Human Physiology
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Week - 08
Lecture - 02

Hello everyone, welcome to another new class in human physiology. In today's class, we will discuss glomerular filtration. You remember that in the last class, we discussed various excretory products, their toxicity, and how to remove them. And then we also discuss briefly about kidney anatomy. In this class, we will start to see how glomerular filtration happens. So, what different concepts will be covered in this class? We will first cover the nephron, nephron structure, glomerulus, Bowman's capsule, glomerular filtration rate, various filtration pressures, and factors affecting GFR, and lastly, we will also see the juxtaglomerular apparatus.

So, nephron, what is a nephron? The nephron is defined as the structural and functional unit of the kidney. As you know, each kidney consists of about 1 to 1.3 million nephrons. So, together we have roughly 2 to 2.5 million nephrons. Nephron has distinctly two parts; one is the renal corpuscle, as you can see, and the second part is the renal tubule. So, a tubular portion called the renal tubule is made up of three parts: the proximal convoluted tubule, the loop of Henle, and the distal convoluted tubule. So, if you see here, you will see that this part of the nephron is the Bowman's capsule, and then this whole part of the remaining tubular structure is called the renal tubule. And now inside the renal tubule, there are two different structural patterns.

One is called cortical nephrons, and the second is called juxtamedullary nephrons. So, this is basically two different types of classifications of nephrons. The cortical nephrons, or the superficial nephrons, are mostly located near the cortex area of the nephron, which is the outer area of the nephron. And in the juxtamedullary nephron, as you can see here, these juxtamedullary nephrons are mostly located a little bit deeper inside the medulla area of the nephron. So, this is two different types of nephrons as you can see.

Then we will start with the glomeruli. The glomerulus is a part of the kidney. You can see here that this is a structure of the whole glomerulus, and basically, this is like a filtration flask. And what is the glomerulus, actually? The glomerulus is a tuft of capillaries. So, basically, it's like a structural kind of tuft with a lot of blood capillaries.

The vessel that enters inside the glomerulus is called the afferent arteriole. So, the afferent arteriole basically carries the blood and brings it into the kidney for the filtration process. And once the blood is filtered inside the glomerulus and across the Bowman's capsule, the rest of the blood will pass through the efferent arteriole, right? So, again the afferent arteriole, which carries the blood from our bloodstream for potential filtration to the kidney, and once the blood is filtered across the glomerulus and the Bowman's capsule in the form of urine, the rest of the blood passes through the efferent arteriole. The diameter of the efferent arteriole is generally less than that of the afferent arteriole. And one interesting thing about the glomerulus and the capillaries of the glomerulus is that the blood capillaries inside the glomerulus are porous in nature or fenestrated in nature.

So, how do they look? If you kind of see the structure of the cells, they are porous. So, basically, why are they porous? So that the molecules or the blood can eventually pass across this porous structure. And what is the diameter? The diameter of this fenestration is about 50 to 100 nanometers. This fenestration of the porous structure allows various water, electrolytes, small-sized proteins, and other nutrients to pass from the blood, and they get filtered. So, if we go into a little bit of depth about the glomerulus structure to start with, if you go again in the last.

So, this is basically like the glomerular basement membrane. This part. So, this will zoom in a little bit now in the next slide here. So, this is like the structure of the glomerular basement membrane. This is a very important part of the glomerulus, and as you can see, it has three distinct layers.

The top part, which is called the lamina rara interna, and the bottom part, which you can see as the lamina rara externa. And in between the dense part, which has a lot of collagen-like molecules, you can see inside; this is called lamina densa, right? So, the outside part is the lamina rara externa, the inside part is the lamina rara interna, and then there is a condensed part in between, which is called the lamina densa and is made of collagen. And you can see that all this laminar interna and the externa are highly negative in charge. Why is that? Because they are made of or built from substances like heparan sulfate, which is highly negatively charged. Due to this negative charge, the entire membrane, or the glomerulus basement membrane, carries a surface negative charge.

Why is it important? Because proteins that are carried by the blood are also negatively charged. Now, what is the basic goal of renal filtration? The basic goal of renal filtration is to remove all the excretory components; for example, ammonia, phosphates, and urea. So, the body needs to remove all these excretory components, which also include urea and uric acid, but it wants to retain all the important components, mostly proteins. Why? Because protein is the most important part that serves as a building block for our tissues, cells, and muscles. So, our bodies do not want to waste any protein.

So, through this initial filtration, the glomerular basement membrane will retain most medium- and large-sized proteins, which will not be able to pass through the membrane. So, which other ions or components will be able to pass? You can see here that almost all positively charged ions, such as sodium, potassium, and calcium, will be able to pass through. Even small negatively charged ions, like chloride and bicarbonate, will be able to pass inside along with other nutrients such as glucose, lipids, urea, and water. So, these molecules will be able to come inside easily. It is also important to know that although large plasma proteins cannot pass, very small proteins, such as hemoglobin or insulin, can sometimes enter.

So, let us see further if we go into detail. So, first we discussed the glomerular filtration membrane, right? As we mentioned, mostly all large-sized proteins cannot pass through the glomerular basement membrane. Why is that? Because the membrane was highly negatively charged, it was composed of heparan sulfate. Now, you can see that once these fenestrated capillaries and the glomerular basement membrane are present, other molecules like nutrients, ions, sodium, calcium, potassium, chloride, bicarbonate, and water, when they pass inside, face another layer of filtration, as you mostly see. This structure after the glomerulus is like a cup-like structure, isn't it? You see, this is like a cup-shaped structure that is also called Bowman's capsule.

So, once those molecules pass through the fenestrated capillaries, they will enter Bowman's capsule. And the Bowman's capsule has some uniquely distinct structural features. As you can see, it has two different layers: one is the parietal layer, and the other is the visceral layer, right? The visceral layer of Bowman's capsule contains typical cells called podocytes. These look like, see the structure of the cells that looks like a foot, right? So, these cells, or podocytes, are also called foot processes. And in between the podocytes, you can see that there are some small netlike structures or loop-like structures.

These are called filtration slits. What are the actual components of the filtration slits? It is made of nephrin, which is basically a protein. This protein interconnects two podocytes and creates this type of thin slit. And these slits are about 25 to 30 nanometers in diameter, but nephrins allow only molecules that are less than 10 nanometers in size to pass. So, what types of molecules will eventually be able to pass? Like less than 10 nanometers, and what are those that can pass across in the same way as sodium, potassium, chloride, and bicarbonate? So, all these ions will be able to pass apart from glucose, right? And then urea, lipids, and some very small proteins, like maybe hemoglobin or insulin.

The majority of the big proteins come inside, even if mistakenly. So, if I consider a medium-sized protein that mistakenly enters this basement membrane of the glomerulus. So, you remember that this part is the glomerular basement membrane. So, in ideal cases, no protein should be able to come through, only very small proteins like hemoglobin or insulin; but if I consider that maybe the nephron has been damaged or there is high blood pressure, then some mid-sized proteins may be able to come inside, but they will not be able to pass through anymore. They will basically cling here, and the nephrin will be able to hold them off, right? So, there is no longer any possibility of those proteins coming inside the Bowman's capsule, and it is very interesting that there are certain cells, like mesangial cells, which, if they sense that any protein clings to the slit or podocyte slit or filtration slit, get activated and chop off this protein and degrade it.

Because if the protein stays with this filtration net or the filtration slit, the next round of filtration will not occur properly. So, the messenger cells will get activated and chop off and degrade all those stuck proteins from the surface, and eventually, the next round of filtration will be proper again. So, once we discuss, just remember that finally, before we discuss the filtration rate, we are filtering the proteins, right? So, protein should not pass from the blood to the urine, and then all the ions, like sodium, potassium, calcium, bicarbonate, and chloride, as well as glucose, lipids, urea, and everything else, will be allowed inside, right? Now, some of you may ask if glucose is also a very important component of our body; lipids are also important components of our body, as are water and all the ions. So, why will they eventually leave our bodies through the process of urination? So, to understand this, we need to go to the next class where we will see that not all of this will eventually come from the urea; the majority of the components will be reabsorbed back into the blood. So, in this class, just try to remember that initially, blood proteins will not be able to get filtered across the glomerulus, but during the process of urine formation in the proximal convoluted tubule, loop of Henle, and distal convoluted tubule, the majority of the ions will be reabsorbed back into our blood.

So, the body will basically retain all the essential nutrients and ions. Hopefully, it is clear. So, let us see what the glomerular filtration rate is, shall we? So, the glomerular filtration rate is the volume of plasma that is filtered from the glomerulus per minute, and the value is about 125 mL per minute. So, this much blood or plasma per minute is basically being filtered, okay? How much blood is coming into the kidneys or the glomeruli each minute? So, if I see the structure and all these capillaries here, the glomerulus, about 1.2 liters or 1200 ml of blood per minute is coming into these nephrons, and then about 625 ml is basically used during the filtration, and the rest, which may be above 575 ml, immediately goes out; but from this 625 ml that is used in the filtration, only 20%, which is about 125 ml of blood, is filtered per minute, and this is called the glomerular filtration rate.

Okay, hopefully it is clear how the glomerular filtration rate is affected; it is controlled by factors such as blood pressure, net filtration pressure, the surface area of the overall structure, and the permeability of the glomerulus, right? If the permeability of the glomerulus is high, then the filtration rate will be higher. If the permeability of the glomerulus is low, then the filtration rate will also be slow. In the same way, if the surface area is larger, the GFR rate will be higher, and if the surface area is smaller, the GFR rate will be lower. Along with that, an increase in blood pressure or GFR pressure will enhance the GFR rate, and a decrease in blood pressure can similarly decrease the GFR rate. And what is the net filtration pressure? Net filtration pressure is the balance between the pressures forcing the substance out and the pressures pulling it in.

So, it is the net filtration pressure. So, you can see what the filtration pressure is first, like 1,200 mL per minute of blood coming in and about 575 mL per minute going out without even getting into the filtration. Out of 1200 ml, about 625 ml per minute is used during the filtration process, and only 20 percent of that, or 125 ml per minute, is filtered, which is called the glomerular filtration rate. That depends on different types of pressure. So, what are some different types of important pressures? One is this glomerular hydrostatic pressure because blood is flowing from this side to that side; right, blood is flowing into this side, and during the blood flow, a certain blood pressure is always maintained.

So, this is called glomerular hydrostatic pressure, which is about 55 millimeters of Hg. The direction of this pressure is from the outside to the inside of the kidneys. In the same way, because the outside part has a lot of high protein content and the inside part has a low amount of protein, as we discussed, the majority of the protein will be retained in the blood, and only a very small amount of protein can pass through. That means there is a lot of high protein concentration outside, and the protein concentration inside is low, which will actually generate osmotic pressure. So, basically, water will try to move backward, osmotic pressure will have an effect, and the pressure of that is about 15 millimeters of Hg.

So, the hydrostatic pressure that pushes the blood inside, which is about 55 millimeters of Hg, and the osmotic pressure, or the colloid osmotic pressure, which actually pushes the water from inside the Bowman's capsule to the outside, are about 30 millimeters of Hg. So, the glomerular hydrostatic pressure is about 55 millimeters of Hg coming in, and the colloidal osmotic pressure is about 30 millimeters of Hg going out. What is the reason? Again, I told you that outside, the protein concentration is high; inside, it is low. So, outside there is a lot of protein, and inside there is only a very little bit, and that is why the water and the fluid will have osmotic pressure on the outside. And then another pressure that actually enforces the fluid outside is the colloidal hydrostatic pressure.

which is like whatever solvent gets retained that also tries to create a very minimal hydrostatic pressure outside, which is about 15 millimeters of Hg. So, you see the total pressure that is coming in is about 55 millimeters of Hg, and then the total pressure that is going out from the kidney is about 30 plus 15, which means about 45 millimeters of Hg. So, what would the net pressure be? The net pressure would be about 10 millimeters of Hg; in which direction? Inside the kidney. Is it clear? So, we always have a net positive pressure of about 10 millimeters of Hg for the filtration process in the GFR process, which always comes from outside to the inside. So, the blood will easily be able to enter using that positive filtration force.

What are the various factors that can affect GFR? Of course, the renal blood flow, right? It is the most important factor; GFR is directly proportional to renal blood flow. Then, glomerular capillary pressure is also directly proportional to the glomerular filtration rate. And we already discussed the colloidal osmotic pressure, didn't we? That is also very important. Eventually, the hydrostatic pressure in Bowman's capsule is important as well. So, whatever I discussed in the last slide, all these factors are very important.

And also, this is very important, isn't it? The constriction of the afferent arteriole will reduce the blood flow to the glomerular capillary, which will certainly reduce the GFR. So, in a case where a certain condition can cause the afferent arteriole to constrict, like vasoconstriction, it will certainly reduce the blood flow, which can also reduce the GFR rate, and if the afferent arteriole, which is going out, is constricted, initially the GFR decreases. Because of the initial stagnation of blood inside the glomerulus and above the glomerular basement membrane, the GFR rate slowly decreases over time. The surface area of the capillary membrane is directly proportional to the GFR. What are the various hormonal and other factors that can affect the GFR? You can see factors that can increase the GFR through vasodilation because vasodilation causes a lot of blood to flow in, which increases the GFR.

So, what are the various hormones: atrial natriuretic peptide, brain natriuretic peptide, cAMP, dopamine, endothelium-derived nitric oxide, and prostaglandin? These are all hormones that can increase the GFR rate by the process of vasodilation. And what are the different factors that can decrease GFR? The process involves vasoconstriction by factors such as angiotensin II, endothelin, platelet-derived growth factor, and prostaglandin E2. These are some of the factors and hormones that can decrease the GFR rate through the process of vasoconstriction. So, at times when blood pressure goes high or low, some of these effects might be needed to maintain the balance of the proper GFR rate, and there are different types of these hormones that can play an important role either through the process of vasodilation or through the process of vasoconstriction to maintain our GFR rate. Finally, this is just a glomerular apparatus inside this basement membrane; you can see the glomerular apparatus in this part, and there are different types of cells or parts, mainly three components: one is the macula densa, which you can see in this area.

It is situated between the afferent and efferent arterioles, and it is mostly formed of tightly packed cuboidal epithelial cells. So, very much like tightly packed cuboidal epithelial cells, isn't it? And then extra glomerular mesangial cells, right? I said this type of extra glomerular mesangial cell. What do they do? They can chop off those hinged or clinging-like proteins that were initially like being clogged in the filtration slits. That is a very important right. So, it is situated in this triangular region where you can see many different juxtaglomerular cells.

So, these cells are specialized smooth muscle cells. So, juxtaglomerular cells, as you can see here, are specialized smooth muscle cells that are situated in the wall of the afferent arteriole just before it enters Bowman's capsule. Juxtaglomerular cells are also called granular cells. These are very important. Why are aglomerular cells very important? Because it also secretes a very important hormone called renin, it plays a crucial role in regulating blood pressure.

Prostaglandins and renin maintain many important functions of our kidneys and blood, primarily through the renin-angiotensin system, which overall maintains blood pressure in the kidneys and the blood filtration process; prostaglandins, which are mostly secreted by the extraglomerular mesangial cells, are very important for producing the inflammatory response. So, the extraglomerular cells are important for the secretion of renin and mesangial cells, apart from their phagocytic property that can degrade leftover proteins; extraglomerular mesangial cells also produce prostaglandins that can elicit an inflammatory response in the presence of bacteria or pathogens. So, these two are very important. We will discuss them further in the next class, where we will try to see the processes of renin and angiotensin in detail. So, do you know that in some kidney diseases, glomerular capillaries are damaged and become so permeable that you start losing protein? So, losing protein is never good, but in cases of disease conditions, you can lose protein, which creates a froth in your urine.

So, sometimes you can see in the early morning urine that there is a lot of froth, which can be due to dehydration or concentration of the protein, but if it occurs frequently throughout the day, you see a lot of froth. That means you are leaking protein, which is also an initial signal that you are having some issues with your nephron and kidney filtration. So, it is recommended that you check in with your home doctor immediately. Activity question: Some of the activity questions you can answer are which part of the filtration membrane prevents red blood cells from entering the capsular space, which part filters the plasma proteins, and how. So, one very important thing to mention here is that if you go back to the glomerular filtration membrane or the glomerular basement membrane, one important component is that none of these large macrophage cells, T cells, or any blood cells, or WBCs will be able to pass across the glomerular basement membrane because the pores are not big enough; the cells are generally larger in size.

So, it is also very important that the glomerular basement membrane retains all the blood cells and all the large proteins in the blood. So, blood cells, WBCs, and RBCs, we should not lose those, right? They are very important components of blood. So, by glomerulus basement membrane they will prohibit that. So hopefully, you enjoyed this class on glomerular filtration, where the glomerulus is primarily important for retaining essential proteins. Apart from that, the glomerulus also retains blood cells and RBCs, while all the small ions and nutrients pass through.

and gets collected in Bowman's capsule. In the next class, you will see how some of those essential ions and nutrients get reabsorbed back into the blood. So, thank you again for meeting with everyone in another class of human physiology. Thank you.