Human Physiology
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Lecture – 02
Mechanisms of Homeostasis - Part : 1

So, what are we looking here? We are looking at the cells, what tissue? any tissue - this can be pancreas, liver, whatever, you can see the different cells. So, there is this plasma membrane, there is a nucleus and just outside the cell there is this fluid. We will call it as extracellular fluid. And then you can see the blood vessels there, and you can of course see this in a transverse section of a capillary. Can you appreciate that this is capillary? In the capillary can you see that blue body there, what does it represent do you think? This is RBC. Why this hesitation? it is RBC, correct? One very simple question. What would be the diameter of that RBC like? Very good, say that again.

About 7.5 micron, absolutely correct, okay that will be the diameter. So, what would be the diameter of the capillary, about the same? Okay, so that is a capillary and these are the endothelial cells. We are looking at the cell and whatever is in the cell, I will call it as intracellular fluid. Very simple.

So, all these cytoplasmic events are happening in the cell. Okay, that is all happening in the intracellular fluid. And then there is plasma membrane and outside of plasma membrane there is extracellular fluid. Some of the extracellular fluid can be right across, right around the cells or you can also have it in blood. It is also extracellular fluid. But to differentiate between the two, I will call this as the plasma. So, what you have is the plasma, in the capillaries, lined by endothelial cells. In between the endothelial cells there are spaces and through these spaces plasma, which is a watery fluid, can ooze out, that is under pressure, okay, it oozes out.

Well, it allows the plasma to go out, small ions to go out, molecules to go out, but large protein molecules cannot go out, okay. So, large protein molecules are always confined to the lumen of the capillary. So, here we have the interstitial fluid, and we will call both as extracellular - we will call this interstitial fluid, we will call this plasma. So, actually in front of us there are three fluids, are you with me? Three fluids, where are they? Intracellular, okay, extracellular and plasma, okay. And of the two, the extracellular fluid here and the plasma, confined within the endothelial cells. What am I drawing? I am drawing a transverse section of a capillary, endothelial cell, another endothelial cell and a gap between the two, are you with me? And because there is a lot of space, there is exchange of fluids in and out. Therefore, the composition of the two is quite similar, okay.

Now, what makes the things really, really, really interesting is - we are going to compare what is in the cell and what is out of the cell. So, here I have a cell, the plasma membrane and this is a nucleus and I am going to compare the sodium ion concentration, how much is outside? 140 what? Got it and how much is inside? 10. So, the difference is how many folds? 14.2 folds, 14.2 folds, there is a huge gradient, huge gradient, appreciate, spend two minutes on just looking at the amount of sodium, any cell, anywhere in your body, any mammal, any reptile, anywhere the sodium in is low and outside - extremely high, 14 times higher than inside, did you absorb the point? Now, look at this, look at the story with the potassium, it is exactly opposite and the difference is much more glaring. Potassium outside is how much? 4 and inside is how much? 140, that is about 30-40 times more, inside is very higher as compared to outside. You will find that there is a huge amount of differences. Okay.

You can see the glucose here is 90 mg that we have seen within limits, and then in the cell, if this is a neuron, what will the glucose concentration be? 0 to 20, okay. So, the brain needs at least 20, brain needs at least 20, okay. Therefore, it is very necessary that you keep the concentration of glucose 90. Are you with me? If it is not 90 inside, you will not be able to maintain it at 20 and if it goes below 20, then you will be in bad shape. Okay, so to make sure that the end user, what is end user? It is a mitochondria in the cell.

Hello, mitochondria in the cell, that is the end user, okay. To make sure that the end user always has a steady supply of glucose, you have to make sure that there is enough glucose in the cell, maybe around 20, you have to make sure that outside the cell it is always about 90. Okay and that should be good everywhere in the blood. So, again, the basic point I want to make is that whenever we are talking of any function in the cell, never ever forget the differences in the ion concentration inside and outside. Tomorrow, if you are a student of neurobiology, if you want to learn how the action potential, how the resting potential happens, how the action potential happens, how the release of synaptic vesicles and all those physiological changes occur, you better remember the differences in the ion concentration and in the concentration of all other entities across. Now, although this is the same, this slide is essentially same as the earlier slide, but here I want to look at the parameter that is given at the bottom - osmolarity.

This one that has more salt, has what? So, I have a glass of water in which I will put one spoon and in another two spoons and what is the difference between the physical properties of two solutions? Osmolarity of glass B is higher than that of A. But now I am going to compare the osmolality between two fluids, one is outside the cell and one is inside the cell and what do I find here? What do I find there? Same. So, this is in sharp contrast to what we have. Are you with me? It is same. It is what? Why is it same? Because if you want to maintain the cell size, it is very necessary that osmolarity should be same. Otherwise water will simply flow from lower to higher osmolarity, and therefore osmolarity is essentially same in contrast to the other parameters.

So, here we have, a very familiar diagram. I am sure you can identify the pair of lungs and the kidneys and the alimentary canal. Whereas we have a system which are and are continuously changing and our environment is continuously changing. There are continuous perturbations and you need to keep on correcting those perturbations. Here we have here a classic example. There are lungs, lungs at the top. So, what do you do? You send the deoxygenated blood to the lungs, sending the deoxygenated blood to the lungs and you get oxygen there, you get rid of carbon dioxide and then the oxygenated blood goes to cells. Let us forget about all cells, let us talk of alveoli. So, the alveoli also have their intracellular fluid, they also have the extracellular fluid and through their extracellular fluid, the lung cells depend on glucose.

They depend on certain sodium, potassium, all their number of parameters in extracellular fluid. They depend on all those parameters. So, what lung cells are doing is on one hand they are getting from the blood everything else and in return they are giving back to the oxygen to blood oxygen. So they are, they are taking it and they are giving it. So, if I take the analogy forwards, just as the blood flows through alimentary canal, the cells whether the epithelial cells, smooth muscle cells, whether nerve, whatever are the organs that are part of your alimentary canal - they also need constancy in their extracellular fluid. They are doing a very wonderful work of continuously supplying the blood with glucose.

You see, you have digested food, carbohydrates as glucose and then not only glucose, amino acids and all the nutrients that will follow. So, the aim of this slide is to show that each and every organ of body, depends on the blood for its own needs at one hand and at the same time it keeps on contributing to the homeostasis, of whatever parameter it can. If it is kidney, it does a very important role of making sure that the urea concentration of the blood does not rise beyond a particular limit. Are you with me? Hello. One very important function, it does not allow the urea concentration, it does not allow the creatinine concentration to rise above limit and it makes sure that the sodium ion concentration and potassium ion concentration is always kept within limits.

It also makes sure that if you have suddenly taken or ingested one litre of water, one litre of water, then suddenly you will find that within another half an hour your kidney produces a huge amount of dilute urine. Why? Because you have taken a lot of water, the water has diluted your blood. As a result of that, your blood osmolality, which was about how much was shown in the previous slide? 281. As a result, because you ingested one litre of water, it has dropped from 281 to say 278.

Hello. Okay. And then, you have a sensor. What do you have? A sensor. Sensor for what? Osmolarity. What does it do? There is a sensor for osmolarity.

It detects. What does it detect? That the osmolarity of blood, osmolality of the blood, which should ideally be 281, is perturbed. It is perturbed. Therefore, it will immediately instruct the kidneys not to reabsorb lot of water. As a result of that, the kidney will generate a large of volume of dilute urine, which we call as the process of diuresis.

Hello. And then the kidney will get rid of the water, so that the osmolality which dropped from 281 to 278 will again go back to 281. So all the organs, whereas they depend on the rest of the systems, they also make their own contributions to ensure constancy. So here we have, again we will go back to our favourite example of blood sugar level. So here we have, to begin with, to begin with, how much is the blood sugar level you are having in your system? Is there 90 mg per 100 ml of glucose, okay, per how much? 100 ml. Okay.

And then you have had, you have had a heavy breakfast, carbohydrate-rich breakfast. As a result of that, the blood sugar level might have gone from 90, 95, 100, 110, 120, okay. And as a result of that, you can see it is stimulating the pancreas, and it is stimulating the pancreas because we have a very interesting group of cells which we call islets of Langerhans. And in the islets of langerans we have another specialized group of cells which we call as beta cells, which is a source for? Say that again? Insulin. So insulin is coming from where? The beta cells. Beta cells are where? In the islets of Langerhans.

Okay, now you all know very well that beta cells of islets of Langerhans are a source for insulin. Now here you can see, here is the most interesting fact. These cells, what do I mean by these cells? Beta cells in the islets of Langerhans. They are also sensors for glucose in the blood. They are sensors for what? They have sensors for the glucose in the blood.

And they do not really get activated as long as the blood sugar level is 80. They do not care, 90, they do not care, 110, 110, then they start caring. Means what? They are now sensing glucose. They are getting activated. So the beta cells of islets of Langerhans, they serve as sensors and once it goes to 110 or 120, they really get activated and they respond by releasing insulin. So do you have a receptor, do you have a receptor for glucose? Very critical question. Where is the receptor located? In the beta cell. Beta cell. I always say that physiology is a science of beauty because you appreciate that the cell which is responsible for synthesizing and secreting insulin is the very cell where the nature has provided receptor. And that receptor is activated, not when it is 80, no, no, no, no, no, no, no, no, no, no, no, no, no, 100, but when it is 110, then the cell gets activated and starts releasing insulin because now the function of beta cells is to release insulin so that it does not allow your blood sugar level to rise beyond 120 or so.

No, no, you cannot do that. Okay, got the point? So you have released insulin, so your insulin secreting cell has a glucose receptor. It has a mechanism by which it can sense the amount of glucose in the blood and as a result of that, insulin has come in the plasma and insulin has gone everywhere in the body. You know something when you are fasting, the insulin level in the blood is almost negligible, almost zero, when you are fasting. What did I say? What did I say? Say that again. In fasting, insulin level is almost not there.

You take the blood, put it through analysis, you will hardly find any insulin. Okay, you start eating carbohydrate rich food. And as soon as the blood level goes 100 and there is a surge of insulin. Okay, there is surge of insulin. Okay, and what does the insulin do? Insulin does lots of things. One, it will act on the skeletal muscle cells, it will act on the liver cells, it will act on adipocytes, and on the fat storing cells.

Okay, and in all those cells, it will make the plasma membrane permeable to glucose so that the glucose can readily go from blood into, so insulin is actually permitting the glucose to pass from the extracellular medium into the intracellular medium where it will be metabolized, it will go to mitochondria, whatever it will be metabolized. This will all help to lower the blood sugar. Secondly, it will also go to liver. So what has happened? You are sitting in a liver cell, okay, and it is about 15-20 minutes after you have had your lunch. As a result of that, insulin has come into play. Insulin will act on the plasma membrane of the liver cells. It will make the glucose permeable, now glucose can enter into the cell.

As soon as the glucose enters, it triggers a lot of things including the stimulation of all those enzymes which will convert glucose into glycogen. So, and we know that part, okay. So, now the liver cell will do to a very large extent, adipocytes will do that. It will convert it glucose into fats and muscle cell will also store some amount of glycogen. So you store it as, so as long as you have it, you store it. Your insulin molecule has half-life of about, we all know what half-life is, okay.

So whatever is the amount of insulin that is released, half of that will be reduced to half because of metabolism, in about 6 minutes. Don't forget, what did I say just now? Half-life of what? Insulin is about how much? Good. So, as a result of that the insulin, the glucose level has fallen. Then if you do not have any food for about say 6 hours, 7 hours, 8 hours and as a result of that your blood glucose level has fallen to 80, 78, 77, okay. Now this time, it is the turn of the alpha cell, which you will identify as the glucagon secreting cell, to get excited. So do glucagon cells have a receptor for glucose? They do, they do, but they are sensitive to the condition in which the blood glucose level has fallen, exactly opposite to that in the case of insulin.

Another beauty point in physiology. How does it work? So what is the mechanism? It is very simple actually. How do you make sure that the blood glucose level remains between 80 to 100? Okay, if it goes down, then the glucose itself, stimulates the alpha cells, glucagon comes in, glucagon comes with the blood, it goes to the liver cell, it acts on the liver cell and that glycogen there, okay, that glycogen was there, it breaks down, take it in opposite direction, convert it into glucose, let it flow into the blood, make sure, that the blood glucose level remains above 80. Okay, so here we have in the pancreas - two hormones, the two types of cells secreting two hormones and the aim of the two hormones is to not to fight with one another. But they just make sure, the glucagon would not allow the blood glucose level to go lower than 80 and insulin would not allow the blood glucose level to rise say above 110. Okay. And therefore we make sure that all the cell, all the cells in the body at any given moment have a steady supply of glucose, it is such an important source of energy, number one, number one candidate, the number one customer in that regard is the brain of course. So you have the concept of a physical and chemical properties of body fluids, intracellular, you can say factors like temperature, blood pressure almost all need to be regulated.

Let us take another example from end to end with reference to how the homeostasis works. This rise in temperature, as I said our body temperature is about what 97.6 Fahrenheit and so as long as our brain continuously knows, knows about what, knows about the temperature of your body. And the temperature of body depends on the temperature of the environment. So you know about the temperature in the environment, how do you know it? There are heat receptors, very simple, heat receptors in the skin, very important, very interesting heat receptor. In other words, how we feel the warmth. We have the heat receptors, the nature has beautifully given us the, just below the skin. Okay.

We have receptor, they are nerve terminals, okay, they are nerve terminals. How do they function, so there are proteins which are sensitive to temperature and whenever the temperature goes from 97 to say 100, 102, those proteins change their shape and then they activate the neurons and once they get activated they can take the action potential to the brain. Then the brain knows, knows what, that the environment is getting warm. Okay. Then there are thermoreceptors. Okay, they are in certain places in the brain, they are in certain places in our major veins, they are in the spinal cord, there are *n* number of receptors in several places in our body. Receptors, receptors for what? Heat, we wear on the skin and you have taken the message. Okay. So let us presume that it is too warm, it is too warm and as a result of that your physiology responds, responds how? By increasing the diameter of the capillaries of the skin and you sweat, okay, you sweat and as a result of evaporation your body temperature comes back. Okay. So here we have a sensor, which we have, which we talked about just now, there is a sensor, okay and then there is a central processor. Where is the central processor? It is somewhere in the brain.

What does it do? It receives the information. What information that it is getting too warm, okay and then what does the brain do? Brain sends information back to what I call as the effector organ. In this particular case, the effector organ happens to be the sweat glands and under the instructions from the brain, the sweat glands are activated and they will release the sweat which will come on the skin, the swear will evaporate. So what do we have here? Sensor, are you with me? Central processor, are you okay? And then the effector organ, are you okay? So these are the three very important basic components of the way we try to maintain our homeostasis. There has to be a receptor, there has to be a sensor, we have to know, our physiology has to know, okay and then inform the central processor that something is going wrong. If it is not going wrong, keep on informing the processor that everything is okay.

If it is getting cold, okay. If it is getting cold, then the brain knows that it is getting cold. It will send the information to the muscles and the muscles will shiver, and you generate heat. So your homeostasis is again restored. So again in that case, in that case you have receptors for cold and mind you, those receptors for cold for different than the receptors for heat, okay. So if you take one square mm area of your skin, in that area you may have say 5000 receptors, okay and for heat and then number of receptors for cold, you have them there, but they are separate, okay.

Alright, so you have receptor, feeds information to the central processor and the central processor takes the information to the effector. If it is cold, effector organs like skeletal muscles can generate the shivering response. Are you good so far? Right. But in the case of temperature, how does the brain know that my optimum is 97.6 F? Are you with me? Because unless there is some standard, how would you know the perturbation? Are you getting the problem? Are you with me?

If it is not that much, then there is perturbation. So how does the brain know that as long as you are 97.6 F, you are good. If it goes down or goes up, you are not good. So how does the brain know? Here comes a very interesting point which you call as the set point.

What do you call it as? Set point. So I am sure you have heard of, you know, these modern cars have what they call as the cruise control. Hello. Okay, so in the cruise control, I set my car at say 50 kilometers per hour, I am on a long drive and that system, that electronic system keeps on making sure that the speed is 50. Okay, if there is a climb or there is anything and the speed goes down, it will instruct, it will note, it will note and give the instruction so that there will be acceleration and the car again will again start driving at 50 kilometers, okay. That I can call it as a set point as far as my car is concerned.

Are you okay so far? How does it happen in the case of brain? Is there a set point? Is there a part of my brain that is always at 97.6 degrees, which my brain will consider as a standard, consider as a standard and will say that look, as long as I am matching with that, I am fine. If it goes down, it is not okay. If I go up, it is not okay. No, there is no such thing. No such thing. Then how does the brain know what is standard? Do you follow the question? I will give the answer. Hello. you are okay with the question? Okay. The answer to that question is we have circuits in our brain, okay.

We still know very little about it. Okay, my disclaimer at the very beginning, we know very little about it. But we know there are circuits in the brain where there is a group of neurons A, there is a group of neuron B, okay, and they keep on talking to one another and the frequency at which they keep on talking to one another, the number of action potentials with which they talk to one another is at a particular frequency as long as the temperature of the brain is 97.6 F.

If it becomes 97.7 or 97.8, then the frequency changes. Once the frequency changes, then the rest of the brain knows that the things are getting warmer. Are you with me? So in this particular case, what is the set point? It is a circuit. That circuit works optimally, okay, with n number of action potentials with which they talk to one another at a particular temperature and that is the set point. And any deviation in the, in the deviation of the temperature and the circuit will start firing at a different rate.