Human Physiology
Prof. Nishikant Subedar
IISER-Pune

Lecture – 27
Kidney and RBC production

So, are our concepts pretty clear regarding as to what are the two mechanisms by which the kidney ensures that inflow of the blood is regulated? What was the first concept that we learned was named as? Myogenic. Myogenic mechanism and what was the other one? Okay. Okay. Okay. And what were the two signaling molecules we talked about and we heard about when we talked about the tubuloglomerular something.

What was it? There were two or three signaling molecules. Okay. Okay. What were the substances that are released by the macula densa? I am reframing the question.

I am just rephrasing my question. ADP. Yeah, very good. Say that again. ADP and ADP.

ADP and adenosine. Adenosine. Adenosine. That is the molecule that reacts with the receptor. Right, right, right.

And fill in the blank. What kind of receptor would you find in the cells of macula densa? What kind of receptor will you find? Listen to the question. What kind of receptor will you find in the cells of macula densa? Your answer is it goes to the smooth muscle. I am not asking about smooth muscles. I am asking about what? What kind of receptors will you find in macula densa? Stretch.

Very good. What is it? Stretch. Stretch, okay. And what is the trigger for stretching those, exciting those receptors? Osmotic pressure. Osmotic pressure.

Because of what? Because of sodium ions. Because of sodium ions. Okay, okay, okay. Done, done, done. We are, let us come to, okay.

Now kidney has, we are just starting with kidney. Now we are just warming ourselves to understanding what kidney really is. And there is very interesting aspect about kidney. I will talk about it and we will go back to the main function of kidney. Kidney is a very interesting function that, okay, it is an endocrine organ.

We already, we are already, and we already know the name of one hormone and what

was the name please? Name name name name name. Renin. Renin. What was it? Renin.

Renin. And what was the source? Juxta. Juxta, say that loudly. Juxta. Juxtaglomulular cells. To yet another equally or even more important hormone which is being secreted by the kidneys and the name of that hormone is, please read for me.

Erythropoietin. Erythropoietin. What is it called as? Erythropoietin. Erythropoietin, very funny. Erythropoietin, erythrocytes.

Erythrocytes. You are talking about RBCs. What has RBCs got to do here is an interesting question you can ask. The question is really interesting. The question is, you see when as long as we are all okay, what do you mean by okay? We are getting enough oxygen. Is there enough oxygen there? As long as my respiratory system and lungs are efficient enough to take whatever oxygen I need, as long as I have enough number of RBCs, as long as my respiratory system is good enough to deliver oxygen to every cell in the body and everybody is good and happy, no problem.

Erythropoietin which is a hormone secreted by the kidneys very low. It is almost very low, very low. So far. Then I have a problem. The problem may not be in me.

The problem is because I have gone to some place in again same - some high altitude and then suddenly I find that oxygen is rare. So although my systems are fine, there just is not enough oxygen there. Or you can have a problem with your lungs. Or your lungs are not working or very simple and most common, particularly common in our Indian women, 80% of the women are anemic. Obviously what, they just do not have, they just do not have enough hemoglobin.

In all these cases then something very interesting happens in the kidney. In the kidney there are certain cells which release this substance. This is a glycoprotein with a molecular weight of about 34,000, molecular weight of about how much? How much? 34,000. 34,000 and this is a hormone that is being secreted by what you call as, I am sure you can decode this figure there. Can you see the Bowman's capsule there, afferent and different vessel and you can also see the capillary there.

There are certain fibroblasts there which are a source for this particular hormone and those cells which are fibroblasts, which are there in the cortex, oh very interesting thing what they have done. They have isolated erythropoietin, step number 1, erythropoietin and then inject it in rabbit. So the rabbit immune system, if it is human erythropoietin, it will generate antibodies. Are you with me? You isolate these antibodies and use them in

immunostatochemistry protocol and then you test them on this kidney and wherever the antigen is there, your antibodies will react. So you are in immunostatochemistry.

And then you can, can you see, can you identify the cortex there and in the cortex can you see the green signal there, fluorescence, can you see the image at the top? What is that, what does that green fluorescence in the cortex of the kidney represent please? Cells that secrete erythropoietin. Very simple, I am labelling, I am immunostaining, labelling. What cells? The cells which synthesize and secrete what? Erythropoietin and I can find that there is abundance of erythropoietin, erythropoietin in the cells. Now what do they do? So if you are short of, if kidney is a sensitive organ or the, or okay, okay. Those cells which contain erythropoietin that we have seen in one of the previous slides, those cells are sensitive to the availability of oxygen, okay.

Availability of oxygen, well, your every cell in the body is, your every cell in your body is sensitive to oxygen. If I cut your oxygen, you will die. Not in that sense. When I say that they are sensitive to oxygen means even if the slight fall in the partial pressure of oxygen in the blood is experienced, the cells will start signaling, giving a signal and the cells will start responding and how they respond? They respond by generating, synthesizing new molecules of erythropoietin and it is a hormone, therefore erythropoietin will go in the blood, it will go everywhere, through the blood everywhere, it will also start acting on the hematopoietic tissue which means your bone marrow. Where are RBC synthesized? In the bone marrow.

It will act on the, it will act on the bone marrow. So here I have tissue oxygenation, okay and tissue oxygenation for some reason has gone low. Why? I told you 10 reasons for which it can go. Actually the author has given the reasons. Can you read for me? Low blood volume, anemia, low blood, low hemoglobin, pure blood flow, any of these reasons, then it will, then it will, that it will be sensed by, and then it will, and the cells of the kidney will start generating what molecule please? Erythropoietin.

Erythropoietin. It will come from the kidney, it will act on the hematopoietic stem cells. What am I talking about? In your bone marrow, okay, there are stem cells. Thousands of them, thousands of them, thousands of them, their function is to keep on every day generating millions and millions of RBCs, okay. Those RBCs from the marrow, they get into the circulation and they better get in the circulation because we keep on losing RBCs in equal number because their life is, because the life is what, numbered 100 days or so. So RBCs will keep on dying, we need to replace them.

So there, so huge amount of, particularly in your sternum, okay, huge amount of hematopoietic stem cells are there, they give rise to, and I will draw your attention to,

okay. So we are talking about what? We are talking about stem cells. So where are we? in the bone marrow? In the bone marrow, there is, this is, this is one of the stem cells is, is graphically shown there. It is called as colony forming unit E stands for erythrocyte, stem cell in the bone marrow. It may be in the femur, in your sternum, it may be in your whatever bone marrow, and then it goes on dividing and it gives rise to a cell called as pro-erythroblast, basophil erythroblast, polychromatophil erythroblast, orthochromatic erythroblast, reticulocyte and finally, what do you have at the end? And one cell may give rise to hundreds and hundreds and hundreds and every day they keep on generating the cells, okay.

Now, I will draw your attention to, can you see the three arrows there? Hello, can you see the three arrows there? The three arrows are pointing at what kind of cell? The stem cell and the second one was pro-erythroblast and third was what? Basophil erythroblast. At this stage, the plasma membrane of those cells will have the receptor for erythropoietin, are you getting my language? So the erythropoietin which is coming from the fibroblasts in the kidney will finally bind where? Here and erythropoietin is the ligand, it will activate those and then the activity of all these cells, so if the cell is generating 100 cells, okay, per unit time it will start generating 500 cells per unit. So you have a huge number of cells and thereby what is your system doing? Trying to generate more and more RBCs so as to increase your efficiency with reference to what? Transport of oxygen, oxygen, oxygen, good, good. This is just for your, this to generate a certain degree of excitement. You know the problem is in the case of kidney failure, so we have a patient, what is the issue? The kidneys are not working, so to deal, so what is the, instantly we will think of what? You have to get rid of the executive product, so you put the patient on dialysis, okay.

So dialysis will take care of removal of the excretory products, will make sure that the blood urea level does not rise, okay. But as a result of kidney failure, now imagine that patient is also has a problem with anemia, let us presume, okay, it is very likely, okay. And if the person is suffering from anemia and if the person has kidney failure, then most probably his kidney as a source of erythropoietin is not working, are you getting the problem? And in that particular scenario, just giving him dialysis is not enough, you also need to give him what? Outside injection of erythropoietin, okay. And now that is available as a biotechnology product, okay. The huge amount of progress that has been accomplished by biotechnology product, you make insulin, you also make erythropoietin and patient who is on, I think you got the message.

Okay, I think I will move on now, you can read this.