Course: Electrophysiology of Heart

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Lecture 4: Cardiac muscle Physiology

So, today we will start our lecture next lecture that is cardiac muscle. So, in this lecture we will deal with the various topics of structure of cardiac muscle fibre and mainly how an excitation contraction coupling mechanism occurs in a cardiac muscle fibre and how it is different from a skeletal muscle fibre in brief we will study. So, generally the cardiac muscle fibre consists of two types of fibres, the fibre which is mainly responsible for the contractile tissue that is the atrial and the ventricular musculature and for the conducting tissue that is the origin of the cardiac impulse and propagation of the impulse. So, we have contractile tissue atria and ventricles, we have the excitatory tissue and the conductive tissue that is the pacemaker tissue or the nodal tissue. So, the two types of cardiac muscle fibres generally the histology of this cardiac muscle fibre or the physiological mechanisms are the same. Except the resting membrane potential which is generated in the nodal tissues and the atria and the ventricular muscle that is the myocardium these two are different, one is the ventricular muscle potentials and other one is the pacemaker potentials.

So, this we will discuss in further lectures. So, generally the characteristics of cardiac muscle is almost similar to that of a striated skeletal muscle with few differences. The first and foremost is it is involuntary in nature, our skeletal muscle is voluntary in nature it also has got striations, it also has got various cell organelles mainly mitochondria because of the contractile property since it has to contract the same is with the cardiac muscle. Now, that mean difference is the skeletal muscle fibres are enclosed in a closed loop and they the each muscle fibres are separated the muscle bundles are separated by the connective tissue, but that is not the case with the cardiac muscle.

Cardiac muscles are branched, but they are interconnected with each other, there is inter vegetations with each other and that is the mainly role and that is mainly required for the functional sensation mechanism which is seen in the cardiac muscle. Now, the heart if it has to pump each muscle fibres cannot pump individually according to their own characteristics or nature, it has to pump as a whole. The atria has to pump as a whole, the ventricle the atria has to contract as a whole, the ventricles has to contract as a whole.

This coordinated action in the cardiac muscle fibres in all the cardiac muscle fibres along the cardiac muscle fibres is mainly regulated by the sensational property or the functional sensational property which is mainly because of the intercalated disc present. The interconnections between the cardiac muscle fibre is mainly done by the intercalated disc.

Now, intercalated discs are usually dark lines which is seen in the light microscope. So, this you can see the intercalated disc the magnified version is shown over here it the cardiac muscle fibre also consists of the thin and the thick filaments that is actin filaments and the myosin filaments. It has also got the Z line, the sarcomere also has got the A band, I band the only difference is the intercalated disc. Now, this is the intercalated disc. Now, this is one cardiac myocyte, this is one cardiac muscle fibre and this is one cardiac muscle fibre.

These two cardiac muscle fibres are joined mechanically by desmosomes and electrically by gap junctions. So, mechanically the two muscle fibres are joined by the desmosomes the inter in the intercalated disc what happens the ends of the adjoining cardiac myocytes are usually joined mechanically by the desmosomes and electrically by the gap junctions. Now, mechanically because so that they will contract as a whole electrically because the electrical impulse should travel across the cell from one cell to another cell. Since we know the electrical event precedes the mechanical event. So, the electrical syncytium is mainly maintained by the gap junctions and the mechanical syncytium is mainly maintained by the desmosomes.

These are nothing but the intercellular junctions. So, gap junctions mainly act as an electrical synapse over here. So, this that is why the cardiac muscle acts as a mechanical as well as electrical syncytium. Now, at this point the intercalated disc as I told you it is an extensive in folding of the membrane. The gap junctions which are which provide the electrical syncytium in the intercalated disc they provide low resistance at intercalated disc.

The gap junctions these are the proteins the channel proteins which are present and they are made up of connexion. The protein is connexion 6 connexions form 1 connexion. So, this gap junctions are made up of this connexion and 6 connexions. So, these is mainly the electrical impulse electrical synapse and the low resistance the low resistance channel proteins or the low resistance vessels. So, that there is no barrier to the flow of the electrical impulse.

So, this allows the action potential to travel from one cardiac muscle to the other cardiac muscle. So, as a whole the cardiac muscle forms 2 separate syncytium one is atria the

other one is ventricles. The atrial syncytium is formed and the ventricular syncytium is formed. Now, atrial syncytium and ventricular syncytium is generally separated by the continuous fiber band except at one place that is AV bundle or atrioventricular bundle. Now, each syncytium obeys all or none law.

All or none law means either it will contract as a whole or it will never contract it will not contract at all. It will contract as a whole or it will not contract at all. So, it is not that it will partially be contracted state like our skeletal muscles the muscle tone is always maintained by the partially contracted muscle it is not like that heart is never like that heart either it will contract as a whole or it will never contract. So, each syncytium obeys all or none law. Now, each muscle fiber is about 100 micrometer and 15 micrometer broad.

The cytoplasm which is present in the muscle fiber is sarcoplasm the same as that of the skeletal muscle fiber which contains abundant of cell organellins. Usually the mitochondria because the contraction needs lots of ATP and each muscle fiber is made up of number of parallely arranged myofibrils and myofibrils consist of both thin and thick filaments acting and myosin filaments. Now, again the difference comes in the circotibular system. Now, the tibular system in a skeletal muscle the circotibular system is usually the formation of triad the triad is formed in the skeletal muscle. There is a t tibule this t tibule is an invagination of the sarcolemma into the deep into the cell and there are two cisternals end in case of triad, but this is not the case with that of cardiac muscle.

In cardiac muscle we do not get triad, but we get diad. Another important thing is the t tibule penetrates sarcomere at the level of z line, but in case of skeletal muscle this penetration occurs at the junction of the a and i band. So, why there is difference of this formation of triad and diad? Now, as you can see in this diagram this is the triad of the skeletal muscle the pink one is the t tibule. This two light green color these are the cisternae. So, there are two cisternae and one t tibule forming a triad structure in a skeletal muscle.

This t tibule is very lean while the cisternae is very much developed. This cisternae is the sarcolelasmic reticulum the storehouse of calcium. In case of diad which is seen in the cardiac muscle the t tibule is very much more in case of diameter. Almost five times the diameter of the t tibule is five times than that of the skeletal muscle which is present in the cardiac muscle as you can see. And the cisternae that is the sarcolelasmic reticulum of the cisternae of the sarcolelasmic reticulum that is not well developed as that in the skeletal muscle.

Also this cardiac muscle t tibules consist of some mucopolysaccharides. So, because of this few reasons their exhibit died in the cardiac muscle and tried in the skeletal muscles. Now, if you see the further detailed molecular structure this is the transverse t tibule. This is the invagination of the t tibule invagination of the sarcolema deep into the cell. This is the cisternae that is the sarcolelasmic reticulum.

Now this is the t tibule, this is the sarcolelasmic reticulum. The channel proteins which are present on the surface of the t tibules that is L type of calcium channels LTCC, this is L type of calcium channels. Since we have already discussed what are the various types of calcium channels. So, this is L type of calcium channels also known as DHPR dihydropyridine receptors. Now, the second channel protein which is present in the cistern and cistern surface of the sarcolelasmic reticulum.

This is RYR2, this is nothing but the rhinodine receptors. So we have channel proteins, these two channel proteins are very specific like t tibules bear the L type of calcium channels and the cisternal end of the sarcolelasmic reticulum they bear the rhinodine receptors. And the connection between the there is a connecting link between the t tibule as well as the cisternae of the sarcolelasmic reticulum that is mainly done by the junk to phyline 2 protein. This is a channel which usually binds the transverse tibule and the sarcolelasmic reticulum of the cisternae. So, with this we will move on to the excitation contraction coupling mechanism in a cardiac muscle.

Initially what I had already told that electrical event precedes the mechanical event. Since cardiac muscle is an excitable tissue the property of excitability is present in the cardiac muscle. So, there is always an electrical event which will occur first that means there will be generation of action potential through depolarization mechanism that will occur first and that will follow the contractile mechanisms or the mechanical phenomenon. Now resting membrane potential of a normal cardiac muscle is minus 85 milli volt to this minus 90 milli volt. This is specifically when we are talking about the ventricular myocardium or the muscle potential the pacemaker potential is around minus 60 milli volt that is different.

So, what we can see most of the thing which has been already discussed. Suppose this is the t-tubule and this is the cisternal end of the sarcolelasmic reticulum. So, this is the sarcolelasmic reticulum and this is the t-tubule the invagination of the sarcolemma. It is bearing certain channels the very important channels that is L type of calcium channels and the cisternal end of the sarcolelasmic reticulum they are bearing the channels that is rhinodine receptors. So, this is the L channels and these are the rhinodine receptors.

Now, whenever there is influx of action potential whenever there is action potential

generated and in traverses the t-tubule this channels are the voltage sensors. Voltage sensors means there is more positive charges over here. So, this more positive charges will cause this L type of calcium channels or other known as DHPR which are nothing but the voltage gated calcium channels. So, this voltage gated calcium channels will open and there will be influx of calcium. Now, influx of calcium is occurring from extracellular to inside the t-tubules.

So, extracellular calcium triggers the L type of calcium channels. So, this extracellular calcium triggers or enters through the L type of calcium channels. The voltage gated calcium channels will open and the calcium will get influxed from extracellularly inside the this t-tubules and obviously, it will stimulate the other receptors that is rhinodine receptors. Now, this rhinodine receptors are present where these are the these are present in the cisternal end. Now, the t-tubules and the cisternal end are very close to each other though there is a gap which is been shown in the figure, but it actually it is present practically it is present very close to each other.

So, they will also sense the voltage since the calcium is also entering because there is more positivity this rhinodine receptors what will happen this rhinodine receptors this will also cause release of calcium from sarcoplasmic reticulum to the sarcoplasm that means to the cytoplasm. So, there will be calcium which is released from sarcoplasmic reticulum to this sarcoplasm. Now, this calcium which is released this will bind to the filaments which are present in the sarcomere that is we have the thin filaments and the thick filaments. And this calcium will bind and will cause the cross bridges formations the same which is occurring in the skeletal muscles also and there will be contraction of the muscle. So, this is usually the excitation contraction coupling mechanism.

Now, the main difference of this with the skeletal muscle is in the skeletal muscles there is only the endoplasmic calcium which is mainly required for the contraction, but in case of cardiac muscle it is calcium induced calcium release that means extracellular calcium is also present as well as sarcoplasmic reticulum calcium is also present. Now, this is the diagram which we can see this is the t tubule and this is the sarcoplasmic reticulum which has already been told. Now, this is the L type of calcium channels and here we have the rhinodyne receptors. Now, whenever these are the other pumps which is mainly responsible for the muscle relaxation. Now, whenever there is generation of action potentials whenever this action potential comes we can see the because of this action potential there is calcium ion which is entering through this L type of calcium channels and that will trigger calcium release from the sarcoplasmic reticulum with the help of rhinodyne receptors.

So, more amount of calcium gets released in the sarcoplasmic reticulum. So, the

sequence of events is action potential moves along the t tubule then we have activation of the dihydropyridine receptors or the L type of calcium channels that is nothing but the voltage sensors which senses the electro positivity. And calcium then binds with the rhinodyne receptors which opens or releases large amount of calcium and this large amount of calcium is nothing but we call as calcium spark. So, this is nothing but calcium induced calcium release CICR. So, calcium induced calcium release that results in calcium sparks.

So, calcium from extracellular fluid contributes in contraction. So, this is mainly through the rhinodyne receptors which is present at the sarcoplasmic reticulum. Now, how the muscle relaxation is exhibited? Now, already we had seen that the muscle relaxation in case of skeletal muscles also the same steps occur in the muscle relaxation that is the cross bridge linkages they detach themselves there is ATP synthesis and finally, calcium is thrown outside. Now, calcium is thrown outside with the help of two mechanisms. The first one is sodium calcium exchanger and the other one is calcium pump that is sarcoplasmic pump.

Now, there has to be two pumps because the calcium which is already entering into the sarcoplasm during the muscle relaxation that should enter into the sarcoplasmic reticulum. So, this sarcopump will take the calcium back from the sarcoplasm or the cytoplasm to sarcoplasmic reticulum. Now, usually this sarcopump is kept inhibited the name of sarcopump comes from sarcoplasmic or sarcoendoplasmic reticulum calcium ATPS pump. So, this is usually kept inhibited by a molecule known as phospholumban. So, this phospholumban is the molecule which usually keeps inhibited which usually inhibits the sarcopump.

This inhibition will removed only whenever there is a phosphorylation of this molecule and this phosphorylation is done by none other than cyclic AMP mediated protein kinase activity. Generally, there is a very common drug important drug known as epinephrine or adrenaline. They usually cause or affect this sarcopump activity or the cyclic AMP mediated protein kinase activity. So, this is usually kept inhibited by the phospholumban molecule. This phospholumban molecule is usually the inhibition is wiped off whenever there is a phosphorylation by cyclic AMP which is protein kinase activity mediated.

And this is usually done in case of drugs by the adrenaline or the epinephrine. Now, the second thing is whenever the calcium is going inside the sarcopump, the calcium should not come out of the sarcoplasmic reticulum. So, there should be a calcium binding protein in the sarcoplasmic reticulum. So, what are these calcium binding protein? The calcium binding protein mainly we have two calcium binding protein. The one is calciquetrin, the other one is calreticulin.

These two we have to remember. The calciquetrin is very important. It is found in most of the muscles, skeletal muscles, cardiac muscles, but most importantly calreticulin is present in smooth muscle, is abundantly present in the smooth muscle calreticulin. So, these are the calcium binding proteins. Whenever calcium will come to the sarcopump, this calcium binding proteins will bind to the calcium. And this calcium will not be able to then move out of the pump.

So, this is the role played by the calcium binding proteins. Now, back into the t tubule also you need to throw out the calcium. So, that is usually done by the sodium calcium exchanger. So, sodium calcium exchanger molecule is there that usually one calcium is exported. For import of three sodium ions, three sodium ions will come inside and one calcium ion will be thrown out.

So, this portion is had already been told that is sarcophasmic reticulum calcium pump is inhibited by the regulatory protein phospholumban. And when phospholumban is phosphorylated by cyclic AMP dependent protein kinase activity, this inhibition of the sarcopump is lost. And this is mainly attributed by the drugs like adrenaline and epinephrine if you want to increase the contractility of the heart and decrease the relaxation rate of the cardiac muscle. So, in this way muscle relaxation occurs. So, this is the main difference which is seen in the skeletal muscle contraction as well as the cardiac muscle contraction in case of muscle relaxation.

The coupling comparison overall the trigger for the sarcoplasmic reticulum release is mainly voltage dependent in case of skeletal muscle. In case of cardiac muscle the trigger is calcium induced calcium release. So, it is the very important question which is asked which is the main influencing factor that is the extracellular calcium extracellular calcium which enters the t tubule and further causes release of the calcium from the sarcoplasmic reticulum. And the calcium release is proportional to the membrane voltage in case of skeletal muscle. While in cardiac muscle the calcium release is proportional to the calcium entry.

It is not that proportional to the membrane voltage how much is calcium is entering. So, the calcium release will also occur in that way that is why we get calcium sparks over there. So, the contractile phenomenon is seen in the cardiac muscle and the skeletal muscles. Mainly in case of skeletal muscles the applied aspects generally we will talk about related to the calcium voltage gated channels that is malignant hyperthermia that is already been discussed with the calcium voltage gated channels, but that does not occur in case of cardiac muscle because of the calcium induced calcium release. So, that is why in this lecture we conclude by discussing the structure of the cardiac muscle.

What is the difference between triad and dyad in the skeletal muscle as well as the cardiac muscle? How the excitation contraction mechanism differentiates distinguishes between the cardiac muscle from the skeletal muscle? So, with this I would like to conclude today's lecture. Thank you.