Animal Physiology
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Module - 1
Lecture – 22

Welcome back to the NPTEL lecture series on animal physiology. So, we are in the section of kidney, and the regulation of fluid, in other word the excretory system. So, we have already done the basic structure of the smallest functional unit of kidney; the nephron. How the how the individual nephrons are, involved in the whole filtration process. So, we have done with the structure, but little bit of a structure is left, because when I drew the structure, I showed you distal tubule, proximal tubule, bowman capsules and all those things. So, what we will do initially in our first light. I will explain all the different cellular structures, which are present at different zone at proximal border, at distal border, and all other places. And then we will talk about the simple driving forces which are regulating this whole process. And then we will talk about the counter current multiplier, and we will close in with the Renin Angiotesin system, which is regulating the fluid.

So, even before I start with the cellular structure. Let us have a simple understanding exactly what is happening. The way it works, is fairly straight forward, if you look it logically. So, the blood which is coming. So, blood is not in physical contact, not in connection with the nephrons. Basically here is the blood vessel, which is entering, and here you have the nephron, if you go back to the structure you will look at it. So, there is a gap between the two. So, see for example, blood vessel is caring something; say molecule x, whose concentration is higher, and whereas the concentration of the molecule x in this vessel, in the nephron is lower. So, automatically from higher concentration, we will move on to the zone of the lower concentration. So, one of the forces, which promotes this whole processes, osmotic pressure. And the second force, you have to realize there is another force which is governing here; that is the hydrostatic pressure.

The amount of water, which is present on these blood vessels, and the amount of water which is present out on the other side into the nephron, because it is the water, which is carrying the ions. It is not that single handedly the ions will move out. So, whenever the ions are moving, along with them they are pulling a stream of water with them. So, hydrostatic pressure and osmotic pressure we will talk about it. and we will talk about one of the very interesting mechanism called counter current multiplier, which is fairly common in biological systems, but we will just you know, kind of go through and I will expect you guys to, consult other advanced textbook to know more about it. So, let us continue, and let us talk about the different cellular structures, which are present in the proximal and distal tubule of the nephron.

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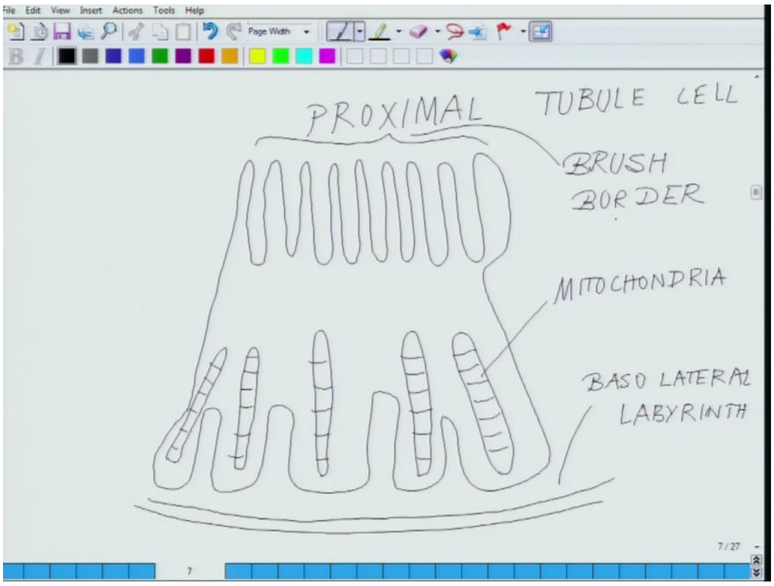

So, coming back to the slides. So, basically in the proximal tubule cells are like this. So, these individual cells have a lot of brush borders like this. These are the brush borders, your tooth brush if you look at it, it is almost like this. So, this is a brush border, which is increasing it is surface area contact, and here it is. This is the basal part of it. And you have bunch of structures like this, all over the place. So, this is how proximal tubule cells look like, which forms a proximal tubule of the kidney, and these structures are nothing, but mitochondria. Lot of mitochondria. There is lot of energy dependent processes are happening, and underneath you have the, basal lateral labyrinth, basal lateral labyrinth actually, and this is the brush borders. So, this is all about the structure of the proximal tubule.

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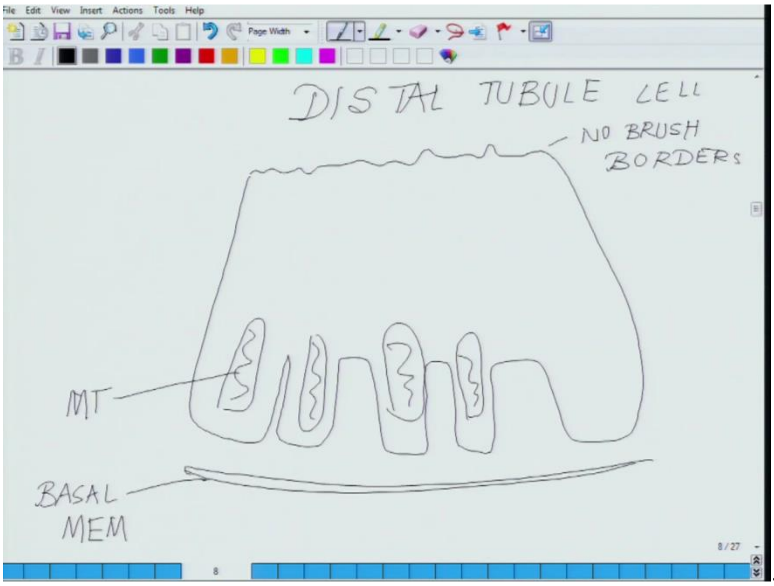

From here we will move on to the structure of the distal tubule cells. Depending on their functions, their anatomy changes; distal tubule cells. So, the distal tubule cells are something like this. This basic structure remains the same, you have the mitochondria likewise, but the star difference comes somewhere else. So, they hardly have any brush borders. So, there are no brush borders, and you have of course, mitochondria sitting here like this, all along the place, and you have the basal membrane. This is the basal membrane. These are the M T stands for mitochondria, and these cells are without the brush border.

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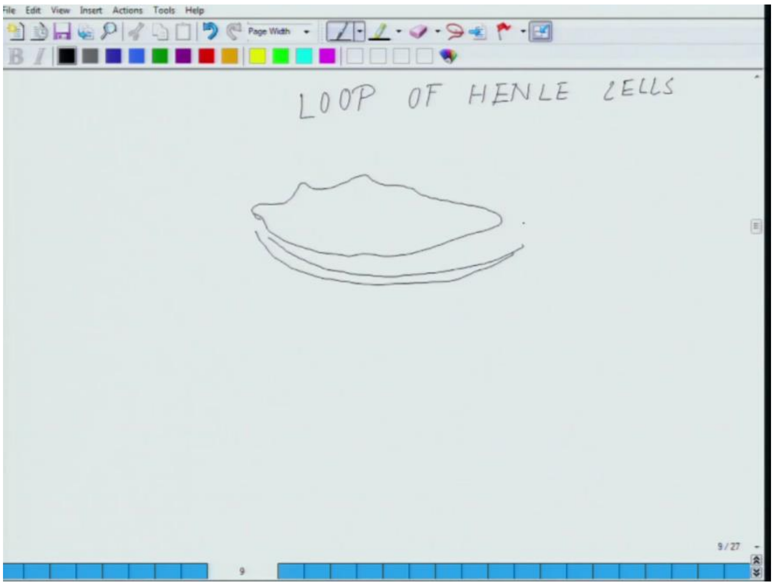

And then there is the third kind of cells, which are present in the loop of henle, loop of henle cells. So, these loop of henle cells are something like this, which is totally different from the distal and the proximal cells. So, after looking at these cells, we are able to appreciate that, how at different part of the whole nephron, the cellular architecture changes. If there is no uniform cellular architecture, and cellular architecture changes, based on the requirement of that particular part, where what is happening. So, now I will just draw another cellular structure to show the epithelial cell lining between the glomerular into the bowman capsule, and the blood vessel how they are doing. So, coming back to the slides.

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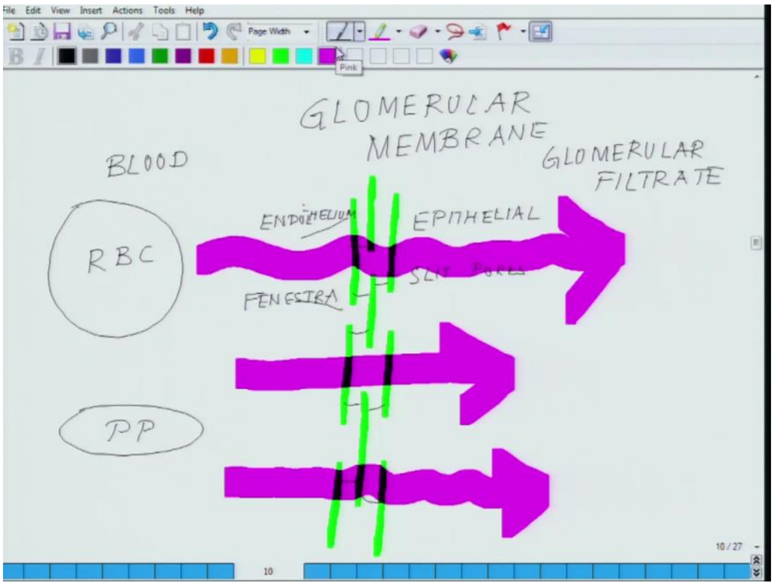

Let us draw the glomerular membrane. So, essentially this glomerular membrane, is something like this. It is kind of a perforated fracture out here, what I am trying to draw, and back to the. So, on this side, so you have the blood on this side, and the glomerular filtrate on the others side. So, what is happening essentially, is these are the R B C's which are there you have the plasma proteins on them. So, R B C's. Let us put in p p as a plasma protein. So, this is the endothelium lining of the blood vessel, and these are the fenestrated capillaries if you remember, fenestra or the windows and on this side, and these are this slit pores are kind of like this, and not fully continuous. There are certain barricades out there, and this side we have the epithelial lining of the glomerular filtrate, glomerular membrane, and these are called the slit pores, and essentially what is happening is, these fluids are moving like this, through this. Maybe in a energy dependent manner, maybe in a energy independent manner likewise.

So, this is how the movement of the fluids, are taking place from the blood vessel to the glomerular membrane. So, there is in essentially what you do, you put a physical mesh around and through the mesh things are moving. Though they are in physical contact, but they too are different entities; like one hand, and this hand. They are two separate entities, but in this junction what I was trying to draw the previous slide was. In this junction all the movement of the fluid along with the solids is taking place. So, and this is a very common thing all across the biology, where you see two individual entities. So, there is no nothing like a gap junction or something. It is there a small pore, and those pores are regulatory pores. They are not just physical pores, like anything can pass through. This diffusion what I just now highlighted, it could be energy dependent diffusion energy independent diffusion, protein carrier mediated diffusion. We will talk about all those things, how these transport is taking place, but this is a simple transport phenomena, which may need energy or maybe independent of energy requirements.

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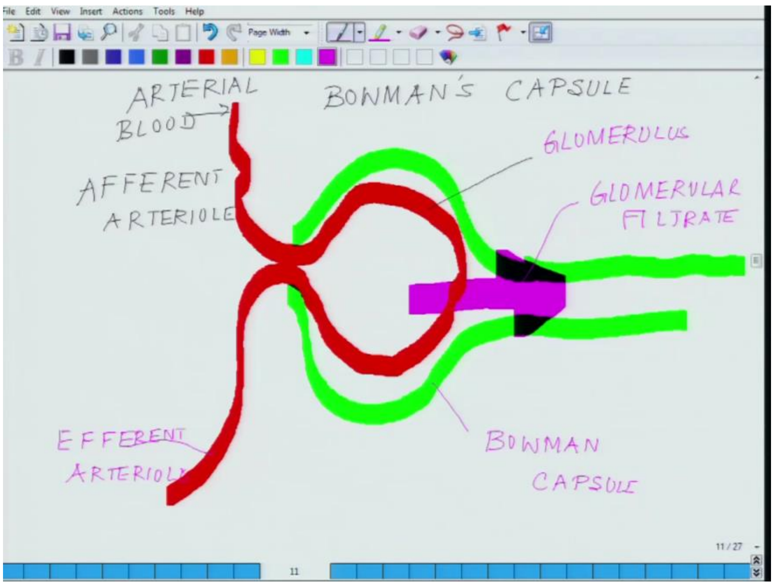

Now, from here I will move on to the next which is the bowman capsule, back to slide. So, talking about the Bowman's capsule. So, Bowman's capsule is something like this. So, the bowman capsule is, if this side is showing the... This is the bowman capsule. This is the membrane, and this side you have the blood vessels. So, the blood vessels are coming like this. They entering like this, and there is a lot of networking of the blood vessel. Then they are almost you know like this. it comes out like this. So, back. So, this is your. This is the arterial blood entering or the afferent arteriole, this is the arteriole blood. And we have the glomerulus membrane here, and what is essentially coming out is the; one second. This is the glomerular filtrate, and this is you have the bowman capsule. So, here you have the bowman capsule. These are afferent arteriole and this is your glomerulus, and this is the glomerular filtrate.

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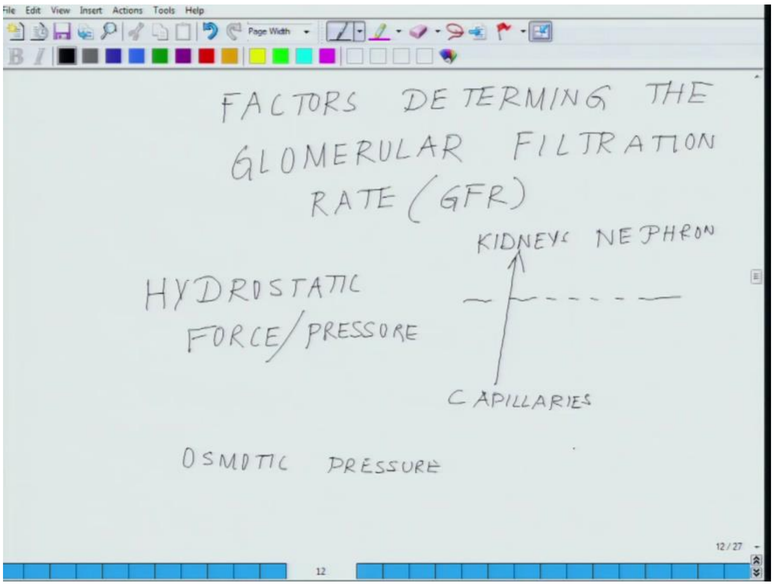

So, after this basic understanding of the structure, I will move onto the next part, which is the forces which are driving this whole filtration. So, as I was mentioning, just in the beginning of the lecture; there are two major forces hydrostatic forces and osmotic forces. So, let us look at it, then let us enumerate all of them, and let us see the relation between them. So, looking back what are the factors determining the glomerular filtration rate. So, the two major factors which are. So, this is also called G F R. this is regulated by two forces; one is the hydrostatic force, and hydrostatic force is essentially between the, capillaries. And here we have the kidneys nephrons, nephron vessel, and individual nephron. So, the hydrostatic force, something like this, (( )) arrow. Then you have the next force which is the, osmotic pressure. You can also call it hydrostatic pressure or force or osmotic force or osmotic pressure.

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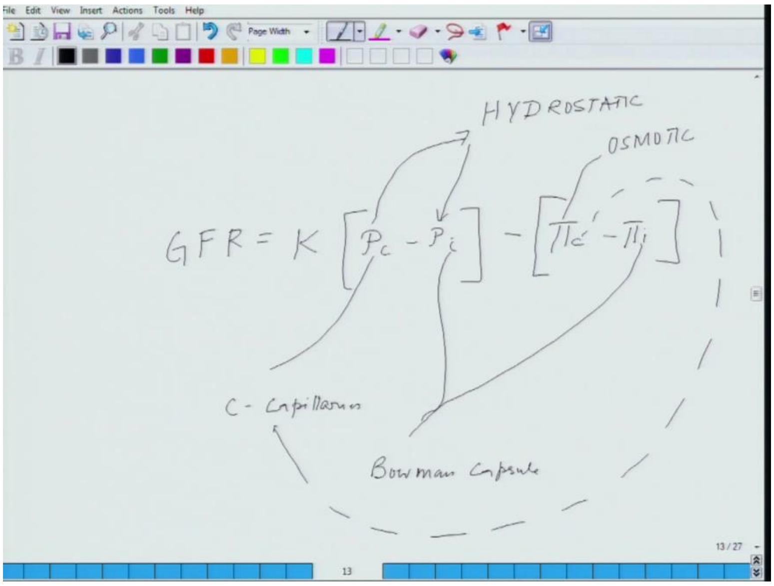

So, the relations stands like this; G F R is equal to k is the constant p c minus pi. I will just explain what is that pie c minus pie i, where c stand for capillaries, p stands for hydrostatic pressure. This p also stands for hydrostatic, i stand for bowman capsule. This i also stands for that, and this c stands for capillaries, and this pie stands for osmotic pressure. So, the differences between hydrostatic pressure and the osmotic pressure, is considered as the glamorous filtration rate.

So, this how at different zone, the filtration process is being executed, while the fluid is moving through it. and what so ever fluid initially moves, at the bowman capsule, is being absorbed reabsorbed, and secreted and likewise it goes through a whole channel, and the whole idea is to, retain as much water as possible, and not to lose the electrolytes. So, electrolytes have to be retained, and in that process getting rid of the urea and uric acid and all other unwanted molecules, which could destabilized or homeostasis of the body. So, from here we will move on to. So, let us coming back to the slides. So, let us get back to the slides. So, after this we will just move on to the next part of it, which is here. Will talk about how the sodium, is getting absorbed at different zone.

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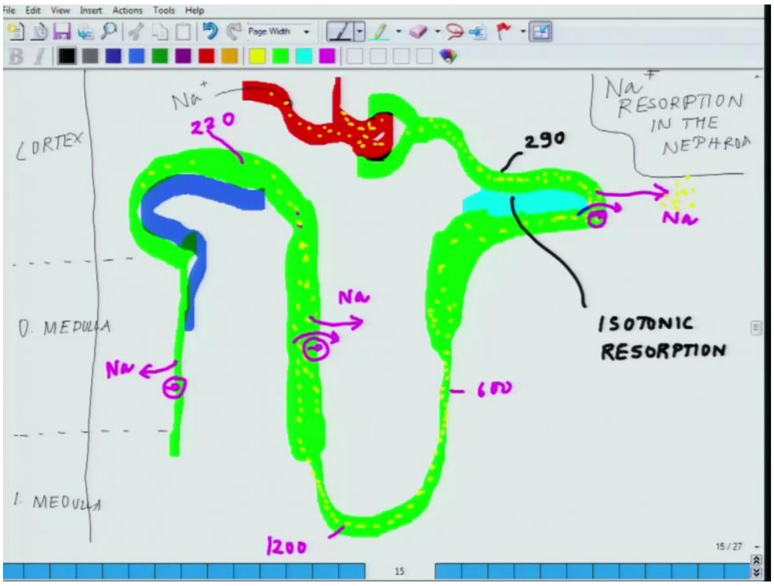

How about this. So, we take an individual case of an individual nephron, and we divided into three parts; the cortical region, the cortex, outer medulla, and the inner medulla. So, this is cortex. This is outer medulla, o stand for outer, and i stand for inner medulla. I will draw nephron now, so that nephron is like you know, out here it is starts, and moving through. So, this is the distal tubule, and it is all the way moving down, and then again it is becomes thicker, and then quires, and here the urine is getting formed; that is it. So, if you look at it. So, this is the zone, where it is much more thicker. This is the thicker segment, which is. Then it becomes thinner. It is continuous to be thinner, and then again it becomes thicker here. So, likewise this is how it goes. So, now what is essentially happening is this. So, this is how let me just much more clear. So, here the blood vessels are entering here. Now coming back.

So, the basically what we will be talking here, is about the; sodium resorption in the nephron. So, this is one of the major molecules which you have to you know ensure that it is regulated right, in the nephron. So, the first thing which is happening. So, sodium is entering through this. Here the sodium is coming in. this is all in the blood. So, from the blood, the sodium molecule. So, if I represent the sodium molecules now let me present the sodium molecule, by I use for example, I use yellow color these are the sodium molecules fine. So, these sodium molecules, then first move here these yellow colors are the sodium molecules. So, they are travelling down, concentrated out here. So, at this point, somewhere out here in the context, part of the sodium is being, using energy driven process, part of the sodium is being reabsorbed. So, here it is getting reabsorbed. So, then again sodium is moving through out here. And if you look at the osmolarity wall value of the sodium, you will see, at this zone this is 290.

So, the value went down further. So, this is hundred percent which has moved out here, then it is 290. And then out here, sodium is moving all the way, all the way through the loop of henle, and out here again at this zone. Second level of sodium absorption is taking place, and this is again energy deviant process. So, this is an energy deviant process, again sodium is getting out. And again sodium is moving all along this vestibule, and out here, this part of the circuit is very important. So, I will highlight it with another color; just to tell you. This is the zone which is under the control of the aldosterone. This is the zone. So, it is purely under the aldosterone control. And the third level of sodium absorption takes place, at this point out here. Out here the third level of energy dependent sodium, absorption is taking place.

The last level where sodium is being, again retain by the system, and osmolarity values of sodium keeps on changing from 290. It becomes around 600 here. The maximum is here 1200, and then out here it becomes 220 and likewise. It keeps on changing, and at this zone, this zone is called. If you, this is the zone where, this is the zone, thus the shading zone what I am doing with the shade. Now this is called, this part is called isotonic resorption. So, this is how the sodium. So, if you look at it the most simplest of all, the sodium is kind of reabsorbed in a very interesting manner, as it is moving through, all the time, it is the two driving forces which are playing critical role; the hydrostatic force, or hydro static pressure, and the osmotic pressure. These are the two key players which are regulating this whole process very tightly.

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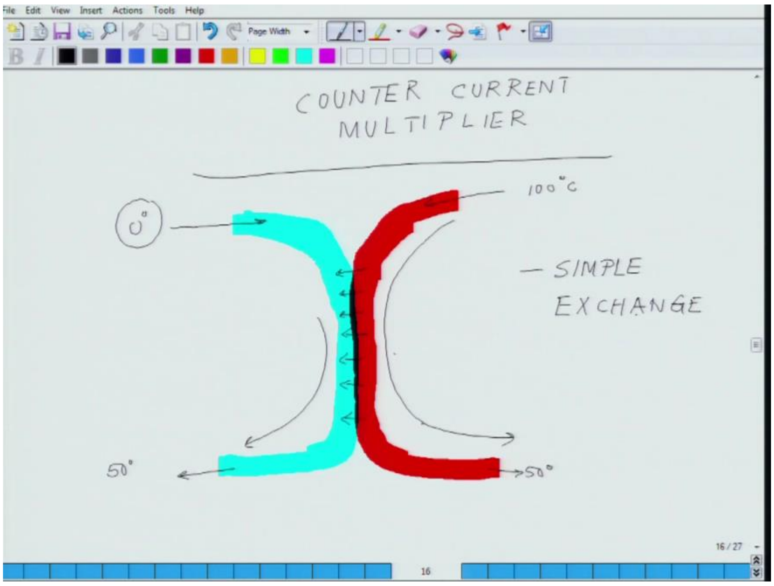

From here we will move on to something called counter current multiplier, because if you realize, these tubes are in close approximately. So, if I am drawing this thing with a lot of space, but in real life they are fairly close, this tubes look of hanley moving. So, what is counter current applier. So, counter current applier is; say for example, you have two tubes. Two tubes like that. Let me draw it to make more sense. So, let us move on to counter current multiplier. So, what essentially is, counter current multiplier. So, let us think of two tubes here. So, let us pick up the color set, or something medium. So, one tube is like this, there is another tube which is like this. They are in touch, but they are not continues with each other. Another word, and out here like this.

Now think of a situation. So, from here a fluid is moving or water is moving at zero degree centigrade, and from here water is moving at hundred degree centigrade. By the time, so automatically the one which is moving with the hundred degree centigrade will dissipate it heats to this side. If there is a possibility of conduction, if they are not very well insulated. So, essentially what will happen; the water which will come out of it, is 50 degree here, 50 degree here. In other word what has happen, the water which is moved at zero degree, has gained heat out here. And the water which has moved at hundred degree has decapitated heat out here, and reduce its temperature. Now think of a reverse situation, so this is a simple exchange. This is a very simple exchange of fluid. There are two tubes which are moving parallel.

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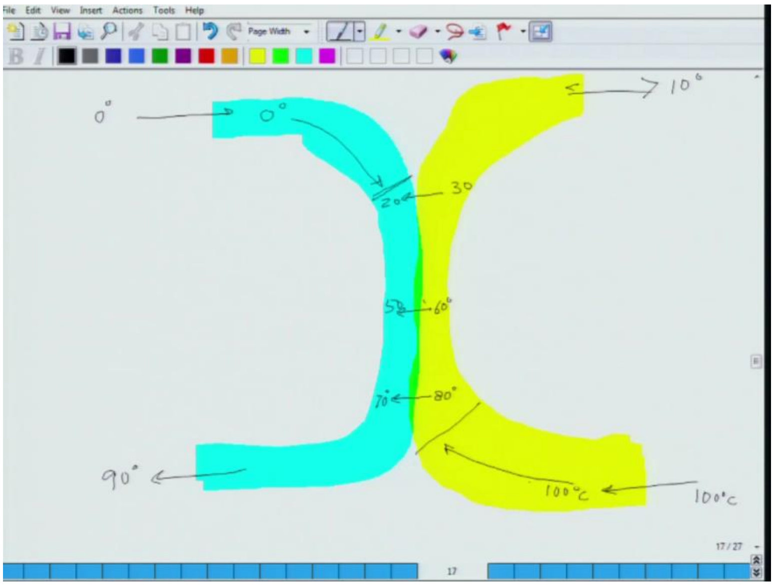

Now think of a reverse situation. So, let us talk about the reverse situation now. reverse is one second take out the this color. So, here is one tube which is moving through, get the tube is thicker, and there s another tube on the side which is in the yellow like this. Now we are reversing the case, of the direction of fluid. What we are doing essentially is, from this site water is moving at zero degree, and from this site water is moving at, rather sorry. From the reverse site water is moving at hundred degrees. Now what will happen. This is move at hundred degree centigrade and. So, what essentially happens is that. So, while water is a entering it is at hundred degree centigrade, and here water is moving, it is a zero centigrade. From the point it is started touching each other, up to this fine, and up to this it is fine along moving this. From here on situation will be something like this. This will be at 80, this will be at 70.

This will be at say 60, this will be at 50, this will be at 30, this will be at 20. End of it, this will come out as 10 degree, and this will come out as 90 degree. So, this is the phenomenon where, the fluid is flowing in two reverse directions, with different parameters; makes change the energy in a different way, and that is what is called a counter current mechanism. And this counter current mechanism, is fairly common in biology, and one of the classic case of counter current mechanism which is being followed, in the kidney, is in the loop of henle. And now we will show how basically this counter current multiplier. Actually it is called counter current multiplier helps in concentrating, sodium and other ions, in the re-absorption, and absorption processes. So, what we will do, we will consider these two tubes now, and we will see. So, this is a basically a loop of henle like this, and we will observe how, with respect to the intestinal fluid, because here you have the intestinal tissue, and here you have the kidney the loop of henle which is moving.

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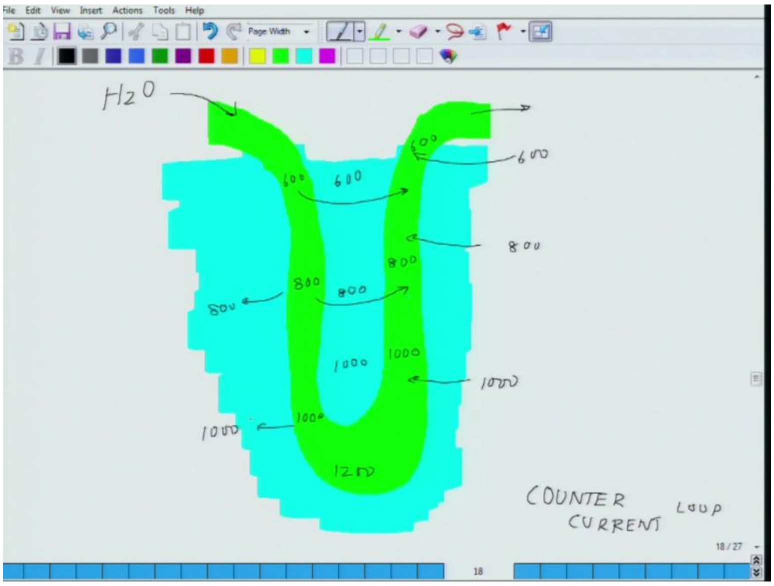

So, if there are two arms of the loop of henley. So, something like let me draw it, the situations like this. So, here you have the two arms, which are moving like this, very close proximity, and you have the intestinal fluid in between. So, this whole part is intestinal fluid, which has a different kind of osmolarity values. Now what will happen? I redraw this part, coming back to the. Now, you have here water moving, so this is the counter current loop of water, and the values which are being shown are the osmolarity values. So, out here 600 osmolarity 600 comes 800, and here you have 1000 1200 here 1000 800 600, and what is essentially happening is that, this is all water molecules here. So, outside it is 600 and from this it is 600, this side also it is 600. Then here you have 800, and you have 1000, and same way from the surrounding 1000 800. So, this is the counter current loop which is taking place. Here we will try to balance each other either side. So, on both sides it is balancing.

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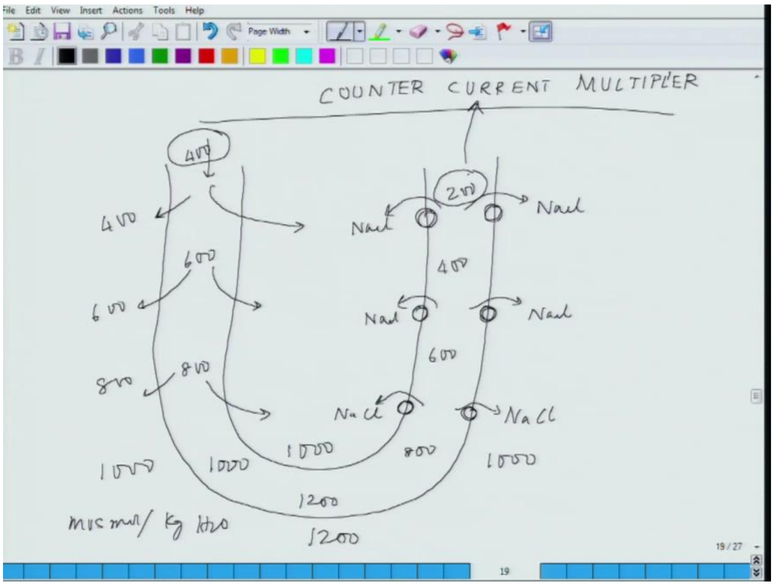

So, now if you see how the counter current multiplier works. Counter current multiplier works like this. As of now we have not introduced any the counter current mechanism. I never introduced any active transport of anything. So, say for example, it is entering at 400 osmolarity value, so water. So, here what is happening, it becomes 600. It is getting more concentrated then it becomes 800, it is getting even more concentrated, then it becomes 1000 osmolarity value. The bottom it becomes 1200, then it again it becomes 800, then it becomes 600, then it becomes 400, and it becomes 200 and likewise. So, what essentially happens at this point. So, these are the zones, if you remember I was telling you that there are energy dependent mechanisms, which are governing several things out here. So, coming to those energy driven mechanisms. So, what is happening here is N a c l is being thrown out, by energy driven process.

So, when N a c l is being thrown out. So, what essentially happen in that process is. So, you have 1000 here, and in between your 1000 and 1000 on this side, because there is nothing is being thrown out on this side; 800 600 400. So, let me just finish this drawing, so that. So, it started with 400, and then it landed up with 200 it is reducing. So, what is happening here, it is basically milli osmole per kilo gram of water, and here you have 1200. So, in the counter current multiplier what essentially is happening. Say for example, water is entering, with a different osmolarity, but if you would have been regular counter current mechanism which was, which I just showed you before this. This is a regular case, where there is no active transport taking place. So, you see 800 here, 800 here, 800 here, 800 here, but think of situation where in out here, where you have these transporters which are setting here; this one, this one, this one, this one.

So, they are continuously regulating, or modulating, manipulating the solute concentration. So, if you look at it out here, it started with 400, and it ended with 200. So, there is basically a fall in the osmolarity value, and sodium has been retained. Similarly, if you look at it, in this way this zone it is all the same, because there are no transporters. As soon as this transporter comes into play, the things it starts changing. So, this is where the counter current multiplier is, one of the mechanisms by which, kidney ensures that we retain as much fluid as possible. So, from here what I will do, I will move on to the aldosterone; the role of aldosterone what it is doing in the kidney, in concentrating the urine, and then we will talk about the rennin-angiotensin system and close in that. So, coming back to the role of aldosterone.

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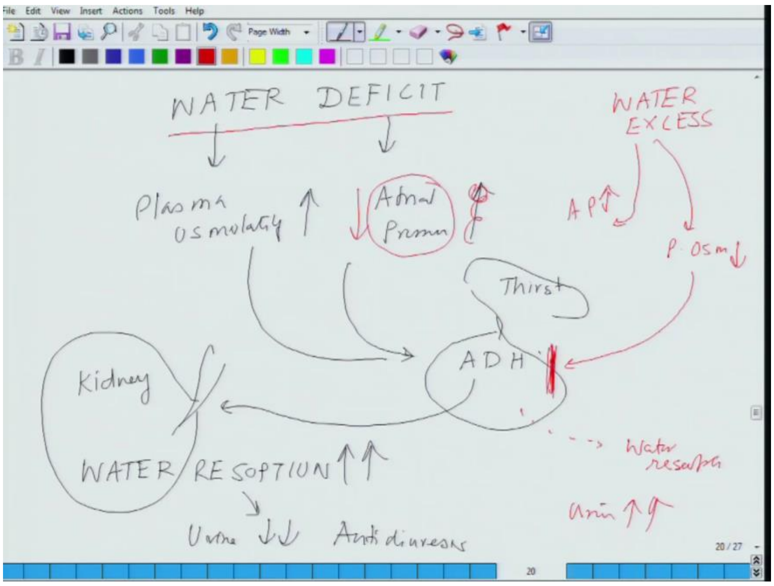

So, say for example, you have a situation when there is water deficit, even in the desert or some kind of a situation; water deficit situation. So, plasma osmolarity will be going up, because your water is shortage, and your arterial pressure, is also go up. Under these situations what will happen, your anti diuretic hormone A D H will be secreted, and that will activate the thirst area. And this A D H which is secreted, will tell the kidney. So, here in the kidney, mediator secreted up in the pituitary. It will tell kidney for water reabsorption. This will go up, maximum water re-absorption and urine goes down, so anti diereses. So, this is how from the brain this is being controlled. And now think of another situation when there is a, I will pick up another water excess. So, under water excess what will happen, the same thing; arterial pressure A P that is going to go down. sorry arterial pressure. So, I made a mistake kindly correct it. So, initially what is happening is your arterial pressure here is going down, and arterial pressure here is going up, and your plasma osmolarity is basically going down. And that situation there would not be any further secretion of A D H, and there would not be any signal, so what will happen, water reabsorption will fall down, and your urine secretion will go up.

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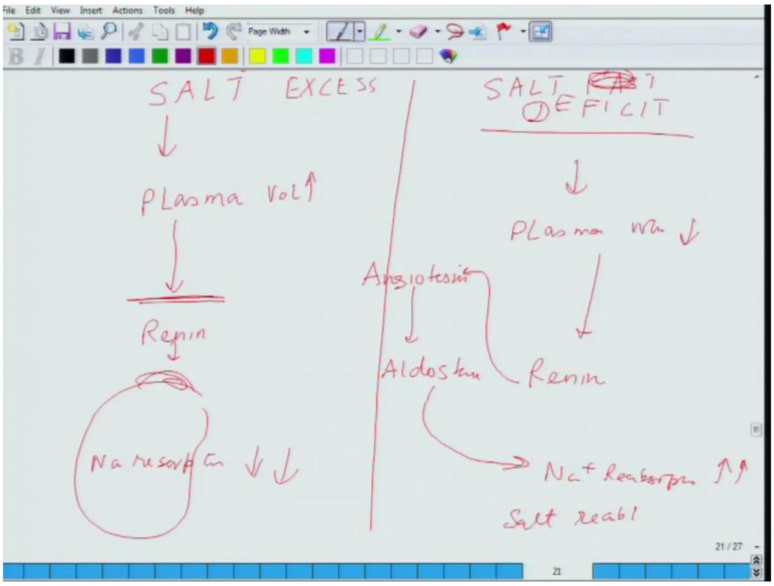

So, this is what is happening with aldosterone route, is a second thing what will happen in the salt excess and salt deficit. So, for example, if somebody is fasting, so there is a deficit, or somebody is eating too much salty food, so there is a salt excess. So, the salt excess is there. So, automatically your plasma volume will go up. It will go up, because it will retain more and more water. Once the plasma volume goes up, it inhibits the secretion of rennin, which is present on top of the kidney out here. So, the renin in secretion. So, sodium resoption goes down. So, you do not need, because you already have excess salt out there. So, you do not really need to activate anything, but think of a situation, where there is excess salt deposit, this is what happens in fasting, salt deficit. Under the salt deficit situation, your plasma volume is going to go down, and this will lead to secretion of renin. So, what renin will do essentially? Renin will activate something called angiotensin, and these angiotensin will secrete aldosterone.

Aldosterone will essentially, will just do the reverse thing; sodium resoption will be increased, and salt excretion will be reduced. Salt re- absorption will be reduced.

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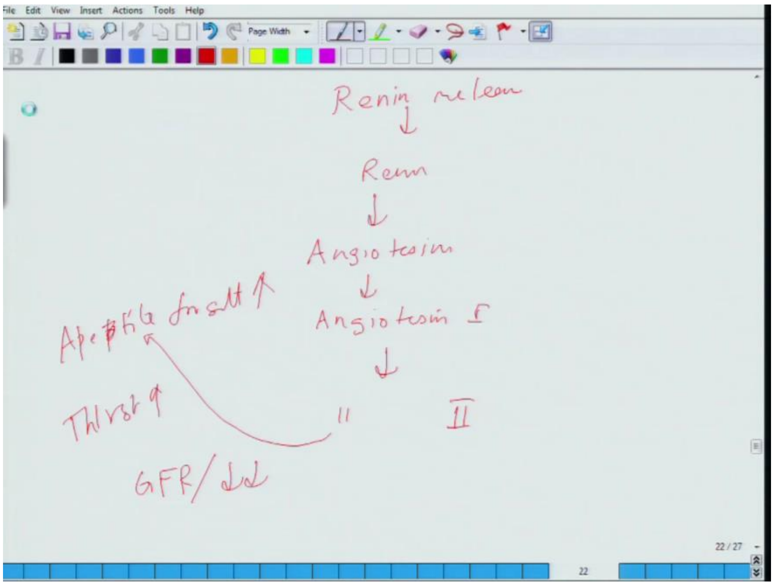

If you look at it in slightly more, what exactly happen when there is a renin release. When there is a renin release, renin essentially breaks down angiotensin. Now after breaking angiotensin something called angiotensin one. And angiotensin one, then transform into angiotensin two, it is this angiotensin two which has multiple function. This is basically appetite for salt is increased. Your thirst is increased. Your glonal filter rate is being reduced. Your aldosterone secretion further lead to salt and water retention, and ensuring that there is no further loss in this whole process .

So, what we essentially see here is that, while from the Bowman's capsule, the fluid moves to the nephron; that fluid has to be processed very tightly. You cannot afford to lose too much of sodium, too much of water. You have to retain as much as water as possible, as well as the electrolyte, all the other electrolytes, and you have to ensure that you lose urea and other unwanted materials. So, there is this counter current mechanism which is coming into play. There is this osmotic pressure. There is this hydrostatic pressure, and then we talked about. These are being controlled by the higher centers of the brain, that brings us to the end of this part of kidney and the regulation of fluid.

Thanks a lot.