Human Physiology
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Lecture – 26
Excretory system : Kidney - Part 3

We have done this but let us do it again. We are again talking about the different pressures at different levels. I am doing this for the first time, it is so important. What are we doing? Pressures, where at different level, at different stage as the blood flows. Let us go there, renal artery 100, afferent arteriole 85, glomerular capillaries 60 and 59 we have done it. Are you okay so far? Now, by the time the blood goes into this capillary network, this also we did today, it is about how much 18 to 8 by when as it enters into this capillary network, the pressure is about 18 mm Hg and by the time it is ready to enter into the veins, it has fallen to about how much? 1

You know something, here the, follow this, Starling hypothesis is operating on a larger scale. I will explain to you. Starling hypothesis, what was Starling hypothesis? The tiny 1 mm long capillary, on the earlier part, on the arterial part, the fluids come out and in the venous part, the fluids go back. And whatever does not go back is the lymph, we did it.

Yes or no? Hello? Are you okay so far? Now, here a very similar phenomena is operating but on a larger scale. Lot of ultrafiltration is happening, lot of ultrafiltration is happening here. So, the amount of blood as it goes eventually, I will ask you a simple question. I will collect blood from the afferent arteriole and I will collect blood from the efferent arteriole, okay, okay, 100 microlitres each and I will subject both the samples for finding out what is the amount of protein in it, which is going to be more and which is going to be less. Tell me.

Did you follow the question? Okay, okay, okay. I will draw the blood from here. Are you okay? How much? 100 microlitres. And then from here, 100 microlitres. The two samples and I subject them to analysis just to find out what is the total protein contained in both.

My question to you is, is the protein contained in both my samples same, A is more or B is more? Same. Yes, same. Concentration would increase with the content. Concentration, content I am asking. Content would be? How it would be same? How it would be same? The protein contained will still be same as the smaller protein.

Okay, let us see one thing. There is a filtration happening, okay, lot of plasma has gone, lot of plasma has gone, but large proteins are still there. So when I go to the efferent end, okay, the blood is actually more concentrated. Hello. Plasma has gone, 20% plasma has gone, okay, but the proteins are still there.

So in the 100 microlitre of sample, I am of course going to get more proteins. Hello. Hello. They are not getting.

Okay. Okay, so we are having plasma, it is containing certain proteins, we are entering into the glomerulus and the plasma goes away. What about the proteins? They are still there. Okay. So the number of proteins molecules per unit volume is more, okay, and that is what I am going to estimate when I collect the sample from the efferent. Now as a result of the, get this, the beauty of physiology, as a result of more protein concentration in the blood that is flowing through the peritubular capillaries, because there is more protein, they exert more oncotic pressure or osmotic pressure, you are right, and the result of that they facilitate and the pressure itself is less, pressure is less, the pressure is how much? The pressure is how much? The pressure is how much? Maybe 8, 10, pressure is low, because the pressure is low, okay, it will facilitate the influx, because the proteins are more, it will also promote the influx.

So the peritubular capillary network makes excellent, excellent ambience for the reabsorption of lot of filtered material from the nephron. You want to take back, you want to take back, you want to take back a lot of water, you want to take back of glucose, you want to, for this is being facilitated by particularly for water, number 1, oncotic pressure has gone up and blood pressure has gone down, it will facilitate. And so in a way, this is like, this is like, again catch the point, this is like earlier part of the capillary, whereas this is like the later part of the capillary, where the Starling hypothesis is operating on the, I think I have done enough, let us move on. So, kidney is such an important organ and blood pressure at which it operates, it is so important that the kidney has said that I do not really want to depend on the blood, I want to free myself from the burden of blood pressure changes anywhere else in the body. I am going to be, I am going to make sure that the blood that flows through me is kept at a constant pressure.

You know what they did? That kidney has almost total, not almost but quite total auto regulatory mechanism, auto regulatory control itself with blood pressure was demonstrated in a very simple way. A little cruel, but a killer dog, kill a dog control, collect its kidney, perfuse the kidney, okay, what do I mean by perfuse the kidney, you have separated the kidney. Just look at the experiment, you know, physiology people does do amazing things. Number one, you have three cannula, plastic cannula, okay, all the proper size, one cannula you insert into the artery, hello, one cannula you insert into

the vein and third cannula you insert which is a thinner diameter, you insert it in the ureter. So, for all practical purposes, the kidney does not know that it is outside, what a funny language kidney knows, it does not, kidney is there, okay.

And now you remove the blood and instead of that you start perfusing, use the language, perfusing the kidney with physiological solution in which the pH is proper, in osmolarity is proper, everything is physiological. So, actually what is happening is that fluid is going, is getting ultrafiltered, okay, some of it is going in the form of urine, some of it is coming back via the vein and now you do something interesting. When you begin the experiment, you start pumping in the fluid. I am just taking for example, you are pumping in the fluid via the renal artery, you are pumping in the fluid at 60 mm Hg, what do you do? 60 mm Hg, 60 mm Hg, good, good. And then you keep on monitoring the urine, actually it is not urine, it is just filter, the urine output or whatever output you are getting through the ureter.

Are you with me? Experiment look at, imagine the kidney, three tubes. One takes the fluid in, another takes the fluid out and third collects the filtrate, done. Now you start with applying the pressure into the renal artery 60 mm Hg, you get fluid filtering in the ureter at a particular rate, good. Now increase the pressure from 60 to 70, 60 to 70, 70 to 80, 80 to 90, you find that the rate at which the ureter is discharging the fluid is still same. Hello, hello, something is happening, something very interesting is happening, means what? Kidney is capable of or if you are in that scenario, let us do something simple.

In that scenario, you insert your fine capillaries to find out as to at what is the pressure at which the ultrafiltration is happening. It is still about same, it is same, the kidney is able to adjust and that is shown in this diagram. Look at this graph, look at this graph, we are increasing the blood pressure from, okay the mean is about how much normal, 80, 120 is about 100, hello are you okay so far, so I am at what point, I am at this point. And then I can increase the pressure 100, 150 or I can go to 100, it is very high actually, this guy is still alive, but he is still okay. But in spite in this range if you see, in this range if you see the glomerular filtration rate is almost stable, can you see the stability, appreciate the point, what is the message here, the message is here is that although the blood pressure can go elsewhere in the body can go from okay from 100 to 120, 150 okay, the glomerular filtration is same.

How is and do not forget this is an isolated preparation, there is nothing coming from autonomous nervous system, no sympathetic, no parasympathetic, no hormone coming from so much, this is a kidney on its own, are you with me, what is the point that author wants to hammer here is that kidney has, kidney is ultra filtration that is happening in the

kidney is so important that the pressure at which the pressure has to be kept constant and for that the kidney has auto regulatory mechanisms. I put this slide and explain the phenomena and explained experiment only to emphasize the point that the kidney has the capacity to maintain the pressure. Now most exciting question, how does kidney do that okay alright, one is of course angiotensin as we said, but I will talk I will come to that a little later. In the literature you will find there are the authors have come up with two different explanations, they are not mutually exclusive, so maybe both are right whatever, but let us study both. One mechanism which operates is called as myogenic mechanism, what is it called as? Myogenic mechanism is muscle, hello, we are talking about muscle, what are we talking about here the point is pretty simple, he says that if the blood that is entering into the Bowman's capsule suddenly pressure goes up, if the pressure suddenly goes up then look at that inlet and look at that outlet, are you with me afferent and different.

As a result of that the afferent vessels will stretch, hello, they will stretch, but then do not forget the basic physiological property of a muscle, if you stretch it will go back and here it goes back a little more that is the property of the muscle and as a result of that this afferent tube will constrict. Once it constricts the pressure is not the high pressure there is not transferred to the inside, are you with me? Since the pressure is more, but you have reduced the diameter of the tube as a result of that the rate at which the pressure in which at which the ultra filtration is happening is now reduced, are you with me? Hello, am I making sense or not? Hello, no, do you want me to do it again, great, let us do it again, no, no this is important, okay, less simple, let us forget all this, I will take a simple tube, take a simple rubber tube, okay and the water is flowing through it at the rate of 60 mm by g that is the pressure, okay. Then artificially I increase it from 60 to 80, as a result of that the tube has now what? So long, okay, because there is more pressure of course, it will stretch, it will stretch, but my tube is a magical tube, it is a magical tube and by magic I have told the tube that if somebody stretches you, you do just opposite, are you getting that message now, just do just opposite, it is muscle, it is a smooth muscle, okay and the smooth muscle has a property, if you stretch it, it goes back, okay and because it goes back it not only means it has gone back, so it was originally so much because of the pressure it becomes so much, now if it remains so much it will take the pressure of 80 mm by Hg to the glomerulus, no because it goes back again, it goes back, the fluid is going back into the kidney again and the same pressure of 60 mm Hg, what do we call this as, are you okay now so far, hello everybody, okay. Sir, let me continue, when it contracts the afferent pressure, the pressure in the afferent artery will increase right. It will, see it will increase, it will increase, but just look at it the amount of, the inflow will be greatly reduced, that will really material influence the, okay, yes.

Not have the opposite reaction, that should decrease the. No, that is the property of all

smooth muscles, okay you stretch them, they will go back, if you want to keep them stretched, okay you have to instruct them accordingly, okay or if you want to get them relaxed or. If you do not stretch them, if we decrease the pressure they do not worry. Oh, they respond to that also.

So they expand. Yeah, yeah, they respond, you mean to say if you are reducing the pressure, if you reduce the pressure they will again constrict, they will, for that you have another mechanism, I will tell you, yeah I will come to that, okay, yeah. In the previous slide if we increase the pressure will ultrafiltration rate also increase. If we increase the pressure the rate of ultra filtration will also increase, that is the problem. You, okay, we have already seen, the effective pressure was 10 mm Hg, okay, if you make that 60, 70 that effective pressure will be more, okay, that 10 may become 20, I do not know, it may become 18, whatever it will become, okay, we do not want that to happen. In, with the, for the kidney to function efficiently these are the optimized parameters and you cannot mess up with them and therefore kidney insists that the kidney gets the input at the, at 60 mm Hg, but okay.

Now whereas this is myogenic mechanism, I will tell you about another. Now hello, hello, wake up everybody, wake up everybody something very interesting is going to happen. Wake up, are you ready? Oh, this is going to be an interesting ride. Okay, stay with me. This mechanism is called as tubule- glomerular feedback.

If you sleep you will not follow, wake up. What am I talking about? Tubulo-glomerular feedback. In this again let us imagine for some reason, okay, the blood pressure has gone up, okay, and for some reason the myogenic system did not work, imagine what is there, it did not work. More blood is going into the glomerular set up, higher pressure, higher pressure, higher pressure means more filtrate, hello, more filtrate, more filtrate means more everything including more sodium, hello. So suddenly now in the tubule you have, okay, I do not know much but I suddenly experience that there is more sodium, hello.

In the tubule there is what? There is more, there is more sodium. So where am I? Okay, I am here, I am here. There is the filtrate is happening, the filtration is happening at a particular rate, are you okay so far? Good. Now pressure has gone up, as a result of that the filtrate is more and as a result of that in the filtrate that is going on or the pre urine that is going is now consisting of more of everything, everything including sodium ions. Now the sodium ions, sodium ions, sodium ions and everything goes, goes, goes, goes, goes, goes, goes here and here we have already said that the distal convoluted tubule talks to the Bowman's capsule, you remember that rule, are you okay with me? What, what? The distal convoluted tubule of the same nephron is going and talking to

what? The same Bowman s capsule, okay.

Now what I will do is, I will now magnify, I will take this tiny part and blow it up to make my story simple and interesting. So where is the urine passing? The urine is passing through this tubule and it is lined by single layer of cells, epithelial cells of the nephron, are you okay so far? And on the, and these are the single layer of cells, I will call this cell which comes in contact with, directly comes in the contact with urine under formation, it is not formed yet. I will call this as the apical side and I will call this as the basal side and it is, and this is of the, this is of the, this is of the tubule. And on the other side there is that Bowman's capsule, are you with me? That Bowman's capsule and in the Bowman s capsule you are having, you are having the, you are having the afferent, afferent input so that afferent arteriole is going this way, are you with me? What am I talking about? I am talking about the cells of the urinary tubule and the urine is going this way, the urine is going this way. On the apical side there is a protein system, very interesting.

I will call that protein, look at, look at, look what is written there. I will call it as NKCC system. What do I call it as? Why do I call it as NKCC? Sodium, potassium, sodium, potassium, so CC, NKCC. Now I am telling you NKCC because this NKCC term is going to come 100 times, NKCC, it is a system of proteins. It is a system of proteins which is a simple system.

That simple system is driven by sodium ions. Why sodium ions? Because sodium ions you would always like to go from outside to inside, 142 times more sodium is from 140 times more as compared to 10 times more. I am sorry about that, 10 times more than that. So sodium ion then so that drives the chloride and potential all those things. So now suddenly those cells, those cells what? The cells which are lining this, can you see this dark patch here? That dark patch is these cells.

And that dark patch of cells, these cells is called as macula densa. What do you call it as? These are the cells of the urinary tubule. Cells of what? Urinary tubule. This also. So the Bowman's capsule, proximal convoluted tubule, loop of Henle comes up, talks to the Bowman's capsule.

This tubule has certain cells which I am going to call as what? Macula densa. So those ready cells are all the cells of macula densa. And the cells of the macula densa on their apical side, in their plasma membrane, they have a protein system which I will call as what? NKCC. NKCC and that facilitates the transport of sodium ions from the extracellular medium within the cell. Within the cell now suddenly you have more sodium ions.

As a result of more sodium ions, the osmolality goes up. As the osmolality goes up, it draws more water from outside and as the more water enters into the cell, the cell what? The cell swells. And as the cell swells, the cell is equipped with stretch activated ion channels. And as a result of that, two interesting things happen. Number one, the ATP escapes from the cell to the outside.

And then the ATP escapes from the cell and then the ATP also comes out of the cell. We have done it actually one of the lectures if you remember. It is converted into adenosine. We have done it in the case of heart, heart adenosine A1, A2 receptors. And then it shows this ADP converts adenosine and what are these? These are the, this is the afferent blood vessel.

The afferent blood vessel just outside has smooth muscles. Those smooth muscles are equipped with receptors for adenosine and can somebody tell me what is P stand for? Very good, purinergic, very good. What do you call them as? Purinergic receptors. Well, ATP, look, look, look, look. I am not looking at ATP as an energy giving molecule.

No, I am looking at ATP as a signaling molecule. And if it combines with its receptor, I am going to call that receptor as a purinergic receptor. And that purinergic receptor is sitting on the plasma membrane of the smooth muscle cells. And those smooth muscle cells are going around the afferent arteriole and when they receive the signaling either in the form of adenosine or in the form of ATP, they will what? Constrict and reduce the blood supply. Hello, have you, are you okay? You want me to redo this? Okay, I will do it.

Yeah, depending, oh yeah, we have enough time. Okay, let us see. Do it again, no problem. This has to be understood. No, actually this has to be, yeah, no, enjoy it.

Have fun, have fun. Okay, I mean this is the beauty of biology as to how the system takes signal from something that is going wrong and take the signal to the right target and give the correction, give the proper correction. In this particular, so what has happened is for some reason the blood that is entering the kidney, it should enter at a particular rate that has gone up as a result of the filtration has gone up. As a result of that one of the products of filtration which is sodium ion concentration has gone up, number of sodium ions in the filtrate are more. They were sodium ions were so many sodium ions were there now suddenly 10 percent increase in the number of sodium ions. And this sodium ions will go all the way down to the tube loop of and they will come up and they will, now the macula densa is only there, not everywhere.

They will talk to the macula densa. Macula densa, no, what the macula, are the macula densa, can I not say that the cells of macula densa are sensitive to sodium ion concentration. Hello, I can say that. They are sensitive to what? Sodium. And how do they respond? They respond because when there is more sodium they just take in the sodium.

I mean they do not know that this is Na plus. No, they do not know that this is Na plus. No, they do not know that. They know that something has come in as a result of that osmolality has gone up that also they do not know. That also they do not know. Then as a result of increase on osmolality there is more water coming in and when water coming in it stretches.

It is a stretch which the cell knows because it has stretched receptors and then it responds. That is a signal that is receiving. What is the signal? It has stretched. And then it gives out the signal. It is a chemical signal in the form of what and what signaling molecules? ADP.

ATP and ADP. That ADP is converted in the outside it is converted into adenosine and adenosine combines with the type of receptor called as A1 receptor. Where is that receptor sitting on the smooth muscle? The signal will go in. It will bring about the cascade of events. Calcium ion concentration will go up. Calcium ions are suddenly available for actin-myosin filaments to slide in that smooth muscle and the smooth muscle will constrict and the inflow of blood in that particular nephron will be restricted.

Are you okay so far? Just appreciate the beauty of the physiological mechanism which the kidney has evolved so as to ensure that the blood flow. Why are we doing all this? We want to make sure that the ultrafiltration keeps on happening at a steady rate. No matter what happens outside. The heart may go up and down, there may be changes elsewhere but as far as kidney is concerned the kidney wants to make sure that the ultrafiltration.

Go ahead with your question. It shows that the macula and the tubule interacts with the capillaries. No, no on the capillary here. This is not a capillary. This is the… Yeah but from that because it is, is not it inside like is not that the level of capillaries at the… Here you mean? Yeah.

Talk to you afterwards. Do not take the time of the entire class. How does the ATP, it just diffuses out like how does it… Oh okay okay okay okay. There are a range of proteins. At this moment I remember the name of one protein system called as panaxin.

We have encountered this once. If you go to earlier slides it is there. It is such proteins which allow, these molecules just do not go. There are channels okay. It is through those channels that the, that ADP or ATP they can flow out and then eventually ATP can directly find its purine receptor or adenosine in the cytoplasm. If you go to your slide on heart you will find how ATP is converted ADP, AMP and finally adenosine okay and that all happens in the extracellular matrix okay and but your question is correct how does ATP go? It goes via certain protein channels and I remember the name of one protein which is panaxin. Yeah somebody had a question here? So the same question, so the panaxin opens up there in stretch.

Yeah yeah yeah yeah yeah yeah yeah yeah exactly exactly. So, a lot of changes happen okay and one of them is opening of panaxin and allowing the ATP molecules to go out. I mean means you see that is a beautiful question but then we actually I am not answering your question but I will give you, I will paint the entire scenario. You find out okay the cell has stretched so what? What next? What next? What next? So there are several steps okay and then somewhere in the end you will find that panaxin the channel open and then ATP goes out and the rest of the things okay.

Yes okay solved okay okay alright yeah. Anything else? Yeah please. After the similar contrast in the afferent arteriole, the rate of blood flow from the afferent arteriole, how does that also reduce the GFR? If okay I will ask you one question. Supposing the afferent arteriole had not constricted, what would happen? You have increased blood flow rate at higher pressure. Higher pressure. So, so, so from 60 you might have gone to 80 okay.

Now by this mechanism you have been able to bring it back from 80 to 60. Make sense? Okay. If you had not done that just imagine what would have happened okay alright anything? Yeah. If we like consume more amount of salt like you said so that it will be less reabsorbed. Which one? Like when you said okay if we it had amount of salt you know say maybe increase the may or variety of more salt in the blood then more salt will be filtered and less of it will be reabsorbed.

So the. Yes yes. More salt. Yes. So, like this mechanism should be triggered even then right and because of that the reduction rate would. See the answer to the question is, I will make a funny statement. Heart is an endocrine organ. What did I say? If I make that statement I am answering your question okay.

Sounds absurd but it is not. Heart is an endocrine organ okay. And you can ask me what is the hormone? The hormone is a protein okay. It is called as atrial nitriuretic

peptide ANP. I am sure some of you have heard. What do you call it as? Atrial atrium.

So the cardiac muscle cells are serving as a hormone. Nitriuretic losing sodium ion, getting rid of sodium ion. So when you have more salt intake that system gets activated okay and that acts on the kidney and facilitates the excretion of sodium. We will talk about it when we talk about the how the sodium homeostasis is maintained.

Even then even in that case sodium will be more in the. Yes yes it will move. Does not that trigger. No no let us see it in that light. Do not go to that question now okay. My argument is you cannot take only this part of the solution and talk about that problem.

No. So if you want to understand how the excess of sodium is being dealt by your physiology, let us take this picture and let us see how what excites ANP and what is the role of ANP in regulating the kidney and then let us take a look at it in totality. Just do not go for this. I cannot answer this in this fraction. I can answer it in totality, but I do not want to do it now.

Do it when we do atrial nitriuretic peptide, but that gives me an opportunity to tell you. So what is heart? It is also an? And what is the name of the hormone? Atrial nitriretic means excretion of urine peptide okay, about 27 amino acids if I remember.