***1st Lecture (renal\_system-tubular\_reabsorption\_l3-l5\_students.ppt)***

last time yesterday we were talking about tubular reabsorption and we reached the peritubular capillary as we said there are certain factors that determine the peritubular capillary's reabsorption .... Starling Forces:-

hydrostatic pressure of the peritubular capillary , Oncotic pressure or the colloid osmotic pressure of the peritubular capillary

we were talking about

* **Determinants of Peritubular Capillary Colloid Osmotic Pressure :**

***We First said:***

Oncotic pressure of the capillary (**πc**) increases the **reabsorption**

Increased **Plasma Proteins** increase oncotic Pressure of the Artery (**πa**) increases oncotic pressure of the peritubular capillary (**πc**). and this will increase the **reabsorption.**

Increasingthe **filtration Fraction**  increases oncotic pressure of the peritubular capillary (**πc**). and this will increase the **reabsorption.**

* ***Summary Factors That play part in the Peritubular Capillary Reabsorption :***

Starling forces says that the net filtration or the net reabsorbtion or whatever equals **(Kf )** multiply net filtration or net reabosrption pressure. So **(Kf )** if we increase it increase reabosrption or filtration.

Also here the effect of increased hydrostatic pressure and decreased colloid osmotic pressure if you increase the hydrostatic pressure you decrease the reabsorption and if you decrease the oncotic pressure you decrease the reabsorption .

**Pc , πc** Reabsorption

This is exactly starling forces

If you decreases reabsorption what will happens ?

The fluid will go back through the gap junction.

We said the gap junction in proximal tubules is not very tight , gap junction tighter in the distal tubule and when we come to the **PH** we notice this is true because if they are not tight that means it cannot maintain gradient (gradient in osmotic gradient or the gradient was hydrogen gradient **PH**) that's why we notice when we come to the **PH** regulation. The proximal tubule doesn't reach to a very low level it reach 6.8 - 6.1 for example at least. But when we come to the distal tubule or the collecting duct because of these tight junctions are tight they can maintain much gradient. The **PH** of the urine there it reaches 4 - 4.5 this we will be talking about when we go on.

If we ask a simple question

1. increase arterial pressure will decrease reabsorption .
2. decrease afferent arterioles resistance will increase **PC** and this will decrease the reabsorption.
3. increase efferent arteriolar resistance will decrease **Pc** at the peritubular capillary which will Lead to increase the reabsorption.

Peritubular capillary here what happens to it?

It will decrease, what about reabsorption?... Peritubular capillary pressure decreases lead to increase reabsorption.

1. decrease peritubular capillary **Kf** will decrease peritubular reabsorption .
2. decrease filtration fraction will decrease the **πc**.
* **Aldosterone actions :**

H+ secretion in exchange for Na+ reabsorption in the intercalated cells.

Aldosterone activates Na+/K+ pump, it activates Na+ reabsorption in exchange for K+.

Aldosterone regulation, it activates H+/Na+ exchange.

* **Abnormal aldosterone diseases :**

Conn's disease (primary aldosteronisim) here we expect increase action of aldosterone.

* **control of aldosterone secretion :**

Aldosterone we take it in the endocrine system which is found at the adrenal cortex which part?

* granulosa
* fasiculata
* reticularis.

It's true if we said it comes from cholesterol through enzyme called desmolase... Aldosterone to precursor for corticoids , androgens.

Desmolaze is activated by ACTH but aldosterone is not controled by ACTH the ACTH mainly control glucocorticoids (cortisol) .

Aldosterone is main mainly controled by angeotensine II this is the main controller, then increasing k+ will increase secretion of aldosterone , very little effect of ACTH.

**Hyperkalemia increase aldosterone.**

**Hyponatremia increase aldosterone.**

**Hypernatremia decrease aldosterone.**

* **factors that decrease aldosterone secretion :**

(ANF) atrial natriuratic factors increase Na+ excretion .

Decreased aldosterone secretion increases Na+ concentration .

Increased aldosterone secretion increases Na+ reabsorption so this will lead to to hypernatremia and will lead to decrease aldosterone secretion.

Increased Na+ concentration will lead to decrease aldosterone secretion.

So tubular reabsorption of Na+ increased either directly or indirectly through making the efferent arterioles resistance high ,constriction of the efferent arterioles resistance. How it works?

Angeotensine II it has receptors on the tubular membrane and peritubular membrane zone .

AT1 (angiotensine II receptor 1 ) we said angiotensin II stimulate Na+ reabsorption in exchange for H+ so it is important in hydrogen regulation it stimulates the Na+/K+ pump and stimulate Na+/bicarbonate Co-transport at the peritubular capillary members so this is the direct actions of angiotensin II.

Indirect was through stimulation of aldosterone the main controller of aldosterone secretion is the angiotensin II.

Mainly aldosterone is controlled by angiotensin II not ACTH, ACTH on only on cortisol. That's why cortisol feedback on ACTH.

* **Effects of angiotensin II on peritubular capillary dynamics :**

Since it constricts the efferent arterioles resistance it will decrease the **Pc** and will lead to increase the reabsorption.

* **Angiotensin II blockers :**

Angeotensin II can be blocked by two ways :

1. angiotensin converting enzyme inhibition.
2. or by blocking it directly on the receptors (angeotensin receptor blockers ).
3. or by inhibiting the renin why?

Because renin converts angeotensinogen to angeotinsin I then to angeotensin II. Soon here we block the whole cycle.

If we decrease aldosterone we decrease arteriolar resistance and by decreasing the aldosterone we inhibit renin absorption.

natriuresis or diuresis decrease blood pressure that's the essence of treating the hypertension by aldosterone angeotensin inhibitors through AC inhibitors antagonist for this at the receptors or renin blockers.

Antidiuratic hormones works on the water reabsorption where? Late distal and collecting duct.

* **Slide 65:**

ADH comes from the posterior pituitary and it is stored in the posterior pituitary .... In the hypothalamus the posterior pituitary stores two hormones (oxytosin - ADH)

How It is regulated... Secretion? By osmoreceptors

* **Slide 67- 68:**

When the osmolarity of the blood increases it goes and stimulates the osmoreciptors in the hypothalamus the stimulated osmoreceptors stimulate the secretion of ADH and the ADH will go to the late (distal) collecting duct and opens water channels and there is receptors (vasopressian receptors) and this stimulates adenylcyclase and this will increase the action of CAMP dependant protein kinase it goes and Phosphorylate channels of aquaporin 1 so when aquaporein 1 is phosphorylated they move to...... Water channels are open and water will move according to its osmotic gradient. this is the mechanism of ADH in distal tubule and collecting tubule . AVP (arginine vasopressin) binds to its receptores binding to its receptors activates G-protein system and this system activates Cyclase and ATP to cAMP protein kinase A induce of phosphorylarion aquaporin-2 and aquaporin once it is phosphorylated move to the membrane and open water channels water moves according to its osmotic gradiant if there is no osmotic gradiant so there is no movement of water, so this is the action of ADH.

And vice versa if there is any disease like diabetes insipidus.. Here ADH decrease and will lead to increase of the urine output or water excretion up to 18 litters and maybe reach to 20 litters who's it the 10% that is regulated by hormones that comes to the distal tubule, increased plasma osmolarity, hypernatremia (relative) because of decrease in the water , excess thirst. And we can say that there is some diseases called inappropriate ADH secretion and this usually sometimes ADH is secreted from abnormal bases like in cancer lung in case of tumors (certain tumors of the lung )they secrete ADH if they secrete alot of ADH what happens ? What really happens that there is an increase in reabsorption of water and what happens to the Na+ concentration it will be low (hyponatrimia) and the blood pressure will increase because of the increase of the extracellular fluids. This is will feedback on the abnormal ADH inappropriate ADH secretion decrease plasma osmolarity, hyponatremia (this is relative hyponatremia) because of increase in water.

* **Atrial natriuretic peptide increases Na+ excretion how does increase Na+?**

Its effects on the GFR increase the GFR and directly inhibit Na+ reabsorption it inhibits renin release and aldosterone formation. So it's action is on the Na+ reabsorption directly increase in renin and aldosterone formation increase GFR. Where the secretion was happening? It is secreted from the right atrium mainly. increase in the blood volume increases ANP as a conclusion for the ANP :

1. **it increase GFR**
2. **Decreases renin**
3. **Decrease aldosterone.**

Increase in the GFR will increase the water and Na+ excretion

Decrease in aldosterone will decrease reabsorption of Na+ and will increase water Na+ lose.

Decrease in renin will decrease the angeotensin II and will lead to decrease in the aldosterone.

Angiotensin II have direct action on Na+ reabsorption, so if the Na+ reabsorption decreased it will lead to decrease in aldosterone and increase the Na+ lose this is how atrial natriuretic peptide works. Slide 71.

* **slide 72 : Parathyroid hormone (PTH) increase reabsorption of Ca++ reabsorption.:**

increase reabsorption of calcium and excretion of phosphate exchange.

Increase Ca++ reabsorption by the kidney.

Increase the Ca++ reabsorption by the gut through activation of vitamins.

Decrease phosphate reabsorption and increase phosphate excreation.

Helps to increase extracellular Ca++

* **Slide 73 :**

Decreased extracellular Ca++ will stimulate PTH (which is a peptide hormone 39 amino acid peptide) secretion it's receptors found on the membrane because the water soluble hormones receptors is found on the membrane and the lipid soluble receptors found inside the cell.. So increases PTH it activates vitamin D , if you remember the functions of the kidney we said that the PTH activates vitamin D converts 25-hydroxycolcalciferol that's coming from the liver and activation of the 25-hydroxycolcaciferol is in the kidney. Activation Vit. D increases intestinal Ca++ reabsorption. PTH directly on the kidney increase Ca++ reabsorption and phosphate excretion. On the bone increase Ca++ release (it is called bone resorption by osteoclastic activity)

* **slide 74: Sympathatic:**

directly stimulates renin release and decrease the GFR and in the end we increase Na+ reabsorption and also the decreased renal blood flow increased the Na+ reabsorption.

* **Slide 75 increased arterial pressure :**

If you increase the arterial pressure what will happen ? Pressure diuresis (pressure natriuresis) that means lose of Na+ and water to decrease and this as a controller for the blood pressure, so if you increase the arterial blood pressure you decrease Na+ reabsorption.

If you increase the peritubular capillary pressure what happens to the reabsorption? It will decrease.

Decrease renin and aldosterone.

Increased release of intrarenal natriuretic factors (prostaglandin - EDRF)and those they are vasodilators they increase the blood flow to the kidney.

* **Slide 76 Osmotic effects of the reabsorption :**
1. Water is reabsorbed only by osmosis.
2. Increased the amount of unreabsorbed solutes in the tubules decreases water reabsorption by the osmotic forces.
3. Diabetes mellitus what will it do! In diabetes mellitus there is a lot of glucose that's is filtered and goes to the proximal tubules what will they do in the tubules! they will increase in the osmolality (osmotic pressure ) if there is a decrease in the osmolality it will decrease the reabsorption and decrease the fluids in the tubules so the fluid will go to the urine, so what happens to the urine? More urine (hypotonic urine or hypo-osmolar urine) this is called osmotic diuresis.

Maybe we can give any substance and this substance in not reabsorbed like (Manitol) manitol is not reabsorbed ,we give it to the patient IV or whatever so manitol will reach the kidney and it will be filtered but not reabsorbed it will make osmotic pressure it will decrease the reabsorption and it will increase the urine (so this is called osmotic diuresis) this substance is used sometimes in brain edema to reduce the brain edema We should increase the water lose how?? We give him manitol because it's not reabsorbed it causes increase in the osmotic pressure (osmotic diuresis).so exactly like glucose.

Osmotic diuretics (manitol) manitol is filtered but reabsorped and it will make osmotic diuresis.

* **Slide 77 abnormal tubular function these diseases is not included as the doctor said :**

in Liddle's syndrome there is excess activity of Na+ channels, that are in the distal tubule these channels are sensitive to amiloride (one of the diuretics)if there is excess in these channels that means there is more Na+ reabsorption through these channels if there is more Na+ reabsorption there is a hypernatrimia, hypertension so what is the treatment here? Block amiloride sensitive Na+ channels.

* **Slide 78 aldosterone escape :**

If the aldosterone was very high the excretion of Na+ should be very low but this happens for a while, if the aldosterone stays very high for long time there will be rearrangement it will be at steady state.... Excretion of Na+ will go back to normal this is called escape from Na+ retention due to aldosterone escape from Na+ retention this happens if we give aldosterone infusion for a long time. The blood pressure was 100 and the urinary excretion is normal. Aldosterone increase the blood pressure and the Na+ excretion decrease and the Na+ excretion will go back to the normal this is called aldosterone escape or Na+ escape from retention.

* **Slide 79 : Conn's syndrome hyper aldosteronism.:**
* **Slide 80: Abnormal tubular function :**
* **Slide 81 :**

Plasma Na+ decrease due to relative hyponatrimia because there is an increase in water, total Na+ does not decrease its just because we did increase the water.

* **Slide 82:**

in **Liddle’s** syndrome the Na+ reabsorption increase, blood pressure increase, the treatment here is to give amiloride or triamteren to block Na+ channels.

* **Slide 83:**

The main stimulator for renin is hypotension... So if there is an increase in the pressure the renin will decrease .

in clearance we talked about two things :

Creatinine concentration in the plasma how do we collect creatinine concentration? We take a blood sample and we measure the creatinine. So what about if I want to measure creatinine in the urine? We collect a 24 hours urine collection and then we measure the urine concentration of creatinine and then we calculate the flow of urine per minute and then we divide it on 1440 . So here we have got three things :

1. Plasma concentration of creatinine .
2. Urine flow .
3. Urine concentration .

now here we can calculate the clearance of creatinin why? Because it determines the GFR

**2nd lecture : (renal\_system\_-concentration\_and\_dilution\_of\_urine-students.ppt)**

* **Slide 1:**

Urine concentration and dilution very important

How urine is concentrated? What is the mechanism of concentration and dilution of urine?

If I want a diluted urine... Where the diluted urine can flow? No early distal and in the third ascending part of loop of Henley in the early distal the osmolarity is very low . why it reaches 100 mOsm? because that area is water impermeable ,that area is solute permeable and it has an active pump which is Na+/K+ 2 chloride co-transport . So the osmolarity in this tubule will still very low. If I want the urine to be diluted it means I have to stop or inhibit the reabsorption of water. If I dont want a reabsorption of water it means I don't want ADH (absence of ADH or inhibition of ADH).

If I want concentrated urine there should be ADH this is the first requirement.

**No ADH diluted urine**

**ADH concentrated urine**

**So ADH is essential.**

2nd the interstitial has to stay hyperosmolar.

* **Slide 2:**

Control of extracellular osmolarity (NaCl concentration )

Increased extracellular osmolarity (NaCl) stimulates ADH release, which increases water reabsorption and stimulates thirst and intake of water.

* **Slide 3:Concentration and Dilution of the Urine:**

Maximum urine concentration, maximum at the tip of loop of Henley, we said it reaches 1200 mOsmol it depends on the length of loop of Henley 1200 to specific gravity almost 1.03 this is highly concentrated urine.

Minimal urine concentration 50 - 70 mOsm/L (specific gravity almost 1.003)

*Specific gravity means الكثافة النوعية*

* **Slide 4:**

If we give 1 litter of water at the beginning it will decrease the osmolarity but will increase the urine flow and increase the urine solute excretion because of excess excretion of water will drag some solutes with it.

Water diuresis is noticed in person who takes large amounts of water and this will lead to water loss this is due to changes in osmolarity.

* **Slide 5:Formation of a dilute urine :**

At the end of the proximal the osmolarity was 300 mOsm which is normal

What happens in the descending loop of Henley? Reabsorption of water

In the cortical it may reach the 600 mOsm.

In the juxtamedullary it reaches 200 mOsm.

the ascending loop is permeable to solutes >>so the osmolarity will decrease.

Urea is reabsorbed in the cortical collecting duct and it's coming to the loop of Henley this is urea recycling. Urea is coming from proteins amino acids.

* **Slide 6 :**

The urine osmolality is determined by the number of particles in the solution. In contrast, the urine specific gravity, which is a measure of the weight of the solution compared to that of an equal volume of distilled water, is determined by both the number and size of particles in the solution.

In most cases, the urine specific gravity varies in a relatively predictable way with the osmolality, with the specific gravity rising by .001 for every 35 to 40 mosmol/kg increase in osmolality. Thus, a urine osmolality of 280 mosmol/kg (which is isosmotic to plasma) is usually associated with a specific gravity of 1.008 or 1.009.

This relationship, however, is altered when there are appreciable quantities of larger molecules in the urine, such as glucose, radio-contrast media, or some antibiotic s. In these settings, the specific gravity can reach 1.030 to 1.050 (falsely suggesting a very concentrated urine), despite a urine osmolality that may be only 300 mosmol/kg.

* **Slide 7 formation of concentrated urine :**

***Note:*** Urea maintains the interstitial hyperosmolarity this is the action of urea.



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**sorry for any mistakes and good luck for you all.**