Human Physiology
Prof. Nishikant Subedar
IISER-Pune

Lecture – 53
Pituitary gland & growth hormone secretion - Part : 2

The growth hormone promotes, let me talk about that point, growth hormone promotes generation of glucose, generation of glucose exactly opposite to the function of beta cells of alloys of langerhans. Are you with me? Are you okay? So growth hormone is also called as a, get the name, diabetogenic hormone. Hello, what name am I giving you? Means what it will produce diabetes. It will produce what? Diabetes. Now here is a very interesting point. If a child is not growing at a proper rate, by the way the child is 6, 7, 8, 9, 10 years old and we expect the child to grow, are you okay with me? And if the parents feel that the growth is not as good as it should be, then why cannot we give growth hormone? Because see the market is full of, if you go to the internet you will find out there are there are marketing people who keep on advising that use growth hormone for growth.

It is full of. If you seriously ask an endocrinologist, a doctor, physician who has specialized in endocrinology, he is rather nervous about it. Because a growth hormone, it will promote growth, no doubt about it. There are every chances that it may produce diabetes.

Are you getting it? So keep this thought deep in your mind that using a growth hormone can be very, I mean you think a lot about it and then finally say I would rather not. Okay, alright. Yes. Go ahead, go ahead. Which one? Yes, yes.

You can, you can but that does not stop the diabetogenic action of growth hormone. Yeah, yeah, it does not. Growth hormone has, growth hormone may kill beta cells under unnatural conditions. Are you getting it? Under unnatural conditions, as long as it is normal biology nothing happens it works fine. Okay, but the moment you give an exogenous hormone, okay you are in what subtle way we are distributing the balance we do not know.

But in that particular case growth hormone may simply kill the beta cells and you have generated diabetes. Okay. Same is the story about, read about testosterone, a very similar story I will not talk about it now. So in the biological system if there is growth hormone release there will be increase in the blood glucose but there will be other mechanism to regulate it. Absolutely correct, absolutely correct.

And then we also get, the beta cells are also protected. It does not, it does not. But if you, okay. So did the growth hormone, like the larger rat with growth hormone extensively given, did it have diabetes? They did have. Oh yeah, yeah, yeah, that is a very interesting question.

We have those animals. They were short lived. Okay, eventually pathological issues developed in them and they had problems. I mean they were on absolute, I mean it is not that you have that advantage and then everything, no, no, that is, that is always the price. So here we have the, okay, so you know just now I talked about the osteoblast and osteoclasts.

Okay. Okay. So the, so the, so here is a, bone is another very interesting subject. You know something very interesting I will tell you. Listen to this. Each and every bone in your body go to every molecule today.

And there is a continuous turnover of the molecules of the bones in your body. And it is roughly estimated that after a period of 9 years, none of the molecules there are, were there 9 years back. Are you getting the argument? Simple enough? Why am I telling you? Just to give you an idea that there is continuous turnover of bones. Slow, it is there, it is there. But the moment that you have, none of them will be there.

There will be every, each molecule will turn off. Okay. So we have a continuous, what you call as a remodeling of bones. And then there are two types of cells, I said osteoclasts and osteoblast. The osteoclasts are the cells which are continuously breaking down the bones.

So they have enzymes and they release enzymes and they will broke down and then that calcium is again sent to the blood. Okay. And then there are osteoblasts and those osteoblasts will take that calcium and keep on making the bone. And any disturbance in this balance in favor of osteoclasts will give osteoporosis. Hello, are you with me? And this process of calcium deposition to a large extent depends on Esteady-all, which is the female sex hormone.

As a result of that, postmenopausal women, because they have lost or reduced source of Esteady-all, they eventually they suffer from what? Osteoclasts. Okay, just remember those, they are very interesting. Okay. So we are talking here about what? We are talking about growth hormone. Growth hormone acts on the liver.

Liver, it gives rise to IGF-1. And that IGF-1 is, so here author tells us that the action of growth hormone on the bone is mediated by what? IGF-1. IGF is a peptide hormone. Being secreted by what organ? Under the influence of what? Growth hormone.

Growth hormone. So let us see now how, very interesting image. You see he is an explorer, a European explorer who is going exploring the deeper areas in Africa and there are certain tribes. And those tribes are called as what? They are called as dwarfs, what do you, pygmies, what do you call them as? Yeah, yeah, what do you call them? They are there, they are still there. What do you call them as? Pygmies.

Pygmies. Now in the, when they took the samples, blood samples, they found that the growth hormone level was normal. But what was, what they were really lacking was IGF-1. And are you with me? So why, why, why? Because those populations have some problems, some mutation. As a result of that their gene for the synthesis of IGF-1, okay, is just not functional. So as a result of that whatever action that you are getting of GH is there.

But the action of GH that is dependent on IGF-1 is not there. And therefore you get, you get this sort of pygmies. Now that IGF-1 that I am calling is called as, was originally discovered as a protein, as a protein which was, of course there are proteins, they were called as somatomedin. What were they called as? To mediate the action, somatomedin. And four different proteins have been found, somatomedin 1, 2, 3, 4.

Out of that we are going to ignore the three and just we are going to focus on somatomedin C. Why? Because, why? Because, tell me why? Because it is same as IGF-1. Somatomedin is what? Same as IGF-1. Okay, alright, alright. So the pygmies of Africa have a congenital inability to synthesise significant amount of somatomedin C.

Somatomedin C. Are you there with me? Therefore even though their plasma concentration of growth hormone is either normal or high, they have diminished amounts of somatomedin C in the plasma. This apparently accounts for the small stature of the people and some of them are dark and for example that is why you can read about it. Is there any environmental advantage this piece has in the plasma? I do not know, that is an interesting question. You are asking what selective advantage they might have had over this. It is an anthropological problem.

I do not know the answer. Okay, but the question is very interesting. Why has nature selected this there? And what were the condition and when did the mutation happen? I mean it is a very interesting question. And I am sure anthropologists have dealt with it but I am not aware of the answer. So let us see. So here we have the amino acid sequence of IGF-1.

It is about 70 amino acid peptide. Insulin is how many amino acids I mentioned? Very good, very good, very good. So the pituitary gives rise to a growth hormone that growth

hormone acts on the, acts on the bone but it needs, it also needs the growth hormone acts on the liver. And then the liver gives rise to IGF and the IGF can act on the osteoblasts and you need the, okay. So here we have the growth hormone has direct effects on what? Fat metabolism, carbohydrate metabolism, lipolysis, blood sugar level, indirect effect, liver and other organs, IGF-1, skeletal muscle adipose, contiogenesis that is the, what is contiogenesis? Cartilage.

Cartilage, cartilage, cartilage and the muscle plus adipose tissue protein synthesis going up, going up. So IGF also, a protein synthesis goes up, cell proliferation goes up. Okay. Now this is interesting figure.

Just look at this. So here we are going to talk about how the feedback control of the release of growth hormone is regulated at the level of the anterior pituitary gland. Growth hormone, how is it regulated? Okay. The answer is pretty interesting.

Okay. So let us see. There are two groups there, paraventricular nucleus and arcuate nucleus, PVN and arcuate. Now life becomes more complicated. PVN, paraventricular nucleus. What is it? It is a group of neurons. Where is it in the hypothalamus? It is mainly known for secreting vasopressin.

Secreting what? Some of the cells also secrete, also secrete SST. SST is what? So let us check. Secrete what? It is very difficult, you know, I mean it is easy to say but it is ultimately when you go to the hypothalamus, it is the same group of neurons, it secretes this peptide also, that peptide also. So it is very difficult for me to say that this nucleus is equal to, no, no, no. Paraventricular nucleus secretes actually six vasopressin also, oxytocin also and SST also and CRF also but it is okay.

So the paraventricular nucleus somatostriatin and that has, that is inhibitory. So the dotted line and then, so the growth hormone secreting cells are being stimulated by ARC, ARC. ARC is arcuate nucleus. What is it called as? Arteous.

If you can remember, fine. If you cannot remember. I would prefer that you remember. Arteous nucleus. What do you call it as? You know why arcuate nucleus is very exciting, I tell you what.

Listen to this. When you have a heavy food which is carbohydrate rich, as a result of that, as a result of that, within after 15 minutes to 20 minutes, the beta cells have, there is a spurge of insulin, that insulin goes everywhere, insulin goes everywhere, follow the story. It goes to the median eminence. In the median eminence it comes out of the bullet-bone barrier and it

talks to the neurons of the arcuate nucleus. Who talks to whom? Insulin is talking what? Two neurons and neurons are sitting where? ARC, you know it is hypothalamus.

ARC, arcuate nucleus. And this is how brain knows that your sugar level is suddenly high. Are you with me? So the question is, the question is, should brain know or not know about your blood sugar level? Answer to that, it should. Come on, it is brain. How can brain afford to be ignorant? It cannot.

And remember this knowledge is not very old. This is all 10-15 years, 15-20 years. I mean for example if you go to the entire literature in diabetes, till almost 2002, diabetes is our periphery. All periphery beta cells going down, insulin resistance, da da da da, hundred things. Brain was not there at all. Brain was not even in concierge, it was not even a candidate to be thought of.

Then these interesting thoughts came up. What is it? That insulin crosses blood brain barrier at the level of median eminence, talks to the neuron of, of what? Arcuate nucleus. And then that information from arcuate nucleus, now once in the brain it is in the circuits. And then the brain knows. Brain knows what? That the blood sugar level is high. And then eventually downstream processes like well if my, if the blood sugar is level I better store it.

So then do I give the instructions to the adipose tissue so that you absorb that sugar, convert it into fat and store it as a fat recycle or give the information again to the liver, make sure that you take in that glucose. I mean of course endoclinic system is working but the brains also now comes into the play. And therefore now in last 20 years the nucleus has shifted as far as the study of diabetes is concerned. From the periphery and the beta cells of course it is important but that brain could also have a very interesting or important role and therefore you cannot really avoid the study of the arcuate neurons and its cells.

Answer my question. Would I or would I not find insulin receptors on the plasma membrane of the neurons of the arcuate nucleus? Yes you do. You do because if you do not find the receptors, finished. That is it.

Yeah. The pudding is good because it tastes good. Insulin receptors have to be there on the, and they are there. Are you with me? Just to complete the story, we have taken a detour but it is very interesting. The other hormone which is equally important is leptin.

What is it? Leptin. Say that again. Leptin. What is leptin? Leptin is again a peptide hormone and it is coming from the endocrine gland is? Very good. What is it? So is adipose tissue the fat cells in your body? Are they a source for hormone? Yes. What is the name of

the hormone? Leptin. Okay. Actually leptin and insulin are the two hormones of the periphery.

Leptin coming from the beta cells, leptin coming from the fat bodies which continuously tell the arcuate nucleus about the energy level in the periphery. How is the blood glucose level? Brain knows by way of these two agents.

Okay. Let us go ahead. Okay. So the pitari will secrete the growth hormone and the liver will give rise to IGF. The IGF will act on. So what is the message in the slide? The message is that the feedback information about the action of growth hormone on the periphery is being taken back to the brain by way of insulin like growth factors. Can you get this image? Insulin like growth factor is being released by what organ? It is going and acting on where? So pitatory is on, pituitary itself is releasing growth hormone.

Okay. If you give, supposing I give a shot of insulin growth factor, what will be its effect on the, will it act on the pitari? It will. It will. Okay. On what kind of cells it will act on the growth hormone cells? Do the growth hormone cells have receptors for IGF-1? Yes.

Okay. And what will it do? What will it do? It is a dotted line. It is inhibitory. Okay. And then the IGF can it also act how? On the hypothalamus.

Okay. How does it go? Again via median eminence. Hello. There is only one way there. Again via median eminence. Okay. It will go and talk to the hypothalamus.

In the hypothalamus it may talk to the somatostatin secreting cells. Okay. Stimulate somatostatin secreting cells, excess of somatostatin will go to the pituitary gland and inhibit the cells of the growth hormone. So this is how the release of growth hormone is being regulated.

Yes please. I have a doubt. Yes. Is IGF going to the pituitary gland through the median eminence? No, no, no, no, no, no. Pituitary gland is completely out of the blood. Pituitary gland, okay. Is anterior pituitary gland a part of the brain? Yes or no? What have we learnt in last one hour? Is anterior pituitary a part of brain? Yes or no? No.

What do you mean? Of course no, no, no, big no, no. Is posterior pituitary part of the brain? Yes. I have, do not confuse that fundamentally. Okay. Is anterior, so there is no question of anterior pituitary being out of the, it is, the capillaries are like anywhere else.

Actually one of the basic criteria of an endocrine gland is that the capillaries which pass through them are abundantly, those capillaries have lots of pores.

Okay and those pores ensure that what all the hormone that is being secreted by the endocrine readily gets into extracellular fluid, gets into the capillary and then it is taken everywhere. So there are plenty of, there is free traffic, free traffic, it is not, it is not. Here let us take a look at the, so what are we looking at? We are looking at a growth hormone secret. So remember we had that fluorescence slide where we had several growth hormone secretes, I take one cell from there, one cell and then blow it up here, okay so far. And this cell will have two receptors, what is it? GHRH, okay and it will have receptor for what? Somatostatin, this is the structure of somatostatin here, same somatostatin which is from the beta cells and I am sorry what cells? D cells, okay or from the stomach, okay and so this will act on and what is the common feature of both the receptors? So, there is some transmembrane G protein coupled system, so growth hormone will have the receptors and then they are, whereas this, okay will bring about stimulate adenine cyclase whereas somatostatin will what? You can see there, it inhibit, okay.

So somatostatin given cyclic AMP concentration will go down and the cell will be inhibited and it acts here and then this gives rise to enzyme, I am sorry, the some genes will be activated and growth hormone and growth hormone will come into the circulation. Here you have the, this is an extremely rare condition but whenever we talk about growth hormone we generally talk about couple of diseases. One is a very famous example of Robert Wadlow, he died very young of course but he had a tumour in the pituitary gland and as a result of that he had excess of growth hormone secretion and that was at early stage, so his height was something like 7 to about 8 feet, okay, are you getting it? And then he had diabetes, are you getting the same argument? So that is called as, that disease is called as gigantism, what is it called as? Then you just put this in Google and you will get the image of Robert Wadlow, an extremely tall person. The second thing is if you have the disease, I mean Robert Wadlow had the disease when in the growing age, as a child of 7, 8, 9, 10 he started growing tall and tall. If the growth hormone secretion is accelerated a little later, what do I mean by little later? I will explain this point and I will stop now.

We have long bones, what do you have? Long bones. Follow this diagram, I will try to explain it very quickly. This is a long bone of your body, maybe in the hands, maybe in the femur, are you with me? And the length has to grow, if you have to grow in the height, it has to grow, okay. Now these cells here, the bone here is still not fully formed at the ends. This part is called as epifacial disk, what do you call it as? Say that again.

And these epifacial disks are abundantly equipped with receptor for IGF-1, okay. And as the child is growing, these epifacial disks, they help in the laying down of the bone and growth, so the bone keeps on growing, growing, growing, growing. And as an individual reaches adolescence, reaches what? Adolescence. Particularly in the case of girls and also in

the case of boys, it is with the onset of menstruation, there is a surge in the case of estradiol hormone and that estradiol hormone completely stops the epifacial disks. So that is the end of the epifacial disk and therefore there is end of any growth in height, okay.

Are you with me? So that is it, that is it. Because estradiol has effect that is exactly opposite to the effect of IGF on the epifacial disk. So you grow, grow, grow, grow, grow to a particular point and then there is increase in the case of what? Estradiol, okay and then what about the boys? It does androgy, does testosterone have a similar action? No, in the case of boys also it is estradiol, okay. Estradiol is the same function which is anti-epifacial disk, okay which completely seals the, which seals the disk epifacial cells are not there anymore and then the bone is completely solidified and then this bone cannot grow.

It can remodel but it cannot grow. Why? Because epifacial disks are finished. The cells of the epifacial disk are cells. There are lots of cells. When you are, we are born with lot of cells, they are just near the ends of all the long bones and they are under the influence of the growth hormone and the IGF and they keep on and that number goes on, number goes on reducing, reducing and reducing as you grow and finally when you reach adolescence, hardly any cells, the reparative hormones, the cells are dead, no more growth. Are you getting the importance of that? Okay, alright, so this is the beauty of the, okay and this is the case in which a person has full, an adult now and has a problem with excess of growth hormones, okay and the disease is in the, then the bones of the jaw and the bones of the face and the bones at here, they become very thick, okay and that condition is called acromegaly. What do you call it as? Acromegaly. Okay, I will stop now.