Human Physiology
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Lecture – 42
Physiology of smooth muscles and digestive system - Part 2

Calcium is the most important that really regulates the skeletal muscle. You remember the skeletal muscle plasma membrane received - what acetylcholine, and as a result acetylcholine receptor has opened. What kind of acetylcholine receptor – nicotinic type and as a result sodium ions have entered and as a result of that the membrane has depolarized. As a result of that calcium spike is there am I ok so far? Here this sodium has relatively less important - the boss is calcium ok. Anything happens I mean if the message arrives from outside from the sarcoplasmic reticulum even from outside - get calcium and start doing your business. Point number 1, is it very clear? So, calcium here is a relaxed cell - here is a contracted cell. I will directly take you to the last point. Whereas the skeletal system is very efficient, very fast and starts acts at the level of milliseconds and it better be because if there is a pin prick and if I have to remove my hand it should happen in shortest possible time ok. But relatively smooth muscle system is comfortable - no rush - what is the rush? If peristalsis is delayed by 2 minutes, I am serious, it does not matter. In some places it may, but it is very slow system ok. Slow system everything is slow - the response is slow then the response will last for a very long time. It will also take time for the response to pass away. It is a very slow system ok. Some are very slow some are not so slow, but as compared to skeletal muscle this is essentially a very slow system. The frequency may be 1 to 10 or to 1 to 300 of the skeletal muscle are you appreciating the point now. The cross bridges have far less ATP activity as compared to skeletal muscles. Of course, ATP has to be there. What am I talking about action-myosin cycling cross bridge hello. And for every cross bridge you are going to need ATP. All that is going to happen, but on a very on a very slow scale. You know the slow scale. Let us take an example ok. I will take one of you and draw 500 ml of blood ok. As a result of that your blood volume has gone down I am sorry blood volume has what gone down. As a result of that if the physiological response is not there the blood pressure is going to fall ok. So, how is the your system going to respond? Your system is going to respond by angiotensin ok, and then immediately reduce the diameter, particularly of your large veins, ok. As a result of that you reduce the volume of the entire vascular system available for the blood. So, that the blood pressure still remains constant - I mean homeostasis is still quite constant are you ok so far.

Now, in that particular stage the blood vessels which have contracted - they are in no hurry to relax ok. They will remain contracted for as long as necessary. Are you with me? Till no new blood comes or till you do something they will remain contracted. Are you with me? I mean that is not a function that comes and goes. No that is a function that has come and that come to stay for some time. The smooth cells have evolved a system in which it works slow. It stays for a very long time. Now here is the beauty of the situation. And it does so by utilizing a minimum amount of ATP. Are you with me? How it does this? I will show you. I

am trying to draw contrast between the skeletal muscle system -very fast very efficient comes and goes quickly. And as long as it comes it is a sort of factory that keeps on using ATP. Are you with me? And since it uses so much ATP that often the mitochondria cannot supply therefore, you need creatine - you remember the creatine we did it in this class. Creatine you need creatine. Smooth muscle system - there is no rush and because sometimes you need to sustain the contractions - you look at the valve - which valve - I am talking about the valve that is lying between the stomach and the duodenum. Stomach and what - duodenum and the food has passed from the stomach after digestion acidification it has gone into the duodenum. And it does not want that the food from duodenum – the digested chime from the duodenum should go back. So the valve closes. Once it closes it remains closed for 5 10 minutes so. During that period if the skeletal muscle were to do it - which means for every second I am going to use ATP. Smooth muscle cell does not do that. So how they do it. I have not answered that question. That is a very important question I will answer it in due course of time. I will just tell you that these cells can sustain contraction for a very, very long time with minimum utilization of ATP – okay. If the angiotensin is removed from the system after inducing contraction they will remain contracted for some period. They will remain contracted for some period they will remain contracted but angiotensin also would not go so quickly okay new angiotensin will keep on coming I mean angiotensin is not like a neurotransmitter. It will come and go. No it is hormonal - one step okay one very simple question for you. Do not read anything just look at the two images and tell me what is the difference is what difference them. Do you notice you are not supposed to read you are only to see the image. You are taking too much time. Your time is done. Every cell has gap junction and no cell has a gap junction okay is the difference clear.

Whereas most of the smooth muscles belong to this category - that is what we have seen - the occurrence of gap junction like in alimentary canal, aorta okay. There are very few tissues - smooth muscles where there is no gap junction. In that particular case every muscle cell has its own nerve supply - this is somewhat like a striated muscle or the skeletal muscle. Are you with me? So far and you see this kind of arrangement - what tissue am I showing you here? what is this tissue here? What is this you cannot see? I will not show I do not want you to read can you identify the image? This is iris and opening in the middle is the pupil, hello and these are the smooth muscles and these smooth muscles under autonomous control. What is their function? what is their function? You go out - you reduce the aperture of the eye okay, and you go into darkness okay you cannot tell your iris that you become small or large - it happens autonomically - autonomous system does it okay. So then you enter into the dark room okay and then there is less light – this is perceived by the certain retinal ganglion cells - they know light is not enough okay. That information is taken to the brain stem and then from the brain stem then that information is taken to the centers of the sympathetic nervous system. Then the sympathetic nerve supply goes and supplies these muscles - so that under the influence there will be increase the aperture okay. Very fine - extremely small extremely delicate cells of smooth muscles of your iris - every single cell has a nerve supply, okay. So the nervous system can control every cell independent of the other okay. And this phenomenon you find in the iris. You know what is goose flesh. Have you ever heard a very nice piece of music and responded by having goose flesh or goosebumps okay? So that

happens - because a hair stands on its end and that happens because there is tiny muscle here can you see this muscle here very tiny muscle in your hair okay. That pulls the hair papilla and then the hair stand there. These muscle cells also smooth cells and it is an autonomic response. And these muscle cells are also of this type and this type are called as multiunit smooth muscles. What do you call? Can anybody stand up and tell me why - what a single unit is single unit and multiunit is multiunit. Use your common sense and give me the answer. They all work in tandem - they all work in coordination to one another - whereas this is not so okay - therefore we will call this as what? So here every cell is a unit. The whole thing is a multi- unit and here all cells put together is a unit therefore single unit. Did you appreciate the argument? There excuse me sir. Why do you need a multiunit system in those eyes and so what will happen if there is single unit system in that? I do not know I do not know. I can try to guess. I have pondered with this question and I think the for fine control - means fine control I will tell you what you want. A cell to contract only so much. Are you with me? you means you are you are going out see how much light is there? There will little more, little more, little more now bright sun okay. So depending on that you are going to reduce the aperture. If it is very bright you are going to reduce the aperture for that precise control, I think nature has thought that this is a better way. I do not know this another wonderful phenomena that you find in the in the smooth muscle system. I will tell you what. I will take a balloon hey listen to this everybody. I will take a balloon and in the balloon I will put 100 ml of water okay. Under the pressure of the water - certain pressure is being exerted on the wall of the balloon yes or no? Okay. I will put 100 ml more okay so the pressure is increased. I do not know whether it is double or not that is the physics problem. I do not know but it has definitely increased okay. So the wall is trying to press the water okay and the water is trying to expand the balloon. And with 100 ml so much with 200 ml far more okay. So far listen to this. If my balloons wall was to be made up of smooth muscles - get this - focus on what I am telling you. If the wall were to be of smooth muscles or instead of balloon I take a urinary bladder from the slaughter house you know get urinary bladder, okay. But you cannot get it because for the phenomena you need the nerve supply. so you just cannot get it from slaughterhouse - that would not work. So you put 100 ml and there is certain stress exerted by the wall on the fluid inside okay. Supposing it is x. What is it is x. And then I put 100 ml more it becomes 2x okay. So far in the case of urinary bladder it becomes 2x After 1or 2 3 4 5 10 15 seconds it goes back - automatically goes back to x. Hello automatically goes - why does it go? I tell you why and how can it happen - how does it happen? Let us see you have to follow the story. It is beautiful. The bladder is here okay. Now you put water in it. It stretches it stretches okay. The natural phenomenon is once it stretches its contracts - once it contracts okay there are n number of actin-myosin filaments - it interacting by way of cross bridges. Are you with me? n number of cross-bridges - now I put 100 ml more it becomes 2n okay. Now when n number of actin-myosin filaments we are talking to another - 2n is much more - whatever had increased - those actin-myosin filaments they separate from one another, hello. So if it was originally 1n with 100 ml it was 1n are you with me so far - yes or no tell me? if no I'll explain again again again. Let us do it again. Put water - if you stretch it will contract - as a result of that happening - because actin myosin filaments are interacting with cross bridges. How many cross bridges are there between - if I actually count how many are there and how many are there and I put 100 ml

more water how much the number has gone to how much 2n. But 2n means those cross bridges are more. After five minutes those additional cross bridges will delink and the number of cross bridges will go back to n. The answer to that question is you will understand the philosophy behind this. You have been to washroom the bladder is empty. Are you okay so far. Now every time the kidney adds a drop and a drop and a drop and a drop the bladder stretches okay. And as the bladder stretches there is more and more interaction of actin-myosin filaments. Is it a good idea to keep on increasing actin-myosin filaments interaction and keep on utilizing ATP for as long as you go to the next washroom again. It is a bad idea. So what nature says is - well the moment there is an increase - it but I'll also delink the actin-myosin filaments this - phenomena is called as stress relaxation of smooth muscles. Take time to appreciate an amazing phenomenon. Let us see what is there. The author gives an example of stomach. In the stomach you add food you are eating food okay. One chapati second so there is there is load on the stomach okay. Now the as a result of more food there is stress okay. But eventually the relaxation happens so is the wall of the stomach pushing the food with the same force with which it came in there which it happened in the beginning. No, there is a great economy in that you do the same experiment on the stomach but at this particular time - you take the scissors and cut the vagus nerve. Are you following the experiment? Cut the vagus and when we cut the vagus - what do you find? So this is the stomach in the stomach the we are measuring the pressure. How do I measure the pressure? By way of manometer. In that manometer I am not using mercury I am using water. Are you with me, and I keep on giving and I measure the pressure to be 20 cm of water - 40 m cm of water and this is my manometer and I find that the food goes on increasing but even if more food is there - the more or less the stretch on the wall has not really gone up. Doesn't mean much, but I'll repeat the experiment by cutting the vagus and then what happens tell me - it is increasing it is increasing - means what? as the pressure kept on mounting within the lumen of the stomach - it gave the information to the brain. Brain kept on calculating that and brain kept on sending the information to stomach - you relax you relax you relax. As a result of that this pressure remains constant. But the moment you remove the input and output via the vagus - so the moment you cut brain out of the system - well the pressure goes up. Are you with me? Amazing biology okay. So you read about the phenomenon okay. Now what we'll do is, we'll take an electrode, what is this electrode? It is a fine capillary we have done this - there is a capillary, in capillary I am going to fill with what solution? I told you once - strong solution of KCl. What is it? Strong solution of KCl. That is because it is a conductor okay. those ions are the conductor. I am going to put here in a smooth muscle and I'm going to connect it to the oscilloscope and I am going to read. You know what happens? It is very simple. What I find is even under resting condition the reading that I get here is - supposing it is minus it is inside the cell and I get the voltage of minus 50 millivolts. How much do I get? Minus it doesn't remain constant. On its own - it goes to about 40 over a period of how many seconds maybe three four seconds 50 to 40 again 50 40 50 40 50 it's oscillating. You don't get this phenomenon in the skeletal muscle. It is oscillating - is the cell responding? Not really it's not really it just oscillating. But if you stimulate the cell either by stretch or by acylcholine or by stimulation of parasympathetic nervous system then you suddenly find that these oscillations between 50 to 40 it starts oscillating between 45 to 35 and then occasionally it gives the spikes and the spike here is the action potential. This is not action potential but

this is action potential. And if you stimulate further then it starts oscillating between 30 to 20 and you can see the frequency of oscillation goes up means what you are stimulating it more and more as you stimulate then the oscillations go towards the zero okay. And as it goes towards the zero - at the at the peak you see it goes here and then it shoots it shoots and then when you are between say 20 30 to 20 it has maximum number. On the other hand, if it goes below 60 or 70 and then you say that the cell is hyperpolarized or the cell is inhibited. Cell is what? Means the cell will not respond even to the regular stimulatory agents or traditional stimulatory agents we will talk about it. We are talking about the smooth muscles okay. Just see what this cell is responding to - it is most likely acetylcholine parasympathetic stimulation or stretch. However, if you give this cell epinephrine or sympathetic stimulation – there is hyperpolarization. Why am I showing this to you? I am showing this to you because in the case of skeletal muscle all you could do is give acetylcholine and stimulate the muscle cell. Are you with me? Do you have a means of inhibiting the cell? Yes or no? No you don't have you don't have. Your only tool is to not to give a signal so that whatever acetylcholine is there it will be broken away by acetylcholine esterase and your cell won't contract. You have no means of inhibiting a skeletal muscle. Get the point. You have no means you can either stimulate it or not stimulate it. When you say not simulated - the muscle cell won't contract okay. So far are you ready for a little interesting detour of the statement. In the case of insects they have an inhibitor transmitter and the skeletal muscle in the case of insects can be inhibited. Just as it can be stimulated glutamate it can be inhibited with GABA. In the case of vertebrates stimulated with acetylcholine, but no inhibition. But smooth muscle can be excited with dada dada dada and inhibited with dada dada are you okay, so far. So here is a patient of asthma and what treatment did we recommend in one of the previous lectures. Say that again - injection of adrenaline - injection of what adrenaline. What will the injection of adrenaline do - look at this graph and tell me relax - what is it? It will relax. The answer is here. It will relax and it will dilate and the person will get the patient will get some relief. We have done this. You have done this. You are talking about what? Isn't this very familiar okay. So this is a branch of the arteriole and we have those smooth muscle smooth muscle, and these are the capillaries - no smooth muscles here, and these are again the veins and you can see the smooth muscles there, okay. This is an examination for you. So this the cells in this capillary - the blood vessels are experiencing shortage of oxygen. How will these cells, if they are say of the of heart or brain, how would they respond. Tell me. Yes, you are right. How that agent that is being secreted - adenosine - you remember adenosine? Yes. The author tells us here that metarterioles and pre-capillaries without nerve fibers - and there is no nerve connection - so these smooth muscles are responding to factors that cause smooth muscle relaxation. Adenosine no hello. Lack of oxygen or excess of carbon dioxide or increase the H+ ions, increase K+ - all those factors can talk to the smooth muscle. The skeletal muscle - the poor guy has only one thing as look only neither relax either contract or don't contract that's the end of the story. But here just see how many how many factors are there to control the okay. This focus on this slide. Then I'll conclude my today's talk. That's myosin molecule you remember that. See the two heads there and the two tails going one around one another in a helix, okay. And then we have also seen that on the neck if that is the head that is the neck and on the neck are sitting some proteins. Actually they are light chains - what do you call them - as you'll call them as light chains - the two are heavy chains

- and therefore these are the light chains. Now please remember these myosin molecules - I should tell you there are 40 different types of myosin molecules have been encountered in vertebrates different proteins. You know how myosin molecules - one protein to another protein okay. To my knowledge I read about 40 myosin - there may be more I don't know, okay. So this is a myosin, this myosin is very different from the myosin. One, two, three, four are there different ways of classifying myosin proteins. So this myosin is very different from the myosin that you will encounter in the skeletal muscle. Have I made my point? It is different, okay. Number one so this is heavy and this is light chain okay. Now you have stimulated this muscle cell. That muscle cell has that the plasma membrane and let's presume that somewhere near the caveoli and as a result of excitation the L- type calcium ion channels. What is that type L-type that's going to open okay. As a result of that calcium is going in - that calcium can act on the sarcoplasmic reticulum which is also a small store of calcium. That phenomena there means this here may be even CICR. Excellent as a result of that more calcium okay. Now this more calcium now okay. Now let us go back to skeletal muscle. There the calcium ions combine with - which protein calsequestrin. It is calcsequestrin. Troponin is made up of three units - one guy talks to calcium, another to tropomyosin and another to actin, okay. So calcium goes to troponin here it goes to another protein which is called as calmodulin. What do you call it as? It is a dumbbell-shaped protein which is thin in the middle and thick at the ends. It can combine with two calcium ions there and two calcium ions there. So how many calcium ions? It will combine with four and then it is activated okay. And then that complex calcium calmodulin complex okay. That will activate the enzyme called as myosin light chain kinase - what is it called as - MLCK. What does MLCK stand for myosin say that again light chain kinase. That myosin light chain kinase will phosphorylate this protein what protein this MLC is that protein is phosphorylated that this protein will be phosphorylated. Once it is phosphorylated it is activated and once it is activated okay. On the head this is a protein of course it's all protein and that protein is ATPase. Hello that protein is what? ATPase. It was inactive now under the influence of this enzyme which is phosphorylated - that ATPase is now activated. So it will now start taking energy from ATP - once it does that - it will bind to the actin filament and it will go over the process of cross-bridge formation. Hello are you good so far, okay. Ad at the same time - there is another enzyme called as phosphatase - that phosphatase will dephosphorylate and it will become inactive and it will give rise to relaxation. Depending on what information is coming from outside it can contract and you can relax the muscle okay. when will phosphatase act - it depends on the incoming information, okay. As long as the incoming information says you contract - it will - once that information goes then phosphatase will get active – dephosphorylate and then the whole system will go back to the relaxed state.