Human Physiology
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Hello everyone, welcome to another new class on human physiology. Hopefully, you are enjoying our kidney class, where we are thoroughly discussing various filtration processes as well as the secretion and excretory pathways. In the last class, we discussed the proximal convoluted tubule, where we showed how the reabsorption process works and how the tubular secretion processes happen. Now, in this part, we will discuss the loop of Henle of the nephron and we will see what the different mechanisms are that happen in the loop of Henle. Let us start with that. What are the concepts covered in this class? So, we will look at the structure of the loop of Henle.

Then we will discuss the function of the descending loop, the function of the ascending loop, and we will briefly discuss the countercurrent mechanism. Then lastly, we will briefly highlight the distal convoluted tubule, or DCT, and the collecting duct. So, you remember in the first few classes about the kidney, we discussed the glomerulus and the Bowman's capsule where the filtration happens. And then once the filtered molecules, for example, sodium, water, amino acids, urea, bicarbonate ions, etc.

, all come out of the Bowman's capsule to the PCT or the proximal convoluted tubule. There we showed you how the reabsorption of the majority of these ions happens, and if you remember, almost 65 percent of the sodium and water reabsorption happens from the PCT. Apart from that, 100 percent reabsorption of glucose, amino acids, etcetera, also happens. We also discussed how the tubular secretion process happens; for example, some drugs or ammonia. Now, we will be discussing the loop of Henle.

So, you see, after this Bowman's capsule area, and then, for example, we discuss the PCT. Now, you see a nice U-shaped structure which is called the loop of Henle, and it has two distinct parts: one is the descending loop, and the other is the ascending loop. So, a descending loop is basically going down from near the cortex area to the medulla part, and then the ascending loop is going upwards, which is more like from the deep medulla area to the upper cortex area. Each of these segments is divided again into two distinct parts: one is the thick part and the other is the thin part. So, you can see that in the descending loop, there is this thick part, and then there is also a thin part.

In the same way as the ascending loop, you can see there is this thin part and this is the thick part. So, the loop extends from the renal cortex deep into the renal medulla, and the medullary interstitial fluid surrounding this loop plays a very crucial role in this function. You may ask me what the primary function of the loop of Henle is, right? So, the primary function of the loop of Henle is to concentrate the urine so that our body does not lose too much water because water is a very essential component of our body. So, in this part, the ionic concentration gradient is maintained and urine concentration occurs. So, you see here, after the structure, we will basically discuss the overall mechanism of the loop of Henle step by step.

So, you see, if you remember, this is the glomerulus capillary, right? So, from the afferent part, the blood is coming in, and then in the capillary network of the glomerulus, it is getting filtered. It is getting collected in the Bowman's capsule. So, do you remember what the osmolality of the near blood in this part of the glomerulus was? It was about 300 milliosmol, right? And do you remember what is called osmolality? So, osmolality was the amount of salt or solute present per 1 kilogram of solvent. So, what was osmolality called? Osmolality was, if I consider x grams of solute per kilogram of solvent. So, this would be called like x milliosmol.

Now, you see that in the glomerulus area where the blood filtration was happening, the osmolality was about 300 milliosmol, and once it gets filtered in the Bowman's capsule area, it gets collected. What was the milliosmole again? It is the same as about 300 milliosmol. And then from here, in this process, what gets filtered, if you remember, is mostly like sodium, potassium, chloride, glucose, bicarbonate, and amino acids. So, once it comes to this PCT area where two things happen, one is the tubular reabsorption. And then the second is like tubular secretion.

But can you tell me how much the milliosmol here is after this PCT deabsorption happens? Again, it is the same as 300 milliosmol. Isn't it fascinating why this happens if you remember that in this PCT area about 65 percent of sodium gets reabsorbed back into the blood capillaries? But if you remember what I said, like water follows sodium in an obligatory reabsorption process. So, in this area of the PCT, even though 65 percent of sodium gets reabsorbed. In the same way, 65 percent of the water also gets reabsorbed in the capillary area. So, eventually the salt or solute amount per kilogram of solvent stays the same, and in this way, it maintains the osmolality at about 300 milliosmol.

A few terminologies that I also want to introduce here are, for example, hypertonic. Right, hypertonic, and then hypotonic and isotonic. So, what are those, basically? In cases of hypertonicity, what will happen? The salt concentration of the solute would be higher. compared to the like initial concentration. So, the salt or solute concentrations should be higher in cases of hypotonic, the salt or solute concentration would be lower than the initial starting position, and in the case of isotonic, it will be equal right from the initial concentration; the salt or solute concentration would be equal.

So, you can say that compared to the initial blood osmolality in the Bowman's capsule and also in the PCT, what we will be calling this solution here is isotonic. Right, because the salt or solute amount per kilogram of solvent is still the same: 300 milliosmoles. So, we will say that for both Bauman's capsule and the PCT, the salt or solute in the plasma or filtrate is isotonic compared to the initial plasma coming from the blood capillary. Is it clear? Yeah. And now you can see there are two distinct parts.

One is the descending loop and the second is the ascending loop. So, let us see how it happens one by one. Of course, there is a lot of information here. So, I will try to go slowly. If you have any questions, please interact with us in the live session and drop them.

We will try to answer and clarify your doubt. So, to understand this whole thing, first we have to understand this ascending loop part. So, this is the ascending loop, and this part is the descending loop. So, first we will discuss the ascending part and then we will discuss the descending part. So, in the ascending part or ascending component of the loop of Henle, it has a lot of sodium-potassium-chloride symporter type of channel, an ionic ion transport channel.

So, you can see that sodium, potassium, and chloride are basically the sodium-potassium-chloride symporter channel. And what will happen? From the higher salt concentration because sodium and potassium are high here along with chloride. So, from this part of the loop of Henle, these ions will move to the tubular cells of the loop of Henle. So, this is like an active ion transport mechanism, a co-transport mechanism, and you can see that sodium, potassium, and chloride are coming to the tubular cells. And inside the tubular cells, they have a specific receptor for each ion.

For example, for sodium, there is a sodium leaky pore channel or sodium ion channel, there is a potassium channel, and there is a chloride channel. And what happens is that the majority of this sodium and potassium from the tubular cells again comes out to this medullary space. This is the medullary interstitial space. So, initially, if I consider this medullary interstitial space. medullary interstitial space.

So, if I initially consider what the osmolality in the medullary interstitial space was, which is almost parallel to this PCT area, it was 300 milliosmol, right? Because I discussed how the osmolality is still the same, even though salt reabsorption is happening. And now, you just think that there is a lot of sodium and potassium coming out of the loop of Henle into the tubular cells and the medullary interstitial area. So, what will it cause? It will basically increase the osmolality, right? So, from 300 milliosmol, once a lot of sodium is coming out, the osmolality of this area will become around 500 milliosmol. And the same thing is happening, right? Because I said, like, across this ascending limb, there are a lot of sodium-potassium chloride type symporters. So, it is basically pumping out a lot of sodium and potassium in this domain.

So, slowly this will add up and increase the osmolality from 500 to 700 milliosmoles, 700 to 900 milliosmoles, and eventually 900 to 1200 milliosmoles. And as you can see, this is the medullary interstitial ionic gradient; this will create a beautiful ionic gradient starting from 300 milliosmoles in the upper area to 1200 milliosmoles in the lower part. And now see, once this osmolality gradient is established, then what will happen. Now, let us come to this descending area. So, you can see in the descending area, there are a lot of water pore channels.

You can see there are a lot of these blue water channels. These are called aquaporins. So, these are aquaporin water channels. Now, if you remember, water goes from low solute concentration to high solute concentration, right? So, you can see here water moving from a low sodium and potassium concentration to a high sodium and potassium concentration in this medullary interstitial area; this water will basically come out using the protein channel called the aquaporin channel, and water will essentially move out. And let's think that initially there are about 300 milliosmoles in this area.

Now, if some amount of water comes out and goes to the interstitial medullary area, what will happen? The salt concentration will build up here, which means slowly. This area of solution, which was initially around 300 milliosmoles, will become concentrated to about 500 milliosmoles. Is it clear? Now, you can consider that a larger amount of water is passing. So, the solution will become more concentrated from 500 to 700 milliosmoles, and the same process will continue. So, as we are going down through this descending loop, you see the concentration gradient will become the same as this medullary interstitial area, which is about 300 milliosmoles to about 1200 milliosmoles, right? This mechanism is called the counter-ion multiplier mechanism, okay.

So, this process is called countercurrent multiplier mechanism. So, see how initially the medullary interstitial plates develop the ionic concentration gradient from 300 milliosmoles to 1200 milliosmoles and how it was developed; if you remember, in the ascending loop of Henle, there are different types of sodium-potassium-chloride symporter channels, and this happens with the participation of ATP or energy. Sodium comes out of the ascending area of the loop of Henle, goes to a tubular cell, and from there it goes to the medullary interstitial space, creating a concentration gradient. In the same way in the descending part, because water goes via an obligatory reabsorption mechanism, it moves from a low solute concentration to a high solute concentration. So, in the same way water comes out, because water comes out, the overall solution becomes more concentrated in terms of the presence of the solute, and hence the osmolality gradient is established here from 300 milliosmol to 1200 milliosmol, and this process is called the counterion multiplier mechanism.

I hope it is clear, and can you tell me what the different types of solution concentration are now in the different areas, for example, in terms of hypertonicity, hypotonicity, and isotonicity? Here, it was the isotonic solution because it was maintaining 300 milliosmoles compared to the plasma concentration of the solute, but as we go down, it is becoming more of a hypertonic solution, right? The same way in the medullary interstitial space as we go down the area where the concentration is increasing would be called hypertonic. Now, very interestingly, the last component is here. So, 100 and 2000 milliosmoles are still here, right? Now, as we are going up across the ascending leap, what is happening? You can see that the sodium is going out. So, if the sodium is going out, what will happen? The osmolality will fall. So, from 1200 it may go down to about 900.

So, as we go up, more sodium is going out, like about 700, the same as 500, 300, and actually it pumps out more sodium and potassium than was initially there. So, the eventual final concentration gradient before this solution goes to the DCT, or the distal convoluted tubule, is that the osmolality becomes about 120 to 200 milliosmoles. So, in this area, the solution osmolality becomes hypotonic compared to the initial plasma osmolality. Hope everything is clear to you. So, this whole process is again called counter ion multiplier mechanism.

So, this is the same thing I will not repeat one more time; hopefully, throughout the whole image, I could explain to you how the process happens. This water channel, a few things I may highlight, is only present in the descending limb. This water channel is not present in the ascending limb. So, the descending limb has a lot of water channels, but this descending limb does not have this type of sodium, potassium, chloride symporter channel; it does not have. It has this aquaporin 1 type of water channel; this is very important.

Next thing in the ascending limb, there are no water channels. So, in this part, there are no water channels present, like no aquaporins are present, but this part has a lot of sodium, potassium, chloride, and symporter channels. So, it is very important that there are certain differences in the ascending limb and the descending limb. In the counter current mechanism, I have already discussed what the counter current multiplier mechanism is, and how the initial concentration gradient in the medullary cavity increases from about 300 milliosmoles to 1200 milliosmoles, right? It occurs first in the medullary interstitial space. And then, once it happens, the water flows out, and eventually in the descending limb, in the same way, the ionic concentration gradient from 300 milliosmoles goes high and becomes about 1200 milliosmoles.

Now, let us discuss another important component of the loop of Henle, which is the Vasa Recta. So, Vasa Recta is nothing but a kind of capillary, blood capillaries that follow the same structure

as vasoducta; if you see, the blood vessels are the same way; they are like a U-shaped or loop shape. Generally, blood vessels follow from upwards to downwards, but in this case, you can see that there is a similar way: one is the descending part and the other is the ascending part. And why is the vasa recta so important? Vasa recta try to maintain this medullary ionic concentration gradient. So, as you remember, the medullary concentration gradient creates a beautiful concentration gradient from 300 milliosmoles to 1200 milliosmoles.

Vasa recta try to help maintain this concentration gradient in the medullary cavity so that water cannot wash away all the salt and damage this concentration gradient, because it is very important for urine to be concentrated in the whole loop of Henle, allowing our body to retain as much water as possible without losing too much, and to facilitate this process. It is highly important to maintain the medullary interstitial concentration gradient of the salt, and the vasa recta helps with that. Let us see how it happens. So, if you remember that there is a lot of sodium chloride right now in the interstitial medullary cavity. So, what happens basically if I consider this as the interstitial medullary cavity is that there is this beautiful ionic concentration gradient of 300 milliosmol.

Now, as for how the water flows, if you remember, water goes from low solute concentration to high solute concentration. So, water from this blood capillary area will basically move out and go to the interstitial medullary cavity. And if a lot of water comes out in the interstitial medullary cavity, what will happen? It can damage the concentration gradient of the medullary cavity. And if this concentration gradient of the medullary cavity is disturbed, it will create a significant challenge in maintaining the whole process of the loop of Henle. So, how will they balance them? Then see, once the water flows out, sodium chloride was also high in the interstitial area compared to the blood capillary.

So, once this water is moving out, a lot of sodium chloride will also come inside the capillary. And where is this thing happening? This is happening in the descending loop. And now, once this ascending loop part what it does is it basically removes all this excess sodium chloride; see, it is removing all this excess sodium chloride which was initially taken up in the blood capillary, and during the process, as it is removing the sodium chloride, it is also accepting the water molecule back into the blood capillaries. So, what is happening? Initially, water is flowing. Like a low concentration of solute gradient from the blood capillary to the interstitial area, sodium chloride, which is high outside, will simultaneously diffuse into the blood capillary as a basic mechanism.

And this is happening near the descending limb, and when the blood flows from the descending to the ascending limb, it is removing the sodium chloride back to the interstitial fluid, and water is getting reabsorbed into our blood capillaries or the vasa recta. The sodium chloride concentration is maintained, and the ionic concentration gradient of this medullary interstitial area is maintained from 300 milliosmol to 1200 milliosmol. So, this excess water, when it comes out, cannot wash away or disturb the concentration gradient. So, in this continuous process of sodium chloride acceptance and removal, the whole vasa recta maintains the concentration gradient, which is also called the counter ion exchange mechanism. So, what is called counter ion, counter current? is also called counter current exchange mechanism.

So, the previous one was the countercurrent multiplier mechanism, and in the vasa recta, as it maintains the overall concentration gradient, it is also called the countercurrent exchange mechanism. Okay, hopefully it is clear, and the last thing is more or less the concentration gradient it maintains; for example, here it is about 300 milliosmol, and it goes out also to about

300 milliosmol. So, there is no significant change in osmolality here that occurs. So, this is the whole diagram of the process I explained: first, the ascending loop and the descending limb of the loop of Henle, how the counter-current multiplier mechanism happens, and then simultaneously the vasa recta and the counter-exchange mechanism to maintain the salt gradient of the interstitial medullary cavity osmolality gradient. So, this whole thing happens in the loop of Henle, and in this way, water reabsorption occurs, and urine becomes more concentrated.

To do everything, the major important part is to maintain the ionic concentration gradient of the medullary interstitial space. Finally, I will quickly touch base on the distal convoluted tubule in the collecting duct. So, basically, in the early part of the distal convoluted tubule, what happens is that the remaining sodium and chloride get reabsorbed. Importantly, this part is also impermeable to water. So, it has a lot of sodium chloride importers, and through which about 20 to 30 percent of the sodium and chloride waste gets reabsorbed.

Also, the early part of the DCT has the site for parathyroid hormone that also plays an important role in calcium reabsorption. We will discuss more about this in our endocrine glands, but just remember that PTH also stimulates the reabsorption of calcium ions to maintain calcium homeostasis. In the late part of the DCT, we just came from the loop of Henle, then the early part of the DCT, and now we are in the final late part of the DCT. What happens is like the late portion of the DCT, and the connecting tibial contains a lot of specialized cells. Like principal cells, these are the primary targets of aldosterone.

This is also kind of a corticoid type of hormone, and you know aldosterone plays a lot of important roles, especially in regulating the sodium-potassium balance. It also kind of stimulates the increased sodium reabsorption from the filtrate into the blood, leading to water retention and increased blood volume. It also helps to increase potassium secretion from the blood to the filtrate during the excretion of urine. So, aldosterone is very important, and it exerts its effect by increasing the synthesis of sodium channels on the apical membrane and the sodium-potassium ATPase pump on the basolateral membrane of the principal cells. So, in the late DCT, you can see how aldosterone has a very important role in the increase of sodium reabsorption, resulting in the retention of water and increased potassium secretion from the blood to the urine.

So, from early DCT to now, we are in the late DCT, and finally, it would be the collecting dirt. The late DCT on the collecting duct and tubule is also responsive to the anti-diuretic hormone, which is ADH, and is very important. So, collecting dirt in the late DCT and the collection of dirt also has an important role to play. Because they are very highly responsive to this hormone, which is called anti-diuretic hormone or ADH. It is also called vasopressin, and what does ADH do? ADH increases the permeability of the principal cells, but what does it do? This segment allows water to pass by inserting aquaporin 2 channels into the apical membrane.

So, what does ADH do? ADH basically increases the permeability of the principal cells to water by inserting the aquaporin 2 channel or by overexpressing the aquaporin 2 channel. And why is this so important? Because from here, the final retention of water can happen, and the final reabsorption of water can happen. So, unless this anti-diuretic hormone, or ADH, plays a role, we will lose a lot of water through our urine. So, why is this so important? If the ADH activity were not present, we would lose a lot of water content from our body, which would lower the blood volume and cause our body to become dehydrated. So, because we should not

lose a lot of blood volume, ADH has a very important role near the late DCT and the collecting duct.

And lastly, collecting the samples is also important for fine-tuning the urea and water reabsorption, eventually to decide and determine the final urine volume. So hopefully you enjoyed this whole part. So, to conclude finally. So, we discussed the whole component of the nephron, right? And if you can tell me what the components of the nephron are, like the glomerulus, then Bowman's capsule, then the PCT, the proximal convoluted tubule, then the loop of Henle, and finally, the DCT, then the collecting duct, okay? So, to summarize, blood is coming from the arteries and initially getting filtered in the glomerulus to be collected in the Bowman's capsule, and a lot of ion reabsorption happens in the PCT, and a certain amount of secretion also happens here, and then in the loop of Henle, urine gets concentrated. and a very important medullary interstitial ionic concentration gradient that establish here to do all this process.

Finally, in the DCT, the remaining amount of sodium chloride reabsorption occurs in the early DCT. In the late DCT and the collecting duct, the remaining water reabsorption occurs, and also ADH, which is the anti-diuretic hormone, helps to retain as much water as possible. Finally, the urine becomes an excretory element, and from the initial blood to the urine, we can see how the systematic process of filtration, reabsorption, and secretion occurs to generate urine. So, hopefully you enjoyed our last few classes on the excretory system, the nephron, and how the process of urine formation happens. So, finally, do you know that the yellow color of urine comes from a pigment called urobilin? Urobilin is also a byproduct of our body breaking down hemoglobin.

So, due to this urobilin, our urine becomes yellow in color. And activity questions what would happen to the urine volume and concentration if aquaporin channels were blocked by some drug. This is very important so you remember, as we said, that in certain cases a lot of aquaporin challenges are present, and ADH also kind of influences the presentation of aquaporin channels in the present cell to help with the reabsorption of water. So, in case these aquaporin channels are blocked by some drug, then what would happen to the final urine volume? So, try to think and find this answer. Thank you again for this class where we thoroughly discussed the loop of Henle, as well as the early and late DCT and the collecting duct.

So, with this, we end the class. Overall, the nephron and how urine formation occurs. Hopefully, we enjoyed the excretory component and the entire urine formation class. Let us meet with you for another human physiology class very soon. Thank you.