

Human Physiology
Prof. Nishikant Subedar
IISER-Pune

Lecture – 12

Cardiac system : From stimuli to rhythmic muscle contraction - Part 3

I am sure you recall this slide which we saw yesterday and where we are trying to, we were trying to figure out the changes undergone by the various parameters across a single cardiac cycle which runs to the length of about 0.8 seconds, okay. And we saw that, we monitored the pressure across the, what ventricle was it left or right that we were monitoring? Left. Very good, left hand. And we found that when it goes into systole, okay, it initially goes into the what you call as iso-volumic contraction and that when the pressure rises to about 80 mm Hg then the semilunar walls of the aorta open and the blood gushes out into the aorta and the pressure mounts to about 120 mm Hg and then because the ventricles are now ready to go in diastole which means they are relaxing, which means the pressure is falling. And as the pressure falls from 120 to 110 to 100 to 90 to 80 then suddenly the semilunar wall is closed so that the blood cannot flow back and in this way the cycle continues and we have seen the pressure changes in the left atria and we have also seen how the pressure changes, the changes undergone by the pressure in the where? In the aorta, in the aorta, that is what we get. This reflects the changes in the ECG electrocardiogram about now, yeah.

OK, systole refers to the contraction of the ventricles. Right now we are focused on that. So during systole – heart goes into contraction and the whole process - when the process ends, systole ends. Maximum contraction, highest contraction, highest contraction. I will come to that in the next lecture.

What you are referring to? Yeah, means you are referring to this blue line? Yeah, means you are referring which point - which point? This point with this? 0.4 seconds. 0.4 seconds, what about this? Yeah. Here again.

Okay. Your question, that is an interesting question. We are talking about this systolic event. Okay, okay.

The point is that this is the end of this systole. See the moment systole ends, there is no question of any further rise in pressure. Okay, so the peak of this systole is going to happen here. It is not going to happen here. Okay, at this point onwards, it is starting to fall because the left ventricle has started going into diastole.

Therefore, the blood pressure is falling. Okay, and then somewhere here, somewhere here, we are already in this diastole. Okay, but why does it stay in the diastole? Which one, which one? In the diagram, the entire portion is still 0.4 even after this.

Do not bother about it. Okay, no, do not bother about it. You see. It will not fall. Okay, that is the way of its nomenclature, that is all.

Okay, so let us see that, let us presume that you weigh 70 kg. Okay, and you have 72 beats per minute and you are in a resting position and it is in a relaxed state and the heart has, left ventricle has gone in diastole and now we are trying to measure the amount of blood. That is the maximum amount of blood. Okay, because the ventricles have relaxed to the maximum extent and you find that the volume of the blood - there is about 120 ml. Get this number straight.

What am I talking about? Left or right ventricle? Left. Left ventricle. In what condition? Relaxed. Relaxed, maximum relaxed. Okay, that is the end of diastole.

The relaxed state and the end of diastole. Okay, so at the end of the diastole and if you are 70 kg, then most likely your heart will, the left ventricle will have how much of blood - read at the top? 120 ml. 120 ml. Are you okay so far? So, now the heart has come to the end of the diastole, now it is ready to go in the systole. Are you okay so far? Now it has gone in systole.

So, it is now contracting, it is throwing the blood as we have seen in the previous slide. Okay, now when it has gone to the end of the systole, does it mean that there is no blood there? No, there is still blood. How much of blood is there? That blood is about 40 to 50 ml, let us take 50 ml. Are you with me? So, there is never condition when there is no blood in the ventricle. There is going to be a blood even at the end of the systole, how much blood is still there? 50 ml.

Let us take the second figure, 50 ml. So, if I subtract second from the first, okay, I can calculate how much of the blood is being thrown out and that will work out to about how much? 70 ml. So, 70 ml of the blood has been pumped out in a single cardiac cycle. Okay, now if you have a very average which means about 72 beats per minute, okay, now can somebody please tell me, 72 beats per minute, each beat is 70 ml, therefore over a period of 72 beats, how much blood has been pumped, can somebody tell me without using a calculator? 5, 5 liters, are you sure? Can you do an arithmetic right? 70 into 72 into 70, if not I will put you in fifth standard, okay, 5040. How much it is? 5040 ml, which means about how much? 5 liters, okay.

So, that I will call this as the cardiac output, what will I call it as? So, whenever we say that this, whatever, that is a standard word in cardiology. So, whenever you talk of cardiac output, what do you really mean? The amount of blood that is being pumped out of the left ventricle over a period of one minute. So whatever your heartbeats may be 60, 70, 80, 85, whatever, okay, and whatever is your, so I will call that as the end diastolic volume, make sense, okay, you have coming to the end of the diastole, okay, and at that stage how much blood is there? 50 ml is there, okay. so it was about 5 to 6 liters of blood is being pumped out of the heart under resting conditions. Are you okay so far? Hello? These are just numbers we are recording. Number 2, now supposing from resting condition you start to get up and then you start walking and as a result of that you find that the heart has started beating at a slightly faster rate from 72 it has gone to 76, from 76 it has gone to 80 and you suddenly feel that if you start running you feel that your heart is really pumping. In that case, in that scenario what is happening is the heart is beating at a higher frequency and with greater pressure, okay, with greater force, with greater force, when it beats with greater force, the end systolic volume, which in the sitting condition was about 40 to 50 ml more will go more or less? Will go less, will go less, it is pumping more blood, so it may be reduced to 10 or 20 ml, okay, what is your body doing? Your body is making sure that the different parts of your body, which now need more supply of blood is being supplied and for doing that the heart has certain mechanism, what mechanisms? Two mechanisms, number 1 increase the frequency of heart, okay, so from 72 you take to 80 to 92, okay, you can 102 you can go, I mean of course there are conditions to that but you can go up number 1 and number 2 also increase the force of contraction and if you do that we are capable of going from what was the normal 5 liters, am I right there? 5 to 6 liters, you can go to 10 liters, you can go to 15 liters, you can go to 20 liters and if you are an athletic person you can go to 25 liters, okay, so our heart has a tremendous capability to keep on adjusting making sure that our heart is capable of pumping far more blood if and when required, so it has to be controlled, how that is controlled? We will come to that a little later, okay, so you just read about all these properties and all these numbers, okay.

We have seen this image but I will show this to you once again because I have some interesting points to make, okay, so this is a heart and this heart is beating 72 beats a minute and every time this, left ventricle goes into systole, it pumps out how much blood? Every beat I am asking how much blood? 70 ml, good, how much blood? 70 ml, now let us talk only one beat, let us not go beyond that, single beat, 70 ml, okay, but this was in the resting condition, okay, now as a result of now you have started walking or you have started running or you have started climbing the stairs, whatever - now your heart is beating more fast pumping more blood, so it is very likely that this very, this very lumen of the left ventricle is now pumping from 70 it has gone to 90, it has gone to 100, it has gone to 110 depending on how much exercise you are doing, are you okay so

far? Now this also means that this aorta which was originally carrying 70 ml of blood per beat is now carrying 110 ml of blood per beat, are you okay with me? Has to, it has to, it is carrying, so now to the rest of the body, so this your entire body, your entire body which includes your brain, your liver, all the visceral organs, your muscle, everything they were originally receiving, whereas as long as you were sitting they were okay with the supply of oxygen and glucose and all other nutrients they were okay, as long as you were resting okay with what? Okay with 70 ml of blood per beat, right? Now you are running or you are doing vigorous exercise, okay, now their need has gone up and therefore heart has said okay I will give you more blood therefore heart has improved its efficiency and now heart is providing to the rest of the body how much of blood now? Say 110 ml, let us take a figure 110 ml, okay. Now if 110 ml of blood is going to the rest of the body, now all that blood will be returned to the right auricle, yes or no? So right auricle will now get how much blood? 110 ml, how much it is? 110 ml exactly same, I repeat exactly same, how much of blood? 110 ml, now if the right auricle has received 110 ml of blood how much? It will go to the right ventricle and from the right ventricle it will go to the, for oxygenation it will go to the lungs, so how much of blood is lung receiving per beat? 110 ml, so the point that I am trying to make is whether it is left ventricle or right ventricle whether the blood is going to the entire body which is much bigger than the two lungs which is much much smaller, are you with me? Lungs are relatively very small, okay, the systemic blood is going to the rest of the body which is 110 ml, if it is 110 ml the blood going to the lungs is at 110 ml, okay, so whether it is the pulmonary circuit or it is the systemic circuit the amount of blood that is being pumped with every beat, by either the left ventricle or the right ventricle, is the same, is same, have I made my point? Is same, never make a mistake, it is same. Now here is the beauty, although it is same the pressures at which the two systems are operating are completely different, I will come to that a little later, that is why heart becomes an amazingly beautiful organ that conducts two systems, pumps the same amount of fluid in the two systems but the two systems operate at different pressure, you have to operate them at a different pressure because obviously this system which takes the blood to the entire body which has far more capillary network as compared to the lungs, you will have to have a higher pressure here, okay. So how is the heart capable of generating at the same time you see the two systole of the left and right are happening at the same time, the two ventricles are going to systole at the same time, both of them are pumping the same volume of blood in every stroke but the pressures are different, we will come to that, okay. Yes please. We will talk about it when we talk about hemodynamics, okay.

Also this is I am sure you understand. We are talking about the valves, okay. Those two are the semilunar and mitral and semilunar and tricuspid valve, these are the semilunar valves, here you talk about the valves, I want you to appreciate the chordae tendinae which are anchored on the papillae. This is very nice animation, it is not animation this is

real, this is real, I mean you know what they did, this is the pig heart, okay. So there is left ventricle, left ventricle when the left ventricle pumps the blood which goes through the aorta, okay and there is a valve there, semilunar valve, so they have introduced a video camera in the aorta, after the semilunar valve and your camera is looking at the valves, okay, so you are looking at the valves. So valves will open, okay, when will the walls open, okay.

If it is human heart, the moment it becomes, the moment it goes from 80 to 81 it will open, I do not know in the case of pig, okay, are you getting my argument, it will open, okay and then when the heart goes into diastole the valves will close and make sure that it does not go below 80, okay. So can you see, okay, so we can see, so they open, so it is continuously, it is a very interesting animation that gives us a very nice idea of how the seminal valves are operating. Now when you have taken a section through the human heart, it is through the ventricles and what is the glaring fact that you cannot escape, look at the diagram and tell me. Thickness of the wall, thickness of wall of what? The left and obviously you will find that the left wall is much more massive, okay, as compared to the right, okay, although the volumes are identical, although what? The volumes are identical and now that will come to, I have already started giving the explanation to the statement which I made earlier. What was the statement? That the pressure in the generated by the left ventricle is more, can you appreciate, can you connect it to this structure? The walls are larger, they can contract more forcefully and they can generate lot of more pressure as compared to that generated by the right ventricle, okay.

Okay, now we will try to answer a very important question which we have been so far sort of postponing as to what is it that makes the the wave of stimulation? What is it that excites? We have seen how a cardiac muscle responds when it is excited, alright, we have seen that in the plasma membrane there are fast sodium ion channels, they respond first, then there are slow calcium ion channels, then they respond under, but we have seen all that, okay, but we have not seen how does the process begin in the first place, okay. So now let us focus on what we call as the pacemaker system or the conduction system of the heart, okay. Very interesting focus on this, do not miss a point, very, very important, okay. Now all we can do a very simple experiment to get a frog and open the animal and anesthetize the animal and then open the animal and then look at its heart. You will find that the heart is pumping and then you take a scissors and do a sort of butcher type of surgery in which you cut away everything, just keep the heart, cut everything, cut everything, okay. So you have cut the blood vessels, the flow of the blood that goes into the auricles, you have cut the blood that flows that goes, everything you have cut, you have cut the nerve supply, blood supply, everything.

And then you remove that heart and put it in a petri dish. In the petri dish what you have

done is already filled it with physiological solution. What do you mean by physiological solution? That solution contains sodium chloride, potassium chloride, calcium chloride, pH adjusted, make sure that the osmolarity of the fluid is similar to that of blood, okay. And also you bubble oxygen in that medium. Your attempt to give some oxygen is OK, but you cannot replace hemoglobin, we are still trying to do that. And you find that the heart is beating, it is beating, okay.

And if you have the physiological solution, that we call - in which the heart is kept, if you have really made good quality preparation, okay, it will beat for two hours. It will beat for two hours. It is, is the heart receiving any input from anywhere? Cut away everything, just cut away everything. It will still keep on beating, okay, which means there is something within the heart, okay, which can generate, heart is an organ of self-excitation. It can generate, it can generate electrical impulse something like action potential within itself, okay, and that can spread to the rest of the heart and excite the cardiac muscles, okay.

And it keeps on generating, it keeps on generating and you can count the frequency, okay. Now, what is that system and where is the system – that is the next point that we will try to address. There is a within the heart muscle, within the heart muscle, now get this, we are talking of heart muscle. There is a certain part of the heart muscle, okay, which the cells there, the cardiac muscle, their myocytes, okay, cardiac muscle. They, when you actually try to study the actin-myosin filaments in them, you find that they are very less.

Are they there? Yeah, they are there, not that they are not there, but they are very few, okay, that is one, they do not have, okay. And some of them, actually all of them, okay, if you place an electrode in them, okay, they show the property of self-excitation, about that I will come to that in the next slide. But where is that tissue distributed in the heart? The answer to that question is you have to follow the green color code which the author has used to show you the conduction system of the heart. It begins with, I am sure you have heard of, you have heard of, what is written there please? Sinoatrial node, so certain tissue of the heart, of the heart, it is not nervous system, it is heart, okay. And those cells, they have, they have certain branches and some of the branches go from the right to the left and then some of, they have two, three branches and they communicate with yet another piece of the tissue which you call as what? Atrioventricular node or the AV node.

And from there the tissue continues and it goes from the auricles to ventricles, and this is called as bundle of His, and then it bifurcates in two and then you call this as the Purkinje fibers. What do you call them as? Purkinje fibers. Look, this is heart tissue, okay, it is

heart tissue, not any, it is heart tissue, okay. Now this peculiarity, this peculiar arrangement is so interesting that I will first talk about it. I will first talk about the SA node. What you can do is, it is difficult in frog because that tissue is not very clear but you can do it in the case of rat.

So, let us do an experiment, okay. Go, anesthetize a rat, collect the heart, from the heart go to the right atria, from the right atria you can isolate a tiny, piece of tissue which may be 1 mm by 1 mm by 0.1 mm, okay, I am just making up the size, I do not really know. You pick up that bit of tissue and then you put it in your petri dish and in the petri dish you have already taken physiological saline and now on that you are going to impale an electrode. Are you with me? Impale an electrode, okay and you will get, you know what I am drawing in the air, the first peak and then the plateau and then the fall and then, and then, and you will find that it is more or less beating like normal heart. Now I am not talking of the entire heart of frog, I am talking of the tiny, tiny, tiny bit of tissue which I have taken from the heart and I know that the tissue I have taken belongs to what node there? Say that again SA node, SA node.

So what is the physiological property of SA node? Those cells are capable of generating action potentials at regular intervals on their own. Is it clear? Okay. Now let us find out how this works. Okay, but before that, before that, very interesting. So what does it do in the animal? Well, I have shown it in the petri dish.

How does it work in the animal? Well, this tiny bit of tissue, which I call as SA node, which I have been working in a petri dish, in the entire animal, those cells are there. Now what do they do? Well, they are associated with the next cardiomyocyte, next cardiomyocyte, next cardiomyocyte. Next cardiocyte is not a part of SA node. It is a regular muscle which is abundantly supplied with active-myosin filaments and the next cardiomyocyte normal, normal, normal cells which you have been doing for the last two lectures and all these cells are connected by way of gap junctions.

Okay, so I am drawing here a cell. Okay, what is this cell? This is the cell I have taken from the SA node. Okay, SA node 1 cell. Second cell is also SA node. Sticking to that, sticking third cell, it is a normal cardiomyocyte with large number of active-myosin filaments. So large number of active-myosin filaments and that is the real contractile tissue.

One tissue, SA node, second SA node, third, fourth, fifth, sixth, seventh, eighth, ninth, hundred, hundred and ten, they are all normal cardiomyocytes. Are you okay so far? Follow the chain of thought. Now they are all connected by way of, they are all connected by our gap junctions. Now the first guy stimulates, second guy stimulates, they

will stimulate at the same time but then second will stimulate the third, the third will stimulate the fourth, fourth will stimulate, I can go on and on till the end of the heart.

Okay and now here is the beauty of the situation. If the first one fires at 0, am I making up numbers? Okay, the second will fire at 0.01, 0.02, 0.03, 0.04, 0.05, 0.06. Are you with me? And they will follow in that sequence. Are you getting it? And the sequence in which each cardiomyocyte in the heart contracts is very necessary for generating an orchestra like contraction of all the muscles because when the muscles contract, when the auricle muscles contract, you do not want the ventricular muscles to contract or even in the auricles you want certain cells to contract a little ahead of the other cell and other cell, other cell so that the entire thing contracts and then the blood goes into the ventricle. You do not want entire auricle, all the cells to contract at the same moment. No, you do not want to do that. Okay, because of this amazing arrangement, it is possible to actually figure out as to how these cells will, each and every cell is programmed to contract at a particular moment with reference to the cell on the left and with reference to cell on the right.

Are you with me? Amazing organization, beautiful. So, the action potential we generate here, we will spread here, so we will spread here, so from this point it will go here, it will go here, from this point. So, these are the points from where the current will flow, action potential will flow into the adjoining area by way of what? Gap junctions and then it will go, the information will go, these three pathways are called as inter-nodal pathways and then it will go to the AV node and from there it will go to the bundle of HIS. Actually, the bundle of HIS, the rate at which action potentials will be transported along the length of the fiber is not uniform. Now, what do I mean by uniform? Well, I have a big road here and there is a bottleneck there, the bottleneck is for a while and again the road broadens and I have my traffic, cars are going at a particular speed, then they slow down, then they slow down and then once they are there, they are again pick up the original speed. Now, let us apply that analogy to the information with a particular speed.

It goes beyond a particular speed and this is the bottleneck. Where does the traffic flow? Traffic flows, but at what speed? At less speed, at less speed. Can anybody use the common sense and tell me what is the significance of this? Why? You are right. Why? He has given the correct answer. You don't want the ventricles to start contracting before you have come to the end of the diastole.

So, the blood has to flow from the auricles to ventricles as long as the blood is still flowing from the articles to the ventricles and ventricles are in the diastole and they are accommodating the blood. You don't want them to contract. You want to go slow till that point. That is why, that is why the speed at which action potential is being carried by this

pathway here is slow, but once it goes here, it all goes there and then the whole heart. Not every cell at the same moment, no? Depending on where the cell is placed, they will all contract and they will pump the blood into the aorta.

Am I talking Greek and Latin or we are same? We are on the same plane. Hello? I hear a very muted yes. Are you okay? Yes.