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$Lecture-41\\ Physiology of smooth muscles and digestive system - Part 1$

There is Science So, we will plan it this way, we will move on now, move on to the physiology of digestion. And you must have noticed that whereas we have made an attempt at understanding the skeletal muscle system and then of course the cardiac muscle system, but third another equally important component that is the smooth muscle system. So, let us - this is our opportunity to take a look at the smooth muscles because they form an integral part of the digestive system which is driven by the smooth muscles. Not only the digestive system, but a range of other systems and let us dive deep into it and try to find out what. So, alimentary canal, movement of food through gut, secretion of digestive juices, absorption of water, circulation of blood, control functions, we will do all this in due course. So I will ask you something, if you take a transverse section of human body somewhere here at the level of the waist, just take a section and look at it and you will get in a diagrammatic view. If I were to draw diagrammatic it will look something like that, look at the top there you see the top that is the spinal cord that symbolizes the spinal cord, just see spinal cord. Below that there is a slightly not so dark circle, below that there are three circles in a row. And then there is space below the three circles. Now top - there is the spinal cord, below that is the centrum which represents vertebral column and below that you can see can you see that hollow circle, tiny circle your dorsal aorta, this is a plan true for all vertebrates. that represents

Take a section you will find that there is what? Spinal cord which is in a vertebral column, below that there is dorsal aorta which is taking the blood backwards from the heart backwards and below that if you see there is this huge cavity, this huge cavity which we call as peritoneal cavity and if you look at that I can say that there is a big tube and inside that there is another tube. So basically all vertebrates have what you call as a tube in a tube organization. Are you getting my argument? Outer tube is your body wall and inner tube is your alimentary canal and it is because of a tube in a tube structure appreciate the point. Therefore it is possible to have the inner tube that goes in and out, in and out, in and out and therefore it is possible for you to have an intestine which is 20-25 feet long are you getting my argument. That is possible and we need that length of intestine because we need so much room, so much space to facilitate digestion. So you need entire we are very long elementary canal and we always wonder how is that elementary canal accommodated in our system it is because this is a tube in a tube, the inner tube can go large number but now this space that you have between the two tubes is called as peritoneal cavity what you call it as? Peritoneal cavity what you call it as?

Peritoneal cavity and all vertebrates have what you call as peritoneal cavity good.

Now you might have heard you know when they give injection or administering into the drug inject drugs into the body often you might have heard intraperitoneal root, intraperitoneal root why what would I mean by I.V. route? Intravenous. Intravenous very good, intravenous very good so there is another - but which is more common is intraperitoneal route means you essentially introduce your needle in this space and you get this plenty of room there so you can give a large volume intraperitoneal root. But you remember if this is the alimentary canal - this symbolizes alimentary canal with this duodenum whether it is duodenum or whether it is a ileum or large intestine it is connected to the rest of the body by means of this membrane which you call as mesentery. So the stomach and the intestine and all that is ultimately supported not anywhere no, no, no it is connected to the rest of the body by what? Mesentery so where is the mesentery coming from? The mesentery comes from the dorsal side - it comes from the dorsal side are you with me? And that mesentery is important because the blood supply to the entire alimentary canal - which is you can say is going to take the blood vessels which will bring the deoxygenated blood back to the heart and also the nerve supply - everything is through the mesentery. So just look at this diagram. This is your alimentary canal it does not have anything so everything is through what? Through mesentery and that is very well shown in here, okay. But before that let us also take a look at the different parts of the different layers. Do you remember we have seen in the histological section the outermost layer was called as serosa - which was a thin layer. What was the layer just below the serosa? Muscular. Muscular.

Very good - longitudinal muscles. Why you call them as longitudinal muscles? So here you have a layer of what serosa - longitudinal muscles - longitudinal means go along those muscles whose length is organized along the length of the entire alimentary canal. What will you call them as? Hello when I say longitudinal muscles your esophagus goes this way okay it goes this way so those cells whose long axis is parallel to the axis of the esophagus will be called as longitudinal muscles and those which go around we will call as circular muscles. So this outer layer of longitudinal muscles then there is a layer of circular muscles, okay. And then there is a layer called as submucosa and then there is the mucosa okay okay. Good - but life is more interesting than that. Listen to this. What was the outer layer - I said longitudinal muscles. What did I say? Follow the point okay. The things are going to become interesting. Outer is serosa which is not muscle inside that is it is a epithelial tissue thick epithelial tissue tough which protects alimentary canal inside that is a layer of longitudinal muscle layer which is pretty thick which plays a very important role in peristalsis. all these muscles they are going to and then inside that is circular a layer of circular muscles in between the layer of longitudinal muscles and the circular muscles there is a very interesting layer of neurons. What did I say? Neurons and there are millions of them millions of them okay - and it is called as myenteric plexus. What do you call them as - myenteric my- refers to muscles enteric refers to alimentary canal, okay - a layer that is there in the muscles of the alimentary canal. What do you call it as - myenteric plexus. What do you call it? You have to this - should fit here what did I tell you just now – myenteric. It is a collection of millions of neurons, okay. And then there are circular muscles okay and then inside circular muscles there is another layer again of neurons which is called as sub mucosal plexus. So again - serosa, longitudinal muscle layer, circular muscle layer, in between can you see this black line with those round dots - what do you call it as? And inside that is another what do you call it as? Submucosal plexus. The entire game of the alimentary canal with reference to peristalsis - when to begin, how to begin, when to terminate everything - is controlled by these neurons. Are you with me? So we have been knowing for very long time that peristalsis happens - who controls the peristalsis - the myenteric plexus and the sub mucosal plexus and these two plexuses in turn get innervation from the autonomous nervous system. So the brain, the autonomous nervous system, sympathetic and parasympathetic - they come they come and talk to the myenteric neurons of the myenteric plexus and the submucosal plexus and overall they will control peristalsis. Secretions very good secretions and well you have been starving so to reduce the blood supply to the alimentary canal. You have just had food and to increase the blood supply to the alimentary canal. Are you with me? Okay. All this happens without our knowledge, okay. Again these plexuses have a very important role in all those actions not only the smooth muscles which line the blood vessels of the alimentary canal so that you can control the blood supply when you want it. And when you don't want it - you stop it. And this of course Iis the mucosal layer. Oh, this is interesting. It is the same thing as the as the original one but you can see the mesentery there. Through the mesenteries you can see the red one which is taking the oxygenated blood there. You can see the blue one which is taking the deoxygenated blood there and that yellow one here - so out of our myenteric plexus - the inner one is the sub- mucosal plexus and then you can see the different layers - the inner most is the epithelial then you can see the different glands. Spend some time on this understanding this. You will appreciate what it is. Okay. Now you know what is at the top skeletal muscle - you know what is at the bottom - what we are going to try to understand right now is what muscle are there, so let us focus on smooth muscle, okay. Now before I start smooth muscles – it is a different world. Smooth muscle is a different world okay. It is neither cardiac - no it is completely different. The only thing that is common is there is an actin filament there is a myosin filament and they slide on one another other. Than that everything is different - hammer the point. It is different okay. Don't carry any baggage from the skeletal system or cardiac cell. No it is a different system and we need to spend time to understand how it is organized and how it is controlled. Just a nice image. The electron photomicrograph showing the top one - you can immediately understand each is a single cell. Are you with me? The muscle fiber and of course you don't see inside - inside there will be one nucleus here one nucleus there okay. Smooth muscle - just how it looks - how different it is there are bundles and bundles and they go all over you can't find a pattern. There is hardly any geometry there, look at the geometry - there hardly any geometry okay. But if you go deep into this and if you try to look - how a single cell looks - like the single cell looks - something like this. This typical shape is called as spindle-shaped. You know how this word come - this word will come very often biology - and I'll tell you how this word came from. You know in the textile okay textile industry you make cloth from the thread, okay. The thread - the axis on which the entire thread goes okay which you put in the machine so that will look - that it's called a spindle - because it looks like there's more tapering towards the end- so the word has come spindle. The word we have borrowed from textile industry so there is a spindle shape cell do you appreciate now goes on tapering to the ends, and thick in the middle. What do we call that spindle but you would wonder as to why that word spindle is coming from therefore a spindle shape - so there are thousands of spindle shaped cells come together and perhaps some of you may appreciate that in the slide that we saw - the smooth muscles very much looked very much look like this. And in a single cell there is a single nucleus okay - not too many nuclei - in a single - as we have in the skeletal muscles. This gives you the dimension what are the dimensions - about two to ten microns in diameter and about hundred two hundred microns in length - but depends on the on the organ. Most not all smooth muscles show another phenomenon with which again we are familiar with and the phenomena is the occurrence of gap junctions. Can you see the gap junction there, hello? Can you see there in the top a neuron - I made a mistake again not a neuron - a muscle cell - a smooth muscle cell okay, is talking to another muscle cell by the gap junction okay - and through which of course the ion can pass ions can pass something like our intercalated okay. And the proteins here are called as annexins okay. So you have one cell connected by gap junction. If I focus here and if I draw diagram I'll say one cell and if one cell is excited - we must see calcium ions have gone up that is the principle still holds. What is the principle? If you want actin-myosin filament to slide on one another you will have to suddenly give a flush of what - your calcium ions, okay. And if that happens within one cell the calcium ions could pass from one cell to another cell and other cell could also - now that calcium ions - it could also respond okay. And then at the top you can see a neuron - can you see a neuron there okay. And this innervation of a smooth muscle is anatomically slightly different from that of skeletal muscle. I will talk about it very briefly. So if this neuron is a part of the post ganglionic parasympathetic, post ganglionic parasympathetic, what neurotransmitter is being released by those terminals. There you can see - very good - what neurotransmitter acetylcholine - so if acetylcholine is released here okay - then if this cell is stimulated, if this cell is stimulated, it may stimulate the next cell, okay. So you don't have to stimulate every cell - every cell need not be equipped with its own nerve supply this doesn't sound very great but it is true for a skeletal muscle in the case of skeletal muscle every muscle cell must have a fiber which is coming okay from the spinal cord or brain or whatever and release what neurotransmitter there again acetylcholine again what acetylcholine. I am sure you can appreciate here I have one smooth muscle cell another smooth muscle cell and author tries to draw our attention - using an image of electron photomicrograph - what is author trying to show us here - a gap junction. What are you seeing here - gap junction okay. So let us anatomically - find out what those gap junctions are? This we have done hundred times hello. Where are we? In the spinal cord okay. And this is your skin and you touch there or prick a pin-yeah I have said something right or wrong? And then you excite the pain receptors and then as a result of the action potential will start okay. So there is a transducer okay? Any perturbation here we will start the action potential - the action potential will go via the dorsal root ganglion - it will enter into the spinal cord via the dorsal root. The processing of information will happen via the interneurons and this particular neuron the blue one there - the cell body is located in the spinal cord is what? It is a cholinergic neuron that you rise to a fiber that will come out of the ventral root - it will go all the way and supply this skeletal muscle. And the neurotransmitter that is being released is again acetylcholine. And it is acting by a what? What receptors - very good - say that again – nicotinic. What receptor? and this is extremely monotonous - very standard whether you are a fish or a bird or a reptile - this is it when it comes to innervation. Now this is so different for the smooth muscle. Because in smooth muscle it can be excited by neurotransmitter it can be excited by a neuron, it can be a tissue hormone by an paracrine agent or just by stretching. It has enormous diversity - when it comes to stimulation of what smooth muscle – it is extremely diverse okay. I will talk about it now - this is skeletal now this is most important now let us compare it with the scenario of the innervation of an organ okay, which is equipped with smooth muscles. One very simple definition of the where you will find smooth muscle is you will find it in the wall of a hollow organ. What did I say? Wall of a hollow organ. Well stomach is hollow - am I right? Duodenum hollow. Intestine - answer - it is hollow okay gallbladder hollow. Pancreatic duct – hollow. Urinary bladder – hollow. Uterus - hollow okay, dorsal aorta – hollow. All these organs are equipped by with what muscles - so one definition of smooth muscle is - means whereas the skeletal muscles will anchor themselves on a bone - the smooth muscles will line the hollow organ. This is the definition. And here is a classic example of a hollow organ. In this particular case all parts of the alimentary canal. And does it have - just as our skin has sensory function - do the visceral organs have a sensory function? What do you guess? What do you think yeah. For example, if food is passing it has a sense that the food is passing and then it has to compare the stretch - in response you don't know about it why should you know about it? why should you? You're right but you don't know why do you need a sensation - for that you don't need - you don't tell the gland to secrete the enzyme - the gland secretes on

its own - what do you mean by that? It is out of your control. You have what control do you have - no it is the autonomous nervous system. When the food arrives okay into the duodenum okay - the wall of the duodenum knows that the food has arrived it will send an endocrine message to the gallbladder. The gallbladder will squeeze and pump the bile out which will pour into the duodenum and do its business. Whatever it is - you have no role. You got it. If stomach pains - gentlemen and ladies - pain - is everything okay something goes wrong. When something goes wrong the system wants to tell your brain okay – tell that something is not quite what it should be. The pain and stretch okay and discomfort you can use all those words. So any such phenomena that is happening here it takes information again by what route again to the spinal cord? So you have this system also this system also in the spinal cord and here it is processed and now this is actually a part of what autonomous nervous system. The autonomous nervous system - it goes to the ganglia are you - in this particular case sympathetic ganglia okay. The preganglionic fiber is going to have what neurotransmitter the preganglionic fiber is going to have what neurotransmitter? Very good and this is since this is sympathetic ganglia - the part of sympathetic nervous system - so this blue guy is going to have what neurotransmitter very good what neurotransmitter and having entered here the terminal here okay. It may either directly talk to the smooth muscles or it may talk to the myenteric plexus neurons. Are you getting the story? Both the possibilities are there. We will talk about it later. Tt can talk to what – myenteric neurons so the then the myenteric neurons they take over the charge because they are sitting right in the alimentary canal. So this was the point I have already made. This is the typical skeletal system and there the nerve fiber that is coming from the spinal cord - they are all cholinergic and each - you see this axon give rise to one branch second branch - third branch fourth branch as many and at each junction it is releasing acetylcholine - look look look - if I cut here then this muscle cell will not get acetylcholine and if it doesn't get - this one contracts - very simple every guy has to have its own supply of acetylcholine every skeletal muscle cell - has to have - not so here. We have already seen - this is a nerve supply and these are what you call as the beaded extensions. They will release their neurotransmitter but if one cell is excited - gap junction - second cell - third cell so it will continue. So what are smooth muscles - they primarily support visceral function visceral means in your alimentary canal. If you open the body wall - whatever you have whatever you have - liver there you have pancreas, there you have different parts of the alimentary canal all those organs we will call as what? Visceral organs and then each fiber is individual small cell. They lack sarcomere, okay. Yeah another interesting point. The sarcomere - you remember the skeletal muscle system. I will say it is the heart and soul of the skeletal muscle, okay. If you have understood one sarcomere - because one sarcomere or hundred sarcomeres - they're all same. We have to understand sarcomere and in sarcomere how the actin filaments are inserted and how in between thick and thin filaments are organized. However, in the smooth muscle there are no sarcomeres, okay. And that beautiful geometry - that you get

in the skeletal muscle sarcomere, sarcomere, sarcomere and then and then perfect distance, okay - all that is not there. No that's not there. Then how does it work? How does it work? I will show you that organization in the next slide. Here - we are looking at one complete smooth muscle cell. Diagrammatic and it is talking to this cell by way of gap junctions. It is also talking to this cell by gap junctions and you can also indicate the influx and outflux of the ions - so that the messages can go some time on what? On a single smooth muscle cell. Look at the smooth muscle cell first of all - I will draw your attention to the plasma membrane - and you'll find that as you go along the plasma membrane - this is certain depression. You get that depression here those depressions are called as caveolae, called as caveolae – it is just a depression in the plasma membrane. But it is a matter of great attraction for the physiologists because whenever this cell receives any information from anywhere - be it from the neuron, be it from a hormone, be it from a local hormone or any information anywhere. Invariably the receptors which are sitting on the smooth muscle cells are located in this part of the caveolae. Those proteins you know which will get a message okay means what means what okay norepinephrine action of nor-epinephrine or action of acetylcholine by way of muscarine receptor, okay, muscarine receptor most probably it is sitting here. What am I trying to do is - I am trying to draw your attention to the anatomical peculiarity, okay and I am trying to emphasize its physiological importance. Why is caveolae are important - because it is the site for accommodating a large number of receptors through which a signal will be received by the cell. Second thing I notice just next to the cavioli there is this deep red patch which are very weakly developed as compared to skeletal muscle - sarcoplasmic reticulum. Yeah it is there sometimes -sometimes it's not there and when it is there it's very weakly developed. Okay why is it so weakly developed as compared to that in the skeletal muscle? What does it contain say calcium. It contains calcium okay. Why isn't it as extensively developed? It is not extensive developed because these cells are relatively small, you know and because they are small - you can always get calcium from outside, okay. So the nature has thought there is no great point in providing a great source for calcium within the cell. You can always get it from outside, okay. Not so in the skeletal muscle, okay. It is so deep inside okay and there you need a burst okay so therefore those cells have an extensively developed sarcoplasmic reticulum which is an immediate source for supply of huge amount of calcium. Not really necessary here okay. Good. Second thing that I want to draw your attention is to these dark blue bodies - which are seen in several places. You will call them as dense bodies. What do you call them as say - that again a dozen or more I don't know much more. I'm sure much more than dozens different proteins okay different proteins. They come together and form - it may be right is it sitting right in the cytoplasm or it may be attached to the plasma membrane. If it has attached to the plasma membrane then we call it as attachment plaque. It is the same thing dense body if it is sitting on the plasma membrane we'll call it as what attachment plaque. It has very important function. The purpose is to anchor the actin filaments - so these actin filaments so if I were still to - it is something like Z membrane. You remember Z membrane. What was the purpose of Z membrane? To allow the actin filaments to anchor okay. And in a perfect geometry. There is no great geometry here okay. But it serves the same function - that it allows and if so this dense body there - I can see here the three actin filaments - there are hundreds and here also and those red rods - what do they represent? This in myosin filaments, okay. And the function is same. The myosin filaments will pull the actin filaments. When it is pulled then of course these two - these two what? These two dense bodies will be pulled, okay - and that's how the cell will undergo contraction. Then of course there are mitochondria all over here is a 3D image - the first one is a smooth muscle is relaxed and I just want you to compare this dense body - that is a dense body over that you can see the thin fibers which are the actin filaments and right in the middle there are dark dark myosin filaments. Can you see there it's very clear actin - myosin filaments and as a result of contraction - whenever it contracts - because it slides - as a result of sliding - can you see in this image there? More of sliding here you just compare that with that and as a result the entire length of the muscle is reduced, okay. So you can you can compare in 3D you can compare the smooth muscle cell in action.