Human Physiology
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Lecture – 13
Cardiac system : From stimuli to rhythmic muscle contraction - Part 4

Sir, how does this system scale up with other large organisms with larger hearts? Oh, that is a very interesting question. His question is how does this system work in elephant, right? Oh, yeah. The answer to that question is I talk about it in animal physiology II, come if you are interested. There we talk about all the animals. As the animals grow in size, the rate at which the heart beats is slow.

So the elephant heart beats about 30 to 35 beats per minute. Because the heart is really large and with every beat the blood has to go through these chambers which is not very difficult. What is really difficult is for the circulation of the blood to happen in the coronary veins and arteries. You do not know what I mean by coronary.

Come you see, this muscle also need blood vessels. We will call them as coronaries, I will talk about the coronaries, okay. So for and heart is large, so you have to take so much blood and then take it out in every beat, okay. Therefore, I will go to the other extreme of your question. If the elephant heart beats about 30, 32 beats per minute, at what rate does the rat heart beat? 300, 300, okay.

And mouse 500, very interesting numbers, remember them. Rat heart beats, how many times I said? And mouse heart, okay. It is very clear, so the smaller the animal, the more rapid is the heart rate. See we have made one observation that a cell connects to one cell from one cell to another cell and that is by way of gap junction, okay. So as far as atria are concerned, okay, the information will start from the SA node, how? I will tell you in 5 minutes.

It will go over the internodal pathway to the AV node, okay. But then from the AV node, the information has gone to all the cells of the auricles. Would it go from all the cells of the auricles to all the cells of the ventricle? No, it is not a great idea. Because then you cannot, in the earlier slide we saw the, you know that bottleneck we saw, okay. If the cells of the auricles are directly communicating with the ventricular cells by way of gap junction, then everything will go from auricles to ventricles and ventricles will also contract rapidly.

So that should not happen. Therefore, the nature has provided a wonderful, a wonderful insulatory membrane which separates the auricles from the ventricle. Hello, where am I?

I am talking about the two auricles. I am talking about the two ventricles and at the separation of the two, can you see that green tissue there? What is that green tissue? Can you, can you read there? Author has given the explanation. Non-conducting fibrous layer means all the cells of the, of the auricles, whereas they talk to one another by way of gap junctions, the cells of the auricles do not, NOT, do not talk to all the cells of the ventricle because there is a, there is an insulator interpose between the two and what is that insulator, insulator, insulator system? You read that non-conducting fibrous layer.

So how will the information go from the auricles to the ventricles? Only by way of the conducting system. The nature has provided a definite conducting system and nature says you better follow that conducting system, otherwise I will not let the information go randomly from auricles to ventricles. No, it has to go from the auricles to ventricles, it has to go only by way of the conducting system and that part of the conducting system which we compared to the bottleneck, okay, where the passage with which the action potential is going is rather slow just to make sure that the ventricles do not contract before they should. Okay, so here we are talking about the, you can read about the SA node, AV node and okay, this is a very interesting diagram. Can somebody look at this diagram and tell me what is happening? What is the message that the author wants to convey in this? The time absolutely correct.

So the SA node has fired. It has given the action potential, it is traveling over the cells of the conducting system, okay. The moment it has fired, I will call it as what time - Zero time, okay. Then the information or action potential is traveling over this internodal pathway by the time it has reached the action potential has reached here. What is, how much time it has taken? 0.03, okay here 0.03, okay. It is say 0.03, it has come here. From here it will go, now from here to here is it going by conducting system or it is simply going by the cardiomyocytes connected to one another by way of gap junction? By way of gap junction, okay.

But it goes, so this will, so this the information goes here at 0.5, the information goes here after 0.07 seconds with reference to zero moment, zero moment of the SA node. Are you okay so far? So if I just ask you to focus on this, will the cardiomyocytes here and the cardiomyocytes there, will they contact at the same moment? That is the ultimate purpose. You want to make sure that this bunch of muscles or this particular should contact first, then this, then this, then this, then this.

Therefore they are, so and then it goes here at 0.03 and then suddenly you see from 0.03 by the time you go through the bundle of His, it has suddenly gone from zero to how much? 0.16. 0.16, why? Because of that bottleneck, okay. And then it rapidly goes from 0.16 to 0.17 and then from here, from it the action potential is spreading locally

from cardiomyocytes and then 0.17, 0.18, 0.19 and it goes here and then 0.21, 0.22. Look, where are we? We are in a single cardiac cycle. Hello? And we have to work within the frame of 0.8 second. Are you with me? Okay. And within that period, so this if you start your stopwatch at this point, okay, the by then the information has gone here, information has gone there. Does it mean that heart has contracted at that moment? No, no, no. This means that that action potential has gone. Then the rest of the things - calcium spark, hello, followed by calcium spark, then followed by availability of calcium, followed by sliding of the actin-myosin filament which means happening of actual systole.

Are you with me? This just tells us how - when it has gone here, this is contracting, this is contracting, this is contracting, not this, okay. And then the action potential and after this, so this is the way by which the current is flowing over the conducting system. This will be followed by eventually within a matter of another fraction of seconds, the actin-myosin filaments will actually slide on one another and you will get the phenomenon of systole or the muscle contraction so that the blood, oh this is another beautiful event. I do not have to tell, I am sure you can understand. What is the author trying to show here? Can you see it comes here? It goes, it starts at the SA node, then it goes to AV node and then it goes over the bundle, it goes here and it spreads, spreads everywhere.

And on the lower figure, I will talk about it a little later, this is your electrocardiogram. So the doctor has put the lead, one lead on the right wrist, one on the left and then one on the leg and the doctor is looking at the electrical information collected from the surface of your body, which is essentially generated by your heart and you are recording it and the author shows when it starts, how it is reflected in the case of ECG, but I will talk more about it later. I will do one more thing. Forget everything, forget everything, just look at the aorta. Take 10 seconds, 20 seconds, 30 seconds, just look at the aorta.

Did you catch the point? What was it? Can you please use the right word? Compliance. What is it? Compliance. What is it? Compliance. Right. Now we will go to understanding the principle of the SA nodes.

What is so special about the tissue? How can it generate action potential on its own? Very important question. We should ask that question. Why? To answer that question, I will draw your attention to two images and the image on the left you already know. What have we done? We have detected a typical cardiomyocyte, which has abundance of action-myosin filaments - a typical cell. We place an electrode inside and the moment we put inside we find that inside potential difference is how much? Read there and tell me.

There, there on the left maybe 95 or something, 90 or 85, whatever it is. That is the

resting potential. And soon, within a matter of very short period, which are the ion channels which are going to open now? Fast what? Fast sodium ion channels will open which will just show you the surge, it will go all the way and a little later which are the ion channels which are going to open? Calcium also called as DHPRs. And they are slow to open and slow to close therefore you get what do you get there? Plateau and then at the end of that 0.3 seconds the calcium ion channels will close and then the potassium and then you have that image.

We have done it 10 times. Now what I am going to do is I am going to pick up that electrode which was inserted in a cardiomyocyte just below the plasma membrane and I was recording. Now I am going to introduce or impale that electrode. My electrode is made of what? Capillary that glass capillary very good that glass capillary is containing what solution? KCL. Now I am going to impale that capillary in the cell of the SA node. Hello, makes sense right? Are you okay so far? And I get a pattern which is very different.

To begin with I find that the resting potential whereas that was almost 90 this is where this is about 65 or so 60-65 millivolts. The resting potential of the two cells is not same. The resting potential of the cells of the SA node which has got the capability of generating action potential on their own have different electrical properties and they have obviously different electrical properties because electrical properties depend on the different types of channels. So amount of the type and number of channels that are existing on the cells of the SA node are different and that is what we are going to learn about in next 5 minutes.

Good. First of all you will find that that was the first difference I outlined just now. What was it? What was it? That the resting potential difference is much less. Number 2 glaringly Plateau is not there. It has different type of calcium ion channels.

Alright. Then I will tell you what. First of all in this diagram the author has started at what millivolt inside? Minus 60. Minus 60. The cell is at minus 60. Does it stay there at minus 60? No. This membrane potential difference is very labile.

What do I mean by that? 60 on its own, on its own 60 becomes 55, 50, 50, 45, 40 when it becomes about 40. Why? I tell you why that is happening I tell you little later but that is happening. By the time inside becomes minus 40 then suddenly the calcium ion channels open. What channels open? Calcium channels open and as a result of that the calcium permeability goes up. Can you read here? Calcium permeability goes up and somewhere by the time it goes to the top then the calcium ion channels start closing.

Are you with me so far? And then as a result of that the calcium permeability goes down and as it is coming down somewhere in this period, the potassium channels which are also there they start opening. When they start opening they will take the ions, potassium ions in which direction? Inside to outside say that everybody I mean I do not like this hesitation. Potassium ions when the channels open in what direction will the ions move? Inside to outside. Inside to outside why? Because inside is? How much time how many times more? 35. 35 say everybody should say how many times more? 35.

35 times more. These facts have to be deeply ingrained on I mean I do not like your hesitation even for a second no not accepted very basic you have to know. So, the as a result, potassium ions will leak out and the potassium ions will carry the positive charge. Therefore, again this electrical charge is going towards positive. How far does it go? Again it goes somewhere almost to because so many potassium ions go out that it almost goes to minus 60. Now, wake up and try to hear every word I am going to utter.

As a result of the potassium current because of the opening of the potassium ion channel potassium ions going out and outside becoming positive with reference to inside and inside almost having reached minus 60. So far in the membrane there is yet another very special ion channel which you do not get anywhere else and those channels are a different type, but they allow the sodium ions to go through and those sodium ion channels open only when the potential difference becomes minus 60 inside. Minus 60 inside means what? Minus 60 means the cell is almost hyperpolarized it is minus 60. It has gone to the bottom it is as much as the highest potential difference you can get inside. These channels open at that voltage means what? There is a protein that protein has all charges on it - is voltage gated and that protein is sensitive to inside becoming minus 60 with reference to 0 outside and that protein undergoes a change in the shape and when it undergoes a change a channel is open and when that channel is open it allows sodium ions and then the sodium ions go in.

Sodium ions in which direction they will go? Out to inside. What charge they will carry inside? Positive charge. Inside which was minus 60? Minus 59, minus 58, minus 57, minus I will go to minus 40. Once minus 40, calcium channels will open you have reached the threshold. Are you getting it? Now this kind of sodium ion channel which is sensitive to the voltage which is minus 60 which is almost hyperpolarized cell is a very rare phenomenon not a very common phenomenon, but it is very special phenomena you encountered it here.

Because of that I will tell you something very funny. Because of that those channels are called as funny channels. What do you call them as? Funny channels and the movement of sodium ions from inside to outside by those channels when they open when the voltage

inside is minus 60 is called as funny current. What do you call it as? Funny current.

Funny current. Very funny. Funny current and funny channels. So would you get this funny current and funny channel in any other cardiac cell? No. You will get only in the cells of the conduction system. Let us go ahead now.

When do these funny channels close? They close. They are operating from here to here. Their purpose is to take it so that the calcium will take over. Then the calcium will take over once they reach the threshold.

Oh they answered that question. Very good question. They are present everywhere. They are present in the entire conducting system. The entire conducting system. I will answer your question.

We will do another interesting experiment. Listen to this. He will again kill the frog. It sounds so cruel, does not it? No, we are just doing thought, thought, thought. Even thought could be a little painful, I agree with that. And I am sensitive to that.

So we will kill a rat which is also equally sensitive. So we will kill a rat and what we will do is in the earlier experiment we had removed a tiny tissue from the SA node. Now this time what I will do, I will have three petri dishes. A, B, C. In the A - I will put a tiny tissue taken from what node? SA node here I will put little bit of tissue taken from where? AV node and here I will take little from the Purkinje fiber, from this part.

I will take some part from here. Same experiment I am doing. So I have three pieces in the physiological solution. And I will put three electrodes in 1, 2, 3. And I am recording and each system is connected to my oscilloscope and I am recording the number of, the frequency on which each is capable of firing. And then the answer to your question is given on the right.

Can you please read for me? There, there. SA node how much it is? 70 to 80. How much is my second sample which is a sample from the AV node? It is firing how many times on its own? 40 to 60. And the Purkinje fiber is firing at what rate? 15 to 20.

Now I am asking you a very simple question. Why does it happen that we have a heart in which, we have a heart in which SA node does its own business, do 60, 70, 80 times and then, then, then AV node do its own business 40 to 60 and then Purkinje fiber is this and we have total chaos. Does it happen? No. Why not? Is that connected and then the signal from the SA node will be very low? Yes, you are right. Can I try this? But why does it? It is decreased. Why does it have to decrease? Oh, what is the answer to that

question, I do not know.

When I do it, I find it. I have no logic, I have no logic as to why. Okay. But I am asking a question. You are on the right lines actually. Go ahead with your thought. Will it decrease the signal from SA node overrides or? Very simple and absolutely correct.

The SA node overrides, it is a boss. Okay. It does not let the normal phenomenon of either the AV node or the Purkinje fiber, okay, to express on its own. Okay. Now, I will ask you a very interesting question. Are you ready for this? Now, let us imagine a situation in which a branch of the coronary artery, are you with me? A branch of the coronary artery that supplies to the bundle of His is ruptured and therefore, the fibers in the bundle of His are not getting blood supply anymore. So the current that is generated by the SA node, it can go over the internodal pathway to the AV node, but, not further, not further, then what will happen? No, you have to do better than that.

Yeah. You see the auricles will keep on beating. Okay. At what, at what, 70 let us presume. The auricles will keep on beating at 70. The information is not going to the ventricle. Normally the ventricle is, ventricle says, okay, you are the boss, since you give the information 70 times, I will beat 70 times.

Now, suddenly the ventricle realizes that I am not getting any information. I am not getting information. So I must do something on my own. Okay. Something on my own means what? It will go, it will now, it will go either to either to, depending on where your damage is, supposing the damage is ahead of AV node, then the rest of the ventricles will start beating at a little after a little while at what speed? At 40 to 60 beats per minute. But then there may be complete asynchrony.

Are you with me? Okay. Therefore, therefore, I am sure you have heard of the word cardiac arrhythmia. What word am I using? Cardiac arrhythmia. Cardiac arrhythmia is a phenomenon in which because of some such problem, okay, the conduction system is not able to take its message to the different cardiomyocytes at the proper time in the proper sequence, in the proper chronology. Therefore, you may encounter cardiac arrhythmia. Do visit this website. There is an YouTube animation is there, which shows you what of the conducting system of the heart. Yes. Is it possible in any way if for example, as a node becomes dysfunctional for AV node to take over? Oh, it does.

It does. It does. Oh, we see in human patients all sorts of things can happen. Okay. All those things can happen. Okay.

And then what is the solution? You raised a problem. You give the solution. Very good. Who said that? Say that again.

Artificial pace maker. Artificial pace maker. Right. It is a tiny equipment which we implant here.

There is a tiny battery which you have to change every 3, 4 years. Okay. But that keeps on giving the necessary signal, so you have artificial place maker. Okay.

So basically the AV node cannot take over as a pace maker. I do not know. Do not know. You have to ask a cardiologist that. Whether how far it can. Okay. The reason I am asking is why does it have its own intrinsic rate in the first place?

Who? AV node takes over as a solution. Does it have its own intrinsic rate in the first place? It is not useful. See, you are not asking a question to me. You are asking a question to evolution. Are not you? I mean he is asking a question as to why this guy beats so many times and why this guy, why is this necessary for this guy to do that when that guy is already doing the job? That is his question.

Ask evolution. And, and. No, no. I am not, I am not sidestepping your question. Answer is there somewhere. Okay. So, since the funny channels are present in all the type of - what, you know, what causes the difference in the intrinsic relationship of all of these things? Oh yeah, yeah, that is a very interesting question. His question is if the, if the funny channels are there everywhere in the entire conducting system, then why is it that one particular part of the system generates 70 action potentials per second and in the case of other 40 to 50 and in the, yet in another case Purkinje fibers 20 to 15 to 20. Why is the difference there is his fundamental question which, with which I very much like the question and I invite anyone to give the answer.

Very good. Say that again. He has given the answer. You see, if you count the number of leakage channels here, here, here, you will get differences. Okay, the number of channels, okay? Their properties could differ, there could be yet other kinds of channels. What I am trying to say or what she is trying to say is the property, the membrane properties with reference to channels in them are not identical. Okay, they are all capable of generating, beating on their own, but they are not identical and they are different across. What differences? Again, you will get this information, that information is there in the literature.

Okay. Look, look, we are, we are talking our entire drama is based on 4 or 5 half a dozen channels. Okay, in reality there are at least 25 different kinds of channels which are

operating in all the systems, okay? So, we are now stepping into the area of research in cardiology where we obviously cannot go here, but information is there. Okay. So, what is your question if I take a membrane, plasma membrane from here and from there, what is the difference between the two? It is there in the literature and the literature and the differences are, broadly I can tell you it is with the differences with reference to the types of channels and the population of channels, density of channels.