Human Physiology
Dr. Sudip Mukherjee
School of Biomedical Engineering
IIT(BHU), Varanasi
Week - 08
Lecture - 05

Hello everyone, welcome to another new class in human physiology. In the last few classes, we have been discussing the kidney, the nephron, how filtration occurs, how urine formation happens, and how various processes of tubular absorption and secretion occur. Hopefully, you are enjoying the kidney class and going through the notes and lectures. Of course, if you have any questions, please let us discuss further in the live session. In this class, we will see how the renal control of blood pressure occurs; along with that, we will discuss some kidney diseases. So, this is very important because some diseases that can affect the kidneys will be covered in this class.

So, what are the different concepts covered? In this class, we will discuss how the renal control of blood pressure happens and what different types of hormones are actually important for that process. And then we will see some renal diseases; we will examine how our kidneys can be damaged by the process of hemodialysis and how we can filter or purify our blood. So, let us go into it and thoroughly see how these things can happen one by one. So, you remember how in the last few classes we discussed that our blood needs to be continuously purified.

Why? Because blood can have an excess of electrolytes, excess glucose, and excess toxic materials, if these continuously stay in the blood, they can eventually damage our cells and organs. So, what blood does via the kidney filtration is that it removes any type of toxic molecules like creatinine, urea, uric acid, and ammonia, but it tries to retain the maximum amount of important essential molecules. What are those? For example, proteins, blood cells, and all those small ions, glucose, and amino acids that can be mostly reabsorbed back into the blood for future use. As you know, this process of filtration requires a continuous proper pressure and blood flow. In case the blood pressure gets hampered or the volume of blood that comes through the afferent arteriole becomes low, then the filtration rate or the GFR will decrease.

And what will that cause? It will cause a significant compromise in the proper filtration of our blood. And if proper filtration doesn't happen, then the toxic substance will keep building up inside. So, that's why it is very important to have proper long-term blood regulation so that in case blood pressure falls, our kidneys can recover and increase blood pressure so that the filtration process doesn't get compromised. And this one thing, this hormone like the renin-angiotensin-aldosterone system, which is also called RAAS, this coupled hormones or this stepwise reaction actually controls directly the blood pressure in the kidney. Let's see how things go.

So, what will happen if the blood pressure decreases? As we described, a decrease in blood pressure means that a lower volume of blood will be able to get filtered at a given time, which will cause the deposition of toxic substances in our body. So, when that happens, our kidneys have a nice sensor and complex hormonal feedback system. If it seems like the low volume of blood is coming in and the blood pressure is falling, the kidney secretes a molecule or hormone called renin. So, this type of enzyme, which is like renin, is produced by the kidney and initially

starts like a cascade. You see, whenever the blood pressure falls, our kidneys release a molecule called renin.

Now, what our liver generally produces is a molecule called angiotensinogen. And what renin does is convert this angiotensinogen to angiotensin-1. So, what is happening? Again, try to recapitulate that whenever blood pressure falls, the kidney secretes renin and the liver produces a molecule called angiotensinogen, which renin can convert to angiotensin 1. Now, it is not like it ends here. One more reaction occurs in which our lungs generally secrete this angiotensin-converting enzyme, which is ACE.

So, the lung secretes angiotensin-converting enzyme, and by the name, you can understand that angiotensin 1 gets converted to angiotensin 2 by the activity of ACE. So, eventually, what is the cascade happening is that whenever there is low blood pressure, the kidney can sense it and will secrete renin, which can initiate a cascade of reactions. By converting angiotensinogen to angiotensin II, this angiotensin II has a potent vasoconstrictive effect. What is vasoconstriction? So, if, for example, our blood vessels normally look like that and have this much diameter after the activity of renin-angiotensin, the diameter would be narrower. So, this basically means that the diameter of the blood vessels will get narrower, and it will help because when the blood vessel gets narrower, it causes vasoconstriction and leads to an increase in blood pressure because the space becomes smaller.

So, initially, whenever blood pressure goes low using this RAS or RAS mechanism through the process of vasoconstriction, the kidney tries to recover the blood pressure. There are some more; let's see. So, what we told was that whenever the kidneys sense any fall in blood pressure, they will create a RAAS mechanism through the initial secretion of renin and the conversion of angiotensinogen to angiotensin-2, which promotes the vasoconstriction of the vascular smooth muscles. Whenever vasoconstriction happens directly, it will try to influence or increase blood pressure, but it also sometimes stimulates the posterior pituitary, which secretes this aldosterone type of hormone. So, what it does is that the process can also stimulate the posterior pituitary.

That can actually stimulate the secretion of hormones like anti-diuretic hormone. So, what is happening is that once vasoconstriction occurs, it can stimulate the posterior pituitary, which basically secretes the antidiuretic hormone. And what is the function of the anti-diuretic hormone? Anti-diuretic hormone basically retains the water. So, what it does is that it reduces the water in the urine and tries to increase the water in the blood. So, basically, anti-diuretics work in terms of retaining water, which means blood volume will increase.

So, what will happen? That blood volume will increase, which will eventually increase the flow of blood and the filtration rate. So, in this way, the filtration rate can also be recovered. Again, this ADH can influence or trigger the secretion of the aldosterone hormone. And do you know what aldosterone does? Aldosterone increases the sodium reabsorption in the kidney. So, if sodium reabsorption happens, what will happen? You remember that water generally follows sodium in terms of the obligatory process.

So, if sodium is reabsorbed from the kidney into the blood, water will also be reabsorbed more and more back into the blood. That will eventually increase the blood volume, improving the GFR rate or filtration rate. And finally, this is like three different ways, actually four different ways, in cases where blood pressure reduces and the filtration rate gets compromised. First, the RAS mechanism produces angiotensin II, which helps in the direct vasoconstriction of

localized arteries or capillaries, improving blood pressure and increasing the GFR rate. Additionally, the posterior pituitary secretes ADH, an anti-diuretic hormone that retains water in the blood, increasing blood volume and improving the GFR rate.

The adrenal cortex secretes aldosterone, which improves sodium reabsorption in the blood; as you know, water follows sodium as an obligatory transport, so blood volume increases, and in that way, the filtration rate also improves. So, hopefully you understood that whenever the blood pressure decreases, there are various cascades of reactions that can neutralize that condition automatically. And then you consider that if blood pressure increases, what will happen because you know that having high blood pressure in the capillaries is not good, as it can significantly damage various parts of your capillaries and also various parts of the soft organs. So, in case our blood is near the kidney, the blood pressure gets high, then what will happen? You see this very important hormone, which is called atrial natriuretic peptide. So, this ANP is like a hormone that is released by the atria of the heart.

In case there is a pressure buildup or a blood pressure buildup, ANP gets secreted by the heart. promotes sodium and water excretion through the urine. So, what this ANP, or atrial natriuretic peptide, basically does is promote more urine formation and the excretion of sodium and water, and if sodium and water are excreted through the urine, our blood volume will decrease. So, basically, blood volume will go down, and if the blood volume goes down, then the blood pressure will also decrease because it will inhibit this renin-angiotensin mechanism, basically. So, if the blood volume goes down, the rash mechanism will also be inhibited, right? That will cause vasodilation.

That means whenever vasodilation happens, remember that in normal cases we may have this type of diameter, and now through this process of ANP, vasodilation will occur; basically, the diameter will be larger, and if vasodilation happens, what will occur then? Blood pressure will go down, right? So, blood pressure will eventually fall because the diameter of those capillaries is becoming larger, which will result in a decrease in blood pressure. So, in this way, our body will neutralize high blood pressure. Okay, hopefully, it is clear. So, the renin-angiotensin-aldosterone system (RAS) will act when blood pressure lowers; it will try to neutralize and bring blood pressure back to normal levels. In case blood pressure goes high, then the atrial natriuretic peptide (ANP) will cause vasodilation by promoting sodium and water excretion, and through this, blood pressure will return to normal from high to low.

Hopefully, you understand this. Then let us quickly discuss some renal diseases, right? We will quickly go through some of these renal diseases. So, the foremost and very important issue is chronic kidney disease, right? What is it? It is basically a loss of kidney function, and there can be several causes, such as diabetes, hypertension, and high blood pressure; many reasons can eventually damage our kidneys and cause chronic kidney disorders or chronic kidney disease. How can we diagnose the problem? We can do blood tests such as the GFR rate and creatinine level; we can also perform urine tests to measure proteinuria. In cases of progressive disease, we can additionally do a kidney biopsy to test the cells and tissue.

Different imaging can also be done, such as ultrasound and CT scan. There are different treatment options available, of course, but CKD is a very ever-growing kind of disease due to our lifestyle and food habits. So, we should be able to improve our health quickly, which is of utmost importance. We should consume proper food, maintain our hydration levels in the body at all times, and also control our blood pressure. So, all these ways, there are a lot of medicines available that can be used to manage chronic kidney disease, but if the disease progresses

beyond a certain point and becomes irreversible, then the only options are to perform hemodialysis or, in some cases of complete damage, a kidney organ transplant.

Diabetic nephropathy, as you know, like diabetes, is a condition when blood glucose becomes higher and persistent, and having high blood glucose is not good because it damages the cells and tissues by changing the osmolality. And overall, the concentration of the molecules in the blood can also attract bacteria and infections, and it also increases inflammation inside our body. So, in this way, the diabetes condition can significantly damage our nephrons, just as a lot of diagnoses can be made using urine albumin tests and, in the same way, creatinine GFR. So, in this same way, the diagnosis can be done to understand the condition. There are controls or measurements that are present; of course, we can control our glucose level, maybe using insulin or some other interventions.

With lifestyle changes, we can also control our blood pressure; we can use this ACE inhibitor because, as you know, ACE can. Convert this angiotensin 1 to angiotensin 2. So, if we can inhibit the AC, angiotensin II will not form, so blood pressure will be controlled, right? And finally, dietary modification should also be done. Then hypertensive conditions like high blood pressure can damage the nephron, the local arteries, and all the kidney tissues and cells. We can monitor the blood pressure; we can do a urine test to diagnose.

And of course, we should control the blood pressure; we can use the diuretics, right? If we use the diuretics, a lot of water will go out from the urine, and blood pressure can fall. Also, there are other types of molecules, right, to control blood pressure. One of them you know, like it naturally happens by the ANP activity. So, we can use drugs that also promote ANP activity. Okay, so basically we can do the vasodilation and reduce the blood pressure; then infection can also happen, and inflammation can occur, like in glomerulonephritis, where inflammation of the glomeruli can happen in the kidney.

This is basically an autoimmune type of disease, which can also be caused by genetic mutations. The same way, urine tests and blood tests can diagnose this type of condition in the body. Steroids, corticosteroids, and immunosuppressants can generally be used for autoimmune disorders, but as you know, prolonged use of immunosuppressants or steroids is not good for your body because they can suppress immune activity and cause a lot of side effects. Kidney stones can occur because, as you know, many of these ions, such as calcium or even oxalate, can get deposited in your kidneys and eventually form a stone, and if there is stone formation in the kidney, it causes a huge amount of pain. Different types of imaging can be done, a biopsy can be done, and a urine test can be done to understand if the formation of stones is present in our kidneys.

Of course, we can do pain management to reduce the pain, and there are also a lot of medications that can dissolve the stone. Those can be used to reduce complications. Finally, UTI is a very common disease that is a urinary tract infection. Even though it happens mostly in the urinary tract or inside the urethra, a progressive stage of UTI can cause damage to the kidneys; this is because the infection is caused by bacteria and other microbes, and we can use antibiotics for treatment. A diagnosis test can be done by a normal urine test by performing a bacteria culture.

So, UTI is a very complicated disease because, you know, bacteria can also become drug-resistant. So, in the case of drug-resistant UTI, the mortality rate is very high, and recently the FDA has issued a cautionary notice that many of the antibiotics have already become drug-

resistant. So, there is a huge amount of issues for those patients who have drug-resistant UTIs. Finally, in cases of any of those diseases or conditions, our kidneys can get severely damaged or compromised, and in that case, if the normal drug treatment or initial interventions are not enough, we can do the process of hemodialysis. So, hemodialysis is a process where our blood can be purified in a controlled setting.

The purified blood can be circulated back inside our body. So, you can see how a hemodialyzer works: your impure blood can be taken in a controlled pressure setting, of course, and then you use this dialyzer filter, where your blood will get filtered, and then the purified blood will eventually be put back into our body. So, this is a basic mechanism of hemodialysis. An important thing to note is that the whole process needs to be done in a controlled pressure situation because low blood pressure will cause a lot of additional time for the filtration of the hemodialysis; similarly, if there is a buildup of high blood pressure, that can cause damage. Our local arteries are like our local nerves.

So, in that way, we should not damage our tissues or arteries. So, the whole hemodialysis process needs to be done in a controlled way. Finally, there can be a lot of issues during hemodialysis. First, you have to properly maintain the sterility of all the elements and the catheters that are placed inside the arm; for example, the catheters that are inserted into the arm to collect the blood need to be sterilized and should not have any clot formation because clot formation can build up in the blood and increase blood pressure. Frequent use of a catheter inside the artery can also cause infections, formation of fibrotic or scar tissue, and in severe cases, it can completely block the veins or arteries.

So, fibrosis, stenosis, central venous occlusion, and infection can happen. So, this is like hemodialysis, although it is a very costly process. It needs to be done in a controlled way with proper sterility and proper observation. Finally, do you know that kidney disease often goes unnoticed just because our kidneys have a very good mechanism to control the process in another way? Even if the regular process is getting hampered by 90% damage to the nephron cells, the remaining 10% of active nephron cells can still manage to perform the filtration process. So, it often happens that whenever the situation or abnormal condition is detected, the damage is already done.

Like almost 90-95% of the kidney is already lost, and then there is no more left, because this is an irreversible process; kidney cells and nephron cells cannot regenerate. Hence, the only other option is a complete kidney transplant. Okay, so you can do some activity questions. Hopefully, you enjoyed the class. That is how our kidneys, through the RAS mechanism, can control blood pressure and maintain the GFR rate.

We also discussed some of the kidney diseases and disorders, as well as the processes for detecting them. If the kidney damage is severe, we covered how to perform hemodialysis. Hopefully, you enjoyed all the kidney classes; in the last few classes, we thoroughly discussed the kidney. In the next class, we will review the new aspects of human physiology.

Thank you again for attending today's class. Thank you.