Human Physiology
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Lecture – 29
Excretory system: Nephron - Part 2

Oh, this is a very interesting slide, look at this. We have said that at the level of the Bowman's capsule when the ultrafiltration is happening, okay, because of the charge on the basement membrane and because of the size of the protein molecules, they resist filtration. But no system is perfect. So in case some protein molecules are filtered, okay, the nature has come up with a beautiful solution. The solution is here, I am looking at a cell.

What cell is this? This is cell from the proximal convoluted tubule. What face I am seeing? I am seeing the apical side. Can I see the villi there? On the villi there, I can, the author has given a tiny brownish patch there. Can you see that patch there? That is a receptor which can identify proteins.

It can not only identify proteins, it can bind with the proteins. So any proteins which by mistake or whatever I do not know, they have been filtered, they will bind to this molecule which I can call as a receptor, okay, and it binds and then once it identifies the protein molecule, it binds to the protein molecule and once it binds it will be taken in by the process of pinocytosis. You have done that in school, pinocytosis and then it will pinch off. It will go in the cytosol. There may be another lysosome, okay, another it will fuse with the lysosome, okay, the lysosome may release certain H ions, the protein will be digested, broken down into amino acids and those amino acids, the amino acids will be finally be released.

Nature does not want to lose any protein molecule. So by mistake if any protein molecule has gone into the, if you do not save it, it will go, okay. So this is a mechanism and you better do it at the level of proximal convoluted at the beginning itself, okay. Let us get rid of all the, not get rid of, I am sorry. Let us make sure that protein molecules that we are afraid of losing, okay, we pick them up and since the molecules are so large, we are talking of protein molecules are so large, okay, it is just not possible to provide a carrier and no, no, we need a bigger system and that bigger system is nothing but this pinocytosis by which we can, this is another very very interesting phenomenon.

I will request you to focus on this. This phenomenon is called as transport maximum. Now listen to this. SGLT2 is there. Hello.

SGLT2 is there in the apical or basal, apical, okay and it plays a key role in picking up the, in picking up the glucose molecules, okay. Now imagine what would happen if the number of SGLT2, am I right? SGLT2 protein molecules is limited, limited, not infinite, not limited.

There is a limit to that, okay. Limit to that means what? As long as certain number of glucose molecules are coming, okay, they will take, but if you give more and more and more, you will reach a point of saturation, okay and if you reach that point of saturation after that what will happen to glucose in the filtrate? It will, you will pass it in urine.

You will pass it in urine. So now I will simply ask you a question that here is a healthy human being, here is a healthy human being whose blood sugar is controlled within the range of 100, 100, 120, 130, 140, whatever milligram, okay and you take the urine sample and find that it is totally devoid of glucose, totally devoid of glucose. But there is another person who is a patient of diabetes and he has blood sugar level of say 200, 250, 300, then you start getting the traces of glucose in the urine and there may be more than traces, you can have higher concentration of glucose. Can you relate this to my earlier observation? What is happening? There are not enough number of SGLT molecules to make sure that all the, all the, okay and this phenomena is called as transport maximum. Mix logic, transport of what? In this particular case, there are others also.

Transport maximum, what do you call it? This phenomena is called as what? Transport maximum for substances that are actively reabsorbed. So let us, let us take, study the phenomena of what you call as transport maximum. We are still in proximal convoluted, we have not gone ahead. We are still in proximal convoluted tube and we are discussing the physiology of the glucose absorption and there is a constraint on that and that constraint we call as transport maximum. Now it has been found that plasma glucose concentration on the x axis and as a normal person, you are, if you are fasting, you are about 80, you are here and it is post meal, you are about 120, 130, you are here.

So normal more or less and that is filtered, glucose filtered load is about also so much. So whatever is being filtered, whatever is being filtered is being absorbed, is being what? Is being absorbed. But once you cross the plasma, glucose in the plasma to beyond 200 or 250 or so, then the absorption is not possible. And then you start, you start, you start what? You start excreting, you start excreting glucose in the urine. It starts appearing.

Okay. I mean this graph tells us actually the values at which you may start and this is, this is, okay, so, okay, so sweet, sweet, sweet, sweet glucose, glucose, glucose, glucose, glucose, glucose, you have reached a point of saturation. It may be about 300, which is a lot. We have a lot of margin. In a healthy person, the blood glucose level never goes up on 120, 140. But you are still okay.

I mean, even if it goes to 200, 250, your SGLT is still enough to make sure that the glucose molecules are being absorbed. But the moment you go above 300, okay, then, then the, then, then, then it starts, you have reached your transport maximum. Okay. And then the, then the glucose will start appearing into the, into what? Into urine. Are you getting the concept slowly? We just, we are just considering the point of saturation of the process of reabsorption.

Can be done, can be done, can be done. Process is at a limit, it cannot be done. Now this process of, this is, this is a classic example of glucose, but that is also true for a lot of other substances which are being reabsorbed. Glucose transport maximum is 375 milligram per minute.

Okay. Are you with me? So much can be, this is the limit, this is the limit, okay, maximum limit this, okay. Then for phosphate, phosphate also is actively absorbed. It is about 10 milli, milli moles per minute. Sulfates, amino acids, amino acids also, amino acids also because the mechanism, mechanism, the proteins are same, but the mechanisms are similar. The transport maximum for amino acids is about so much, urate is so much, lactate is so much, even plasma proteins is so much.

Okay. So we, here we consider the limit within which the cells of proximal convolute tubule can, can reabsorb and beyond the limit it is, it is just not possible, okay. Are you okay so far? We are done? Good, good, good. Okay, this is very simple. We are just talking, we have done it already. We will do it once again.

We have seen this image. This the author makes a point in this slide that water reabsorbs from the osmosis coupled mainly with sodium. So if sodium goes, the water will go. We alluded to this point already.

I can just move on. This is a box diagram, but we have done it, but let us do it once again. Sodium reabsorption, why sodium goes? Luminal negative potential and then because sodium goes, then water goes, which the chloride go by the luminal concentration, the urea goes. This just tells us as to how are the different substances reabsorbed across the, one very interesting point. Please remember, bicarbonate ions are important for us.

What for? pH. They play a very important role in nature. But what am I talking about? Bicarbonate ions. So we want to conserve them. So here author tells us as to how are we going to reabsorb the bicarbonate ions.

We do not want to lose them. So here we have the lumen and here we have the apical surface and on the apical surface we have an antiport system and that antiport system does what? It is there. Exchanges, antiport exchanges. Sodium will of course come. How sodium will come that we have already seen. And it will, against that it will go the hydrogen ions will.

Now on the basal side, of course we have the pump. Now here we have another protein system in which again it is an antiport system which will, let us see, carbon dioxide water abundantly there, carbonic anhydrase, H_2CO_3, carbonic anhydrase, carbon dioxide and water, carbon dioxide and water absorbed in again carbonic anhydrase within the cell. This gives rise to H ions and the bicarbonate and here something interesting happens. Whereas these H ions are exchanged for the sodium ions and H ions are being thrown out.

Remember, two issues. We want to keep bicarbonates and we want to get rid of H ions. Why? Our body keeps on generating huge amount of H ions right from stomach to the metabolism of amino acids. We keep on generating H ions and in the interest of pH we better get rid of H ions and keep on conserving what? Bicarbonate ions. So there you have the, so here what we do is, here again we break up bicarbonate into H and CO3 whereas the H ions will go by help of this antiport system, we have already seen this H ions will go there whereas the bicarbonate ions. Now there is another system of proteins on the basal side which will exchange, which will, no this is a simple system where sodium and bicarbonate will be taken from the cell towards the blood side and this, okay.

Can somebody please tell me what does this system signify? It is exchanging what and what? Bicarbonate and chloride. That makes sense. Why? Because it is negative for negative. So you are bringing about the transport of substances without really making any change in the ion. So you are exchanging sodium for chloride.

I am sorry, not sodium here. Here the bicarbonate is exchanged for chloride. So what is the message in the slide? These cells play an important role in the recovery of the bicarbonate ion. We do not want to lose the bicarbonate ion and at the same time we are making sure that the H ions are got rid of. Sir, in the last slide, carbonic anhydride was shown on the lumen side. Since it is a protein, is it on the say luminal membrane of the.

It is there on the villi. On the villi. Everywhere, everywhere. I will just explain this slide and we will close today's talk. What I will do is, my proximal convoluted to be starting here and it is ending here. I will take these 2 points, take these 2 points and I will put them here and from 0 I will divide it into 0 to 100.

The distance 0 to 100. So 0 is right at the level of Bowman's capsule and 100 is where the loop of inlet is beginning. Number 1. Number 2 what I will do is, I will collect the fluid, the filtrate here, here, here, here, here at 5 different points and those points I will call as 20, 40, 60, 80, 100. What I am doing, I am just collecting these samples filtrate along the length of the proximal convoluted tubule. From the beginning 20% distance 40, 60, 80 and 100.

Are you with me so far? I am collecting that fluid filtrate there and I am subjecting it to, I will take it to atomic absorption or whatever HPLC I have and I am trying to subject it to analysis. And the concentration that I have here at 0 position, the fresh filtrate, what a dirty word, the filtrate. I will call it as whatever is the concentration sodium, whatever is the concentration I will call it as 1. So whatever sodium I have here is sodium is here is 1. And I have sodium here evaluated here, here, here and here is my last sample.

And I find that my sodium is almost 1. Why is it still 1? Because lot of sodium is already absorbed. Lot of sodium is already absorbed. We have seen that huge amount of sodium has been absorbed. Why is it still 1? Water is also absorbed. Water is also absorbed, very simple, very simple.

Water is also absorbed in the same proportion. As a result of that the amount of, the concentration of sodium ion is remained same. But if I see the amount of glucose here, amount of glucose here and amount of glucose here and I compare the amount of glucose here with the amount of glucose here, what picture do I get? 99% of glucose is absorbed. Are you with me? And same is also the story for yet another valuable molecule. What is the other valuable molecule? Okay. Are you getting it? Are you getting the profound importance of proximal convoluted we have absorbed completely by the time you are done with the proximal convoluted tubule, glucose is completely absorbed, amino acids are completely absorbed.

At the other end if you go to the top, you have another interesting story to tell what is going up? Creatinine. Why is it going up? You do not want it back? You do not want? You see exactly the water has gone, creatinine has not gone up. Creatinine per se has not gone up. But because the water has been absorbed therefore the concentration of creatinine is relatively more and therefore creatinine will go. And we have already seen the importance of creatinine.

I am making continuously making a mistake. It is what? Creatinine. Creatinine. What is it? Creatinine and creatinine and then here is the osmolality. Osmolality is same. It is just one and bicarbonate is here and sodium is here etc.

So this gives us an idea as to overall what is the rate at which the different substances are being absorbed as the filtrate moves along the proximal convoluted tubule from one end to another end. I will stop now. Thank you.