involved in acid-base balance.
* H execration in exchange for bicarbonate(HCO3-) "bicarbonate reabsorbtion".
* Reabsorbtion of urea so it will go to the interstitial fluid in the medulla then to loop of henle then go back to make concentration of urine.
* ***CHECK SLIDE 41 "NORMAL RENAL TUBULAR NA+REABSORBTION***

Here we have to know the percentage NOT the numbers.

* In proximal loop of Henle is 65% reabsorbed.
* In loop of Henle 25%.
* What is remain controlled by aldosterone.
* ***CHECK SLIDEs 42,43***

***I***f we follow the osmolarity and concentration through the hole tubules , we should know how much is this part permeable to water or permeable to ions? How much is reabsorb? what is reabsorb? And so on.

\*If water is reabsorb to greater extent than solute, what will happen to osmolarity?

Osmolarity will increase, and this solute become more concentrated in the tubular.

\*If water is reabsorb to lesser extent than solute, what will Happen?

The urine will be dilute "less concentrated".

\*In proximal tubule the concentration of glucose and amino acid and protein is zero.

\*lope of hinle divided into two part :descending part and ascending part:

1-Descending part permeable to water (the concentration will increase because there’s relatively more reabsorbing to water)

2- The ascending part permeable to electrolyte.

\*inuline concentration continues increasing (because it not reabsorbed) (clearance is 125).

\*createnine will secreted.(clearance is 140).

\*PAH increase in proximal (because it fully secreted) >>(clearance is 585).

\*\*ascending and descending part of the lope of henle is very important.

\*from inulin we can know what we call tubular fluid.

\*inulin not reabsorb and not secreted and it freely filter.

\*If you want to know how relative to inulin (concentration of other substance is reabsorbtion or secretion or whatever:

( inulin concentration(tubular inulin) / plasma inulin)

if there’s **reabsorb** : inulin concentration(tubular inulint or tubular fraction of inulin / plasma inulin) will be **high**.

* **Slide 44:**

-in part A: 1/3 of the fluid is reabsorbed so concentration of inulin will become 3 times so A remains 66.67% reabsorbed.

\*\* this same in any part of tubule(depend on how much is going to be reabsorb).

-in part C: we reach very high concentrations of inulin.

\*\*if you measure the inulin conc. Referring to the plasma inulin you will see how much is reabsorbed.

***Check slide 45***

***Extra note:***

1-Peritubular physical forces like starling forces: in peritubular capillary there is hydrostatic pressure and oncotic pressure, if we have a lot reabsorbtion there will be high hydrostatic pressure in the interstetium, so the fluid will be pushed to the peritubular capillary "reabsorbtion"..the other will be pushed out…if it push out the reabsorbtion happen in that area…in the concentration-dilution it will become very important factor in the interstitium of the medulla; because the interstitium of the medulla must remain hyper polar.

***\*reabsorbtion of water not*** happen without ADH; ADH will open the water channels or water channels are already open, but if the interstitium around it is not hyper osmolar water will not go from the tubules to the medulla cause there is no osmotic gradient, if the interstitium around it is hyperosmolar if you open the channels water will move according to their osmotic gradient…so the other requirement for conc. Of urine is hyperosmolarity of the interstitium which happen if there is avtive reabsorbtion Na, Cl, K co transport.

2-Hormones:

-aldosterone:regulate the reabsorbtion of NaCl.

-ADH: regulate the conc. Of water.

-Parathyroid control the reabsorbtion of ca.

-ANF "atrial nitriuretic factor" decrease reabsorbtion of Na.

-Angiotensin II :main affect is vasoconstriction, BUT in the kidney it increases Na-K reabsorbtion of water (like aldosterone ) it stimulate secretion of aldesterone from adrenal cortex, important in Glomerulotubular balance.

-Sympathetic effect both Ra and Re

***CHECK SLIDE 47***

-ther is no tubular balance and Glomerular balance.

-if there is increases in the GFR the reabsorbtion stay the same, the execration will increase.

-if there is good tubular balance with more reabsorbtion.

-what is left in the urine almost the same.

***PERITUBULAR CAPILLARY REABSORBTION :***

\*what control the reabsorbtion in the peritubular capillary is the osmotic forces (Pc: hydrostatic pressure in the capillary,,πc: oncotic pressure of the capillary,, πf: oncotic pressure of the interstitial fluid,,Pif: hydrostatic pressure in the interstitial fluid".

These control the reabsorbtion that comes.

What goes through the peritubular capillary still go forward…. if it does not, it will stop after a certain time; because the forces will become in balance….what is being reabsorbed here, it reabsorbed by **bulk flow** , because the capillary’s channels are very wide and the capillary is permeable to a lot of substances "so it is bulk flow".

***CHECK SLIDE 49***

If the reabsorbed is 125 ml/min "GFR" , what is left is 1ml/min as urine volume.

***CHECK SLIDE 50,51,53***

