Human Physiology
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Lecture – 33
Excretory system : Regulation of Osmolarity and counter-current mechanism - Part 2

Let us do this once again. What are we trying to understand from the counter current mechanism? It is a mechanism by which the kidney is capable of being very high, full of very high osmotic value. As you go deeper from the cortex into the medulla and further deeper the osmolarity increases, how is kidney capable of doing that? That is a wonderful question, very interesting question, we are trying to answer that question and for that we have this example in front of us. So here you can understand there is a nephron there, you can see the loop of Henle and to begin with what did we say? To begin with what did we say? Let us presume that the fluid is at what osmotic value? 300 milliosmoles per liter everywhere. And then as the fluid goes here, as the fluid goes here, then on the ascending side what is the peculiarity in what is the ascending side different from the descending side? It has what? It has what? The ascending one.

What is it? Pecularity of the ascending one. It has what? No aquaporins. Yes aquaporins or no aquaporins? No aquaporins. What is it? No aquaporins.

So this particular in the thick segment, it is abundantly rich with the system that can keep on exporting the sodium. As a result of this you keep on building a certain concentration difference between the interstitial fluid and what is the content of the ascending limb. And when the pump is working at its best efficiency it is capable of building how much of difference from across the wall of the tubule inside is about 200, outside is about what? 400. 400. Now but since there is no barrier this equilibrates with the descending.

So the fluid that is going in the descending fluid and the interstitial comes to an equilibrium so everything becomes 400. So you have 400 in the descending, 400 in the interstitial but 200 in the ascending fluid we have gone there for. And then eventually as we know the fluid flows look at this arrow and then you have here so you have even 400, you have 400 because in the descending it was 400, it comes in the ascending that is 400, it keeps on building the difference so that becomes eventually from 400 this will become 300 but that will become and the process goes on repeating till what time the fluid, the interstitial fluid it goes to about how much? That is the limit to which 1200, 1300, 1400 it is the limit to which it can go in the case of human kidney to what extent it will go in the kidney of that hopping mouse? 10,000. 10,000 okay that is why it is able to okay. So now I will take this story forward and I will ask you okay okay. In this then we had introduced another character and that character was called as what? Vasa recta what did we call it as? Vasa recta.

What is vasarecta? It is a blood vessel it is a blood vessel okay it is a part of the peritubular capillary network which is a peculiarity of the cortical nephron or the juxtaramedullary nephron? Juxtramedullary nephron that is the peculiarity that is the peculiarity okay and then we had seen that the two vessels go parallel and the flow of the current in them is opposite to one another and that is what we are looking at it now okay. So we have a blown up image of this is the nephron that you can see so we will start with 280 okay to be more precise 280, 400, 600, 600, 1000, 1200, 800, 600, 400, 200, 150 okay you can clearly appreciate the thick blue line which indicates what the absence of? Absence of what? Absence of aquaporins and as a result of that it goes as far as as far as 100 if you actually beyond it actually goes to may 100 or even less whatever it is. Now I am going to ask you one question what may be the nature's rationale in diluting the whole thing? It is diluting okay I mean you went all the way you concentrated the fluid to how to what extent? 1200 and then you take up again to the cortex into the distal convoluted tubule and then you have diluted the fluid to what extent 100, 50, 100 or whatever even less than that? I am posing the problem in front of you and I am asking one of you to answer my question. Please go ahead. Sir, in the absence of ADH the you can excrete out the microfluid. You got the answer because if you have taken lot of water then you need to excrete dilute urine so dilute urine is very important okay. So you dilute the urine here okay and if the and if the osmolality of the blood is less and if water is a burden on you and if you need to get rid of the water just making sure that you do not use the sodium ions you have diluted it.

So, make sure that you do not absorb any water and throw it out of the body in what form you can extremely dilute urine so that with that from that point of view diluting it makes sense. You have to dilute it okay. But then what do you do when you need concentrated urine or when you are deprived of water we will come to that in a few slides down. Now so let us go back to this figure so here we have this and coming so this is vasa recta this actually this vasa recta are very close they are very close the two tubes one in which the descending tubule and next to that is the vessel of the venous component of the blood vascular system that is taking the blood supply up so there is opposite direction. We have seen that in one. Now let us talk about what happens actually when the blood flows - so what is this red one it is a branch of the peritubular capillary. Good what is it? It is bringing oxygenated blood good. What is it doing? It is sending a branch it is sending a capillary down down down down deep into the medulla into that part of the medulla where the osmolality of the fluid is 1200 it is going there. Now as and now this capillary let us see now. You are here say the blood is going down the blood is going down the blood as it enters what is the osmolality? 300. 300 okay. Now the blood is going down and its capillary and that capillary has many pores outside what is the position outside there is more outside osmolality it is 400 and it is 500 okay. So equilibrium will start happening means what outside salt will get in and inside water will go out. so what is it bring to the blood the blood as it goes down goes down it keeps on taking the same osmolality as that of the fluid outside. So, as it, I am not going to try to keep my identity. No let me become the same way as the fluid outside - consumes less energy, okay. So the salts enter and the water goes down and then in the vasa recta also. What is the osmolality of the fluid by the time you reach to the lowest or lower most point of vasa recta 1200. You are okay so far good. Now what have you done in the process in the process you have lost your oxygen that is the purpose of your capillary you have to give oxygen and give oxygen to what? Well you have to give oxygen to this you have to give oxygen to the loop of Henle - they are the cells they need oxygen so you give oxygen to them, so all the tissue that is there as you go deeper and deeper into medulla they need oxygen you give oxygen and become yourself what deoxygenated. Now you as you get deoxygenated as you start travelling upwards you do exactly opposite means what as you go, you are in 1200 ok I am 1200 and there are windows all over hello, are you with me and as I go up osmolarity becomes 1200, 1100, 1900, 800 are you with me the water gets in ok and the salts go out very simple ok. And by the time it goes to the top it is about 325 almost same as blood ok. So, so the so what beauty you have to appreciate here is where as one hand, as long as cells - they need oxygen you have to have the blood supply, but if you just send - imagine if you and I were to design it I will say 300, 300, 300 outside is 1200 ok you will dilute you will dilute the fluid outside no I do not want to dilute the fluid outside, because the pump and that system, has worked very hard to make sure that the osmolarity goes as high as 1200 I do not want to dilute it I am interested in preserving the high osmolarity of the fluid as you go deeper and deeper into the medulla. Have I conveyed to you the paramount importance of vasa recta yes or no. Good. Now second important point which I discussed with you yesterday, is we always talk of homeostasis, and we always talk of blood always being at 300 milliosmoles ok. Then how do you then how do the blood the endothelial cells how do those endothelial cells dealing with blood which is having osmolarity of 600, 700, 800, 900, 1100, 1200 milliosmoles? How are those cells coping up? Or even for that matter - how are these cells coping up with the high osmolarite? Very simple question. There are cells in loop of Henle - yeah they are there and to what osmolarity they are exposed?

1200 this is 4 times more concentrated than elsewhere. How is this part of the medulla coping up with the problem? The solution to that problem is as amazing. These particular cells are adapted by having in their cytoplasm as many 4 times more solute molecules. So that the intracellular osmolarity of these cells - so if I go here the cells the osmolarity of these cells is 400 or 600, 900, 800, 1200. So even those cells are, as far as the osmolarity of the cytosol of these cells is concerned, they are very different from elsewhere ok. Are you getting the point? So how these cells have evolved and that is this is the kidney from the kidney you take the you do the osmolarity from you take samples from 4 places ok. Here, here, here and this is the deepest part in the medulla ok. And you see the osmolarity of the cytosol collected from 4 different cells and look at the graph yourself do you get the answer.

I mean you see if you were to do this experiment of collecting sample from different cells from different issues anywhere say skin, brain, liver, pancreas, muscle it is 300, 300, 300, 300, 300 are you with me. It is only in your body this is a unique collection of cells which is either in the vasa recta or in the loop of Henle where those cells will show you what? Show you what? Osmolarity, osmolarity, very high osmolarity. I want you to hear. The author tells us about what are the different solutes which are there - polyhydric alcohols and what? methylamine. So, these are some of the solutes which are highly concentrated in the cells as you go deeper into the medulla which add to the osmolarity.

So, that the osmolarity can be taken as far as - so, that these cells are capable of dealing with the highly osmotic fluids which is surrounding ok. Now, move on 5 minutes back I spoke about the dilute blood and its importance and its relevance ok. Now, we are moving on. We are going to the other end of the spectrum when the osmolarity of blood is rising because there is loss of water through skin, it is through lungs, it is through faeces, it is through dehydration from whatever. So, let us see how does your body react when you are being dehydrated.

Got the problem? Now, let us see - as a result of that the blood osmolarity, which was let me take let me go to more some precision - the osmolarity – you are well hydrated - osmolarity of the blood is about 280 milliosmoles how much it is? 280 milliosmoles. 280 milliosmoles. Now, as a result of dehydration the osmolarity of the blood has gone from 280 to 281, 282, 283, 284 even remember the rise of about 3 to 4 milliosmoles was good is good enough to trigger some of the cells in your hypothalamus. So, what you have here is - the just see this - if you take a knife and run it through this plane. So, that the human brain is cut into two symmetrical parts ok.

I will call that plane of section as mid sagittal plane. So, cut into part and you look at the brain and you will see on the ventral side of the brain this part is called as the hypothalamus, this part is called as the optic chiasma, this part is called as the mammillary body do not bother about it and this is the pituitary gland. And of the pituitary gland of the human being is facing that way. So, this becomes the anterior pituitary, this becomes the posterior pituitary - are you OK with the basics of anatomy? There what are we doing? We just know in one minute we had we had brief encounter with the hypothalamo-hypophysial system of the humans. This is the most important neuroendocrine system of your brain. Part of the brain – hypothalamus - pituitary is the endocrine gland which is controlled by the hypothalamus.

So, are you good so far? In the hypothalamus now I will introduce you to very important groups of neurons ok. I am going to tell - I want you to remember ok, few things you cannot have forget ok. Two groups of neurons there are many groups of neurons ok. I want you to remember two groups of neurons one is called as supraoptic nucleus what is called as what is it called as? It is called as supraoptic neurons because there is in the hypothalamus there is optic chiasma ok. Let us do a little bit of anatomy - you have eyes in the eyes you have retinal ganglion cells - hello retinal ganglion cells the retinal ganglion cells give rise to axons those axons they gather together and form what you call as the optic nerve.

Optic nerve is also is the second cranial nerve. Some of the fibres of the second cranial nerve cross right in the middle of the optic chiasma what you call it as? Optic chiasma. And optic chiasma cut in transfer section is here so this actually visualise what? A large number of fibres from the right retina going to the left side of the brain and from the left going to the right side of the brain, good so far. Now sitting on the optic chiasma, slightly on the lateral side of the optic chiasma, there is a group of neurons. Supra optic nucleus - are you getting the rationale why it is named so. What is the name I I teld you just now? Supraoptic nucleus. Supraoptic nucleus - so we have bilateral symmetry right half left half in right in the middle here somewhere here somewhere we have a space in the brain which we call as third ventricle what you call it as? Third ventricle.

Third ventricle why call it is called third ventricle? Sometime in future. There is a group of neurons on the left there is a group of neuron on the right. Paraventricular group. Makes sense at the level of ventricle so I am talking about these two groups of neurons. What are the two names can you please recite for me? Supraoptic and paraventricular neurons - these are very interesting because they secrete two hormones namely oxytocin and vasopressin. What are the hormones? Two hormones? So, there are some cells some neurons which secrete a hormone which secrete a neuro hormone which we call as what are the two names we recited just now? Oxytocin.

Oxytocin and. Vasopressin. Let us forget about oxytocin for a while and let us focus on vasopressin. Now, this both the hormones are nonapeptides each is made up of 9 amino acid residues. So, how many amino acids are there in vasopressin? 9 how many are there? 9.

9 amino acids. So, these neurons I am sorry these neurons - they give rise to axons they go down the hypothalamus down the hypothalamus and they terminate in the posterior pituitary gland where do they terminate? Posterior. Posterior pituitary. These neurons - their cytoplasmic machinery which means endoplasmic reticulum, Golgi, da da da everything they synthesize a big molecule, that molecule cleaves and then you have a small molecule, which we call as vasopressin. And those molecules are then and then trafficked. They travel all along the axon and they get into the posterior pituitary gland and in the posterior pituitary gland, what is the action that is happening? Can somebody look at the diagram and tell me? It is there, there is the figure on the left what is happening to the hormone there? It is going into capillaries. It is going into capillaries come on it is so simple it is going into what? Capillaries. Capillaries ok. It is going into the capillaries.

Now that hormone I will call as a I will call it as neurohormone. Why do I call it as a neurohormone? It is a neuron. It is a neuron, from a neuron and a hormone is going into the blood ok. I can also call therefore I can also call the neurons of the superoptic and paraventricular nucleus as neuroendocrine cells, good. Neuroendocrine because they are having a secretion that is going into the blood, so they fulfil both the conditions, ok. That they are coming from a neuron and they are going into the blood so neuroendocrine ok. So, vasopressin gets into the blood and then it gets into the kidney and it undertakes its function. So what function does it do? Let us follow the block diagram. What is point number one? Water deficit very simple. Number two extracellular osmolality goes up means from 282 how much what I said? 282, I gave you an example what example did I give you? 285.

285, 284, 285 very good. So then and then it stimulates osmoreceptors. Where are the osmoreceptors? Tell me now. Tell me the name. Supraoptic. So the neurons of the neurons of the supraoptic and paraventricular nucleus - they serve as osmosensors - they serve as what? Osmosensors and they are excited and they give rise to what? Which is also called as antidiuretic hormone also called as what? Antidiuretic.

Which is abbreviated as what? ADH. ADH ok. As a result of this arrow upward what does it say? What is happening to plasma ADH? Increases. Increases what is happening to what is happening to - now we are at the level of kidney. Water permeability in the distal tubule distal tubule, collecting tubule - what happens to water permeability? Increases. Increases means in the collecting tubule water is will be absorbed, how? It will be received which means water absorption which means which means which means that the osmolarity which was going in the direction from 280 to 281, 282, 283, because now water is reabsorbed, it may go back from 284 to 283. So this is our this is our physiological response to the challenge that we are facing. What was the challenge - dehydration what was the physiological response? To look for the water that you have and there is another equally important response which is to generate thirst that generation of thirst will induce a behaviour and the behaviour is to look for the water and ingest water. So that your osmolarity which was deviating from 280 in the direction of 282, 283, 284 will be returned back 280 on consumption of water. A beautiful image you will enjoy taking a look at this image. We are looking at the same cylinder three positions number one on the left - let us see we have the biological fluid in the biological fluid you have a solute and the author has very nicely coded here is some solute and some osmolarity. I will call it 280 just call it 280 and if it goes towards from 280 it will goes to 281, 282, 282 can you can go in that direction can you can - you count the number of solutes you can and if it becomes dilute it goes in that direction or as if we have given a scale different osmotic values of the extracellular fluid of the blood.

Now, as you are dehydrating then you are going in that direction, so the blood is going from 280 to 285 inch means very hyperosmotic. So, now, you will go to the neuron of the superoptic nucleus and the and the blood in the capillary and the extracellular fluid and the osmolarity is going from 282, 281, 282, 284, 284 that particular neuron I will begin with this. Let me go to this point when it was 280. This cell is about 280. I put an electrode outside I put an electrode inside and what reading do I get minus 60 millivolts. And when it is minus 60 volts it is 280, it is not a challenge here - my neuron keeps on firing with the frequency of let us see how much it is there see 3 action potentials per second are you with me? Just take a number 3 - 3 action potentials per second. Now, if you move towards dehydration, as a result of that that there is hyperosmolarity - now can you see the difference between the size of the neuronal cell body there what is the difference. The cell will be shrinking because inside osmolarity was 280 outside is 285 water will move out and as a result of that this cell will shrink. The plasma membrane of that cell is equipped with is mechanoreceptors so beautiful there is no other word. How do you convert how do you convert the change in the osmolarity - how does this cell respond to that. So, it is a mechanoreceptor - so there is a mechanical change once it shrinks from minus 60 it goes to how much minus 55 or minus 50 means it is going towards zero - hello it is going to once it goes it is going towards 0 it is getting depolarized, once it is getting depolarized what will happen to the frequency of action potentials per unit time- increase.

Once that increases, what will happen to the amount of vasopressin being released - more increase let us go in opposite direction. You have taken suddenly 1 liter of water as a result of that osmolarity has fallen from 282 to 275 as a result of that - now the same – has gone into what condition? Now tell me what is the inner reading now minus 65, which means the cell is hyperpolarized hyperpolarized cell is an inhibited cell. When it is a inhibit cell, number of action potentials are reduced which means the vasopressin secreting cells are now inhibited and that is exactly what happens when you drink a lot of water. But let us go back to the scenario in which, yes, I want to answer that question. Now I will send you a paper okay. So here we have, we have okay. This is interesting we are monitoring the plasma vasopressin concentration under what conditions? Under the conditions of normal and dehydrated, more more dehydrated - okay more dehydrated. Then what happens to water excretion - can you see here when this dilute urine you are excreting lot of lot of what lot of water dilute urine, okay. Eventually, the water, the amount of water that is being excreted is less and less because the vasopressin concentration is increasing. We are looking at two conditions, we are looking at this – this indicates what? Absence of aquaporins. We have done it what is it absence of what? Aquaporins. Aquaporins and there are no aquaporins we have already seen that urine is diluted that is the function of the diluting segment. It is diluted okay. And are there any aquaporins here in the collecting duct collecting duct cortical collecting duct here here here here here here are there any aquaporins? Are there here? Say that again. Not constitutionally. I will tell you that as a result of no aquaporins, will the water go out? Water won't go out so that dilute urine will pass out as it is okay. Therefore we have the okay, no, I am sorry I made a mistake here. There is no aquaporin here no aquaporin and so what is the strength of the urine that is going out? 65.

65 which is very dilute okay. Now here you introduce the aquaporins and then let us see what happens when the aquaporins are there.