Human Physiology
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Lecture – 10
Cardiac system: From stimuli to rhythmic muscle contraction - Part 1

We are trying to understand how the heart works basically. We know the heart has to work because it has the pump the blood everywhere in the body and it is a very basic fundamental function necessary for life and we saw that the heart cell plasma membrane is polarized. What do you mean polarized is that inside is negative. If you introduce an electrode inside you find that the inside voltage is about how much? Minus and as compared to outside which is how much? 0. Which is how much? 0. Outside is what? 0. If by any chance for any reason or supposing I inject ions directly into the cell, just do it somehow.

Then what was that 85 will become 84, 83, 82, am I right? 82, 80, 79, it is going towards 0. I will call it as depolarization. What will I just call it as? It is getting depolarized. On the contrary, if I further inject negative current in it, then it will go from 85, 86, 87, 80, 90, 95.

I will call it as hyperpolarized. Just introducing ourselves to the terms. Also remember that whenever cell is getting depolarized, it is going in the direction of being activated, being excited. Depolarization will lead to basic terms of neurobiology and this muscle physiology, basic. So whenever the potential difference inside goes from 85 to 80 to 75 to 70, it is getting depolarizing and a moment of threshold will happen when suddenly the lot of sodium ion cells will open and the cell will excited, get excited and the cell will respond.

If it is a nerve cell, it will carry action potential from one end to another end. If it is a muscle cell, it is going to contract. But if opposite happens, means what? Inside is minus 85, 86, 87 by the introduction of negative ions inside, then the cell is hyperpolarized which means the cell is inhibited. It is difficult to stimulate the cell. These basic facts must remain in there, there.

Got it? Hello? Everybody? Okay. Maybe you have done it, but let us. Okay. Now the second point is, let us go back to this figure once again. So in the plasma membrane of what? Of muscle cells.

Okay. One thing is for sure. What is it that everywhere? Proteins, proteins, proteins. And this what I am drawing your attention to these proteins. What is their peculiarity?

They are fast sodium ion channels. Where are they? In the plasma membrane.

Of what? Of this cardiac muscle cell. Are you okay? So protein system. Okay. And if for any reason if it gets excited, why it should get excited, I will tell you a little later when I talk about the conduction system.

Okay. It will, the channel will open, it will allow the sodium ions to go through. What ions to go through? It will open temporarily is very fast, very fast. Therefore, we call them as fast sodium ion channels. So as a result of the large number of sodium ions going in, originally it was minus 85. Now large number of sodium ions are going in.

Okay. Okay. As a result of that minus 85, minus 84, minus 80, minus 75, minus 70, minus 65, it is going towards 0. It is depolarized, the cell is going towards getting activated. Okay. Are you with me so far? Now as that happens, okay, and it happens so quickly that whatever was around 85, okay, it rapidly shoots.

Okay. And it goes how far almost? You can see that? It goes to plus 20. Okay. When it goes to plus 20, okay, we will say that the polarity is reversed. Originally it was minus inside, now it is, just see it is minus, it is, it inside has become, inside how much is, previously how much was it? Now how much is it? Plus 20 inside, okay, it is happening so quickly. Are we okay so far? Now why is it happening? Why is this happening? It is shown in this graph.

Look at the yellow, yellow peak there, yellow spike there. What does it indicate? Well, the action potential has come, the membrane is stimulated, the sodium ion channels have opened and we are just evaluating the amount of calcium ions which are going in. Look, it goes up, huge number of, okay. And because of that, so actually this steep peak here is actually because of this. Got the point straight, why is it going? Why is it going from minus 85 inside, why is it going to plus 20? Because huge number of sodium ions are getting and how much, and if we try to quantify that, we will get this peak.

Okay. But it goes up and comes down quickly. Why does it come down quickly? Because the channels rapidly close, as a result of that no more sodium ions are going in and therefore the peak comes down. So why does it shoot up? Because of sodium ions. So far, okay. Immediately after that another interesting event happens, the DHPR channels which are also there, again we will go to the plasma membrane of the skeletal muscle cells, there is a system of proteins which I call as fast sodium ion channels, another system of proteins I will call as slow calcium ion channels, done. And these are slow, they act a little slow, okay, and they open and when they open the calcium ions will go in, we know why calcium ions will go in, we know very well because there the

calcium ion concentration is how many times more than that of inside? 1000.

Huge, okay, as a result of that calcium ions will go in, okay. And then the channels have been open for a while, as a result of that you will get this plateau. So, so this plateau, so actually this plateau which tells you what, what does this red line tell you here? The red line tells you when the DHPR channels open, calcium ions are going in, going in, plateau, plateau, almost for 0.3 seconds if you are recording from the ventricular cell, hello. And then after that the calcium ion channels suddenly close, potassium channels open, potassium ion channels will now go in opposite direction because they are far 35 to 40 times more inside, they will go outside, okay, along with them they will carry the positive charge, outside will become positive like the original state, okay.

And inside will again be restored to minus 85, so what have we done? We have undergone through a cycle of electrical changes. As a result of those electrical changes within that tiny period of about 0.3 seconds, there is a surge of calcium ions, those calcium ions are suddenly available to the actin myosin filaments. As a result of that the actin myosin filaments will slide on one another, it will contract, okay. And that contraction is represented in that reddish curve there.

Can you see that there are two curves there in the first one? The first one tells us what? The first one tells us the electrical events that are happening across the plasm membrane of the cardiac muscle cell. What does the second tell? As consequence of that the muscle cell is actually contracting, contracting, actually we are interested in the contraction, we are interested in the contraction so that the heart can undergo through the systole, you want to generate mechanical energy so that you can pump the blood. That is being represented by the second curve. And that tells us what is the time difference between the sodium going in, okay, then the abundance of calcium becoming available and the actin myosin filaments sliding and generating mechanical contractive force in the heart, that is being represented in the red curve there. Am I okay so far? Hello? We are good? Now, let us again see this figure for some time.

This is a very interesting figure we did yesterday, let us do it once again. So we know that as a result of, so that plasma membrane there, they are all there, what, what is that? The fast sodium ion channels are there, DHPR is there, they are all there. So protein, and fast sodium ion channels next to that maybe there is a slow calcium ion cell, they are all getting activated and here is the representation where the author has shown one DHPR, there are thousands of them, okay. And as a result of opening of DHPR, the calcium ion, calcium ions are going from where to where? From the extra cellular compartment into the intracellular cellular compartment. So suddenly there will be excess of calcium ions in this part and those calcium ions will readily talk to another protein system which is

sitting on the sarcoplasmic reticulum and that system I call as what? Say that again loudly.

Ryanodine receptor 2. Rhinodyne receptor 2. So what is the, how does it differ from the ryanodine receptor that I, what is the type of ryanodine receptor that I find in the, in this calcium muscle? Rhinodyne 2 is in Cardiac muscle. I am not going to let you forget that, right? Okay.

And we know, we have already done what ryanodine receptor does. Because of the influx of calcium is stimulating the RYR2, okay, RYR2 is responding how? By opening and allowing another flush of calcium ions come out of sarcoplasmic reticulum. This flushing out of the sudden rise in the calcium is also called, we saw it yesterday in a very amazing video yesterday and what do you call the phenomenon as? Calcium spark. Calcium spark. So what is actually, why do I see the light there? I see the light actually light there if I am viewing an isolated cell in culture, a cardiomyocyte in culture, I see the flash.

Why do I see it? I see it because within the cell I have introduced a special kind of dye, a chemical, I have introduced a chemical. What is the peculiarity of that chemical? The peculiarity of that chemical is the moment that chemical combines with calcium, what? It gives light. It gives light. I will call the dye which is I am introducing in that cell as calcium sensitive dye.

Very simple. Okay. Calcium sensitive dye is very important because it is a tool to find out whether my cell whatever it is, a nerve cell, whether it is a nerve cell or an endocrine cell or a secretory cell, if I want to find out if the cell is getting activated, a very important state in biology. I have a tool. What is my tool? If only I can introduce the calcium sensitive dye, the chances are that if your cell is getting activated, calcium is going up. That is the thumb rule that you can do. You can ask your question, you can ask a question any time you study any activity in the neuron or cell or any other cell, you ask yourself a question, okay, something is happening here.

Is calcium going up? Ask yourself a question and look around for the biochemistry of that cell and ask yourself a question is going up and if it is going up, if calcium is going up, most probably it will, if it is going up, I will ask you a question. What is your tool to detect it? Calcium sensitive dye. And when the calcium sensitive dye combines suddenly with the amount of calcium that comes up, it is always transient, okay, it will emit fluorescence, okay, and that fluorescence and I can read on the fluorescence microscope, great. Now, at the end of the plateau, at the end of the plateau, I want again that the, then I want to remove calcium. I do not want the cell to contract forever, I want

to remove the calcium, okay.

What is my method for removing the calcium? I have done it by placing a large number of what? Calcium pumps. Calcium pumps, where are they, where are the calcium pumps there? They are placed there in sarcoplasmic reticulum. What is not shown in the diagram is that the calcium pump which is an ATP, ATP system, okay that ATP system can pump the calcium ion from the cytosol into the sarcoplasmic reticulum. There are several of them in the plasm and also which can pump the calcium from inside to the outside.

Why do you need ATP? Because you are pumping calcium from lower concentration to higher concentration, okay. You will need energy, so you need ATP, okay. So where do I have the pump? It is clearly shown here. What is not shown here is the pump is also located there.

What pump? Calcium pump. What does it do? Pick up calcium, okay. So that, so the calcium ion concentration in the cytosol is readily reduced and as a result of that it is not available for actin-myosin filaments. No sliding on one another and as a result of that my actin-myosin filaments have relaxed. Are you okay so far? Good. In addition to that there are a couple of interesting systems which have to be there in the plasma membrane, number one.

A lot of sodium has come in, we also talked about a lot of sodium has come in. First you know I need to get rid of that sodium as well, okay. How do I do that? I do that by having one more protein system in the plasma membrane and I will call it a sodium-potassium pump. We have done that, okay. And that system what does it do? It does one ATP, one ATP and it throws out, throws out against concentration gradient sodium is more outside, throw it outside.

How many ions of sodium? Three. And against how much of potassium? Two. So three, three ions of sodium are thrown out and two ions of potassium are brought in and the pump is working 24 by 7 and for every cycle you need one ATP. One ATP, okay, three potassium outside, two sodiums, I have made a mistake, what mistake did I make? Three sodiums to the outside and two potassiums to the other side, again another ATP and the pump will keep on working and the pumps are terribly efficient. You can't imagine how many time cycles it can do per second, huge number of cycles, okay. Then there is also in the plasma membrane, there is an antiport system.

That antiport system there, this is the antiport system. What that antiport system does - is that every time the sodium ions, actually I am, have you ever done secondary active

system in say first year or second year anyway? Yes or no? Good, good, good, good, I am talking about that but let us talk about it too. Let us do it once again, okay, no problem. There is already too much sodium ions outside, okay, okay. Thus those sodium ions are being attracted in because of concentration difference 14 outside to 1 inside and number 1 inside is negative. So that carrier system, that antiport system there you see I am talking about this antiport, this antiport system, okay, the sodium goes in.

But it is antiport because every time 3 sodium ions go in, what did I say? What did I say? 3 sodium ions go in, the system works in such a way that one calcium ion goes out. So what am I talking about? I am talking about a system of how to take the calcium ions away from the cytosol, okay. But as a result of that you are also paying a price and your price is that sodium ions are coming in. So how do I get rid of that? Well, I have pumps.

What pumps? Sodium potassium pump, okay. So, so we are having different protein systems to make sure that the sodium ion concentration inside is kept low, calcium is kept low. Yeah. Along with this antiport system there are also calcium ions, will they be there when present calcium ions are there? They are there, they are there, both the systems are there, both the systems are there. What was the point. I will not talk about this, can somebody tell me what is the point we wanted to make in this slide? Drugs, what drug? I gave you some names. calcium antagonist, calcium antagonist, they are family of drugs, calcium antagonist, they are useful for what, treating what sort of, what sort of - anti-hypertension, you want to reduce pressure. Okay.

And looking at the slide, look at the slide and tell me can you name one of the drugs which is available, which is available in the market? Nefedipine. Nefedipine, great, great, very good, very good. Okay, okay. You see when the heart pumps, particularly when the ventricles pump, okay, okay, okay, if I am the model here, okay, this is my right side, here, here, this is the midline, hello, okay, this is the right side, okay.

So somewhere here is the right auricle, okay. Somewhere here is what? Right auricle. Right auricle. What right auricle? What does it, what does the right auricle do? It continuously, it continuously receives, it keeps on receiving the deoxygenated blood from all over the body. What do you - know all over the body? From the head etc by the superior vena cava and from the lower part of the body by the inferior vena cava and the blood keeps on pouring into the, into the right auricle, okay. And then I have another system on the left side of my heart, here on the left side, okay, and that is the left auricle and that keeps on receiving the oxygenated blood from lung, very simple, very clear, okay.

And then when the two ventricles go in systole, systole, okay, the blood from the right

ventricle goes to the lung for oxygenation, hello, am I okay there? Yes or no? You go there, okay. And the blood from the left ventricle will go everywhere for the systemic circulation. So there is systemic circulation we have done, we have done this in the school, systemic circulation and pulmonary circulation, that is what I am talking about, okay. So there are two systems, the pulmonary system and the systemic system, they are in series or in parallel? Look like parallel, okay, they look like parallel, but if you look this diagram, it is actually in series, okay. So let us see, so the blood is coming from the, the deoxygenated blood comes from the rest of the body, okay, pours into the right auricle, goes into the right ventricle and then goes to the lungs and the same blood comes back, okay, to the left, okay, it is in a series, okay, it is the same blood will come back and then from there it will go to the rest of the body, okay, supply oxygen, carbon, whatever and then take.

So in a way, if you are sitting on an RBC, if you are sitting in an RBC and if you follow that you are actually going in a series, okay, and heart actually can be considered as two pumps, two pumps, the nature has brought them together, developed as one pump, they are two independent pumps, okay. So the blood goes to the rest of the body, okay, then it has lost its momentum, okay, the blood has lost its energy, the blood has lost its pressure, why does the blood, so the, - I am talking about the left ventricle, left ventricle, the blood is here in this, in this systemic circulation, what is the, what is the pressure with which the blood is being pumped? 120 mmHg, 80 mmHg, 80 not less than that, okay, 120 mmHg, so your brain is continuously getting blood, okay, this rush of blood 120, 80, 120, 80, but by the time the blood enters into the capillary network of your body where the capillaries are in millions and in tiny, tiny, tiny, tiny, so tiny that the diameter of each capillary is about 6 or 7, 6 or 7 microns, RBC is 7.5 microns, capillary is 6 microns, are you getting the argument? So how does the RBC pass through the capillary? Hello, a very interesting question, what is the diameter of capillary I told you? 6 microns, 6 microns, okay, 6 microns, maybe on 5.5 and what is the diameter of RBC? Then how does the RBC pass through the capillary which, whose diameter is less than the diameter of RBC itself? Yeah, say that. Change in, change in shape, you saw that the, and the change in shape is, change in shape is, this is your RBC, look at the beauty of the nature, just appreciate, this is your RBC, okay, it goes and encounter, finally it will encounter a capillary, which capillary which is, which is less than the diameter of this RBC, did you get the beauty of the situation? What did the RBC do on itself? It folded on itself, it what? It folded on itself and would that folding be, now I can ask you a very interesting question, why the mammalian RBCs are disc like and not globule like? If it were globule like, would it be able to fold? No, so again you have to appreciate the beauty of the nature, which has come up with a bio-concave RBC which can fold on itself so that it can pass through the capillary but at the end, but the whole purpose is to make sure that the plasma membrane of the RBC rubs, rubs, rubs, rubs along the wall of the

capillary which is necessary for the release of oxygen.

Are you getting my argument? I will talk about more about this when we talk about what? When we talk about hemodynamics and how the gaseous exchange happens at the level of the capillary. But let us come back to this. So what the point I am trying to make is, by the time the blood has gone into the venous system, the blood pressure which was in this part, in this part it was 80, 120, 80, 120, 80, by the time it branches and branches it goes to 60, 40, 60, 40, by the time it goes here it falls to about, there is no pulse now, it is about 20, it is about 20 to 30, by the time it goes through the capillary work here, the pressure has fallen to 2, 3, 4 mm Hg. What are we doing? We are keeping track of the blood pressure changes as it goes from the heart to the different organs. It has been through the capillary and now it is in the what? It is in the veins now.

It is in what? venules and then venules will get together into larger and by the time the blood is pouring into the superior or inferior vena cava, the blood pressure has dropped to 1, 2, 2, 0 Hg, it is very low, it is very low and as the blood enters into the, into the what? Into what? Right auricle. Into right auricle. Actually, the blood is flowing in a steady, steady, steady stream. The auricles are in a diastole, so they are slightly expanding and the blood is pouring in and pouring where? Pouring where? Into the lumen of the right auricle, coming from where? Superior, inferior vena cava. And then at the time the, The valve.

The valve. What valve? Tricuspid. Say that again loudly. Tricuspid valves are open. Tricuspid valves are open. So we find that of the total amount of blood that is arriving in the right oracle almost 75 percent. How much? Simply straight way flows from the right auricle into the right ventricle, just goes, just goes.

Okay. Then after 75 percent has gone, then the right auricle, right auricle goes into systole, goes into what? Systole. And as a result of that, that balance 25 percent of the blood which was still in the right auricle now is also pushed so, so almost all the blood that entered into the right auricle has now moved on or has been pushed into where? Right ventricle.

Right ventricle. Where? In the right ventricle. Okay. Now for this to happen, for this to happen, the right ventricle has to be in, has to be in a relaxed mode. Are you with me? You cannot have, you cannot have the auricles and ventricles contracting the same time, does not make good, does not make good mechanical sense. So when the auricles are under systole, okay, the right ventricle has to, has to relax in diastole so that it can receive the blood.

So it is receiving the blood. And this is going to take time. You see, you are actually moving certain ml of 60, 70 ml of blood from here to there - you are going to move, it is going to take time. It is not possible in milliseconds. Okay. So therefore, that we have seen yesterday, you know, the heart pumps within a period of what? 0.

3, 0.3 seconds, the whole cycle is about 0.8 seconds. Okay. That is why, that is why the things are, because there is so much mechanical component involved, therefore the heart, the electrical activity is relatively very slow. Okay. Now, so the, so the, the right ventricle has relaxed fully.

Okay. And now it will go - and then it will receive a message. How it will receive a message? We will come to that in the next lecture. But then, then it suddenly goes into, into what? Systole. Means, it is going to contract.

It is going to, the pressure is going to increase. Okay. But the moment, the moment it is, it is going to contract, the first thing it does, the first thing it not to have the blood go back into the atria. You need to stop it. Therefore, you have the valve. What valve do you have there? Tricuspid valve.

So the tricuspid valves have to close. Okay. And because of that, when the tricuspid valve has closed, then the blood has only one passage to go and the, and the passage, and the passage, this is the only passage, this is the only passage. Okay. And, and what is this passage? This is the pulmonary artery, which will take the deoxygenated blood to the, to the lung for oxygenation. Are you okay so far? Good.

So the blood has again got certain amount of pressure. Who generated certain amount of pressure? Right ventricle. What is the aim? The aim is to make sure that the blood reaches the lungs. So we are talking about the pulmonary, pulmonary circuit.

Okay. So it has to develop certain pressure. How much pressure? Very important. I will come to that, I will come to that a little later. So it goes there, then it goes through the, the blood goes in my lungs, in my lungs I have alveoli, in my alveoli there are capillary, the blood flows through that capillary. Again the diameter of the capillary is very low. Again the RBC have to go like this and in the process they, they get rid of the carbon dioxide, take the oxygen. How that happens? We talk about it when we talk about respiration and the oxygenated blood now comes, it comes there, where does it come? Where does it come now? It is coming back by the, by the pulmonary vein, oxygenated blood is coming into what? This side, this side of my heart.

Okay. Now this blood also very much like that, it just flows, the blood just flows, flows

from the auricle, 75% of the blood just flows from the auricle into the ventricle. Okay. Ventricle goes on expanding till it can receive the amount of blood, whatever it can and then it goes into systole so that it can now pump the blood. Now it can pump the blood, okay, through this from here going into the ventral aorta.

Okay. Ventral aorta and with every beat, with every beat, what is the pressure it is going to develop? 120. 120, 120. It will go to 80, again to 120. Good. So when the blood is pouring either into the right auricle or into the left auricle here, the blood has been through the capillary network which means what has happened to the blood pressure? Very low, very low.

I told you how much? 1, 2, 3, mmHg, very low, very low, the blood that is appearing. So, what should be at any given moment, if you are sitting in the, if you are sitting in the atria, sitting in the atria, okay and you want to receive the blood, okay, if you are on the left side, okay, if you are, if you are, if you are on the left side, you want to receive it from the lungs, if you are on the right side, you have to receive it from the rest of the body. And the blood that is coming is already in 2 or 3 mmHg. So what should be the pressure around you? Still low, low, low. So the pressure, the pressure in the, in the auricles is always, always extremely low. If it is rises, how will the blood come in? And the blood that is coming is already in the very low pressure.

So you have to, you better make sure that the pressure is extremely low, okay. And then when the blood flows from, at the same time the blood will flow from both these chambers into the right and left ventricle respectively, okay, now it has to generate pressure and the pressure is, pressure is how much? 120 mmHg, okay, so that the blood will go into the aorta, okay. But before that, before that, the moment the ventricle goes into systole, the first thing you have to do is to make sure that the mitral valve or the bicuspid valves are closed. Otherwise, otherwise the blood will go, go back towards the lungs, you do not want that to happen, okay, alright, alright. And then you have to, okay, now this is, I just gave you an overview of the things.

Now I am going to show you some, some videos and I am going to ask you some questions. Okay. Thank you.