Human Physiology
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Lecture – 55
Thyroid gland : Part : 2

Oh, this is a small word model of human pendrine protein. This also is how many I don't know. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11. When there is endocytosis happening how do you make sure that you are only taking the iodinated thyroglobulin and not non-iodinated? Is there any comfort? The answer to that question is, that is a very good question. The answer to the question is, it just takes it randomly. No, no, I will tell you.

No, no, no, no. It just takes, that is a very good question. It takes, his question is, when the process of endocytosis is happening and the cell is taking in, are you sure that it is taking only T4, T3 or only tyrosine? The answer to that question, it can take anything. But if it takes tyrosine, it will be sent for processing again.

If it is T3, T4, it may be used for sending it to the blood. You got it? So this is a quick look at the pentrine molecule and let us see. We are still looking at, look at the beauty of this slide. We are again talking at what? I am sure you know what this is. We are looking at thyrocyte.

Done? On the, on the basal side, so this is, this is what? This is the capillary. From the capillary which molecule is coming? TSH, the thyroid similar to carbon, it acts on its receptor. And what kind of, I can see it going up and down 7 times with G protein coupled system. And this is, this is what? This is what? This is simple, this is simple system, 13 times up and down. It will take sodium and iodine.

And oh yeah, the author has drawn here, the pump has drawn here, author has drawn the pump here. And to make sure that sodium inside is low so that this simple system can work. And then you have the, and then you have, what do you have? You have the, okay, okay. And okay, and then this is the thyroglobulin molecule which is going here and this is the iodine molecule. This is the iodine molecule is going there.

Can you tell me the name of this system there? Pentrine. That is the protein, pentrine system. You are right. Now pentrine as it goes, okay, the apical cell, the apical site of the, the apical site of the thyrocytes is thrown into villi. Can you identify the villi there? That villi there? Sitting on the villi, right on the villi, okay, is an enzyme.

Can you please read me the, read for me the name of that enzyme there? Thyroid. Thyroid what? Thyroid peroxidase. What is the name of the enzyme? Thyroid. Thyroid peroxidase. So what, and what is the message author wants to give here that right on the villi is sitting this enzyme, the oxidation of the iodine is promoted by the enzyme thyroid peroxidase, okay.

So that iodine has to undergo a little change there. Because of that little change, had that not happened iodine can still combine with tyrosine. But at an extremely slow rate, okay, that oxidation makes sure that the reaction really goes fast and then as a result of that we have, we have thyroglobulin molecule has, is this, do you find any iodine here? No, this guy has got iodinated and as a result of that you can, you can get mono and diiodotyrosine molecules which are all over into the. Sir, what does an arrow show? Which one? The torque between two OH. Oh, this is the, you mean, I am not getting your argument, you are talking about this arrow? I do not know that, I do not know that, it is chemistry you deal with it, okay.

So author tells us the importance of the peroxidase enzyme and oxidation so that iodine can combine with the, this process is also called the organification, let us move on. So okay, the pituitary has released TSH, why has pituitary released the TSH? Pituitary, of course, steady TSH is always going, okay. I suddenly put you in a cold place, so there is a challenge on you, what is the challenge on you that you need to maintain your body temperature, okay. So how do you realize it? Well, you have thermo receptors, they are on your skin, they are on your hypothalamus, they tell your brain that there is an assault, there is a challenge with reference to temperature, it will trigger many things including behavior, okay. And then one of the important things it will do is to stimulate, is to tell the hypothalamus, okay, hypothalamus, follow with me, hypothalamus.

Hypothalamus will release a peptide called as TRH, what is it called as? Thyrotropin releasing hormone. And this peptide is particularly interesting because it is made up of only three amino acids, one of the shortest peptides, how many amino acids? Three, very short peptides, extremely short. And it is coming from the hypothalamus, it goes to the median eminence, hello, are you with me? And in the median eminence by way of hypothalamo, hypophytial portal system into the anterior pituitary gland, in the anterior pituitary gland you will have the TSH cells, those TSH cells in their plasma membrane will have a receptor, the receptor is for TRH, that receptor is also 7 transmembrane G protein coupled system. Hello, are you with me? Very simple, same, biology is very repetitive, same thing, G protein coupled system, but the receptor and then the cell will release TSH, okay. Now why is your system releasing TSH because your system wants, so that you can meet the challenge of the cold around you, you need to raise your metabolism, okay.

And the, the, the system that will help you to adjust your physiology to the lower environmental temperature is TSH and eventually T4 and then T3 and then it will have its effect on all the cells so that metabolism everywhere will go up so that now your body is capable of generating more heat, literally generate more heat, okay. So, so under, so we are

looking at a follicle, can you see the follicle there? It is interesting, just do not, do not miss the point. Can you see the follicle there, single follicle there? When you look, can you see the collide there in the middle? You find something interesting on the periphery of the collide? Can you see there? There are certain punches, you know, there are certain hollow areas, okay. That hollow area is because these cells of the cell will release enzymes. Those enzymes will chew up that part of the collide which means actually what T3, T4, okay and take them by endocytosis.

But when the harmony is being broken down in the collide and being taken in, the collide looks like this with these vacuoles, those holes. They are actually not holes, we call them as vacuoles. What do they represent? Are you with me? So there is a complete collide. Let us see. We are looking at a, let us see, we are looking at a resting thyroid.

Okay, so far no problem, resting thyroid. No TSH, just resting. Now suddenly the TSH started coming. So thyroid is excited. So thyrocyte is excited.

What will it do? It will release enzyme. So these cells will release enzyme. Originally this was a smooth follicle, smooth, I am sorry, smooth outline of the collide. Under the influence of the enzymes, this part of the collide is digested, can you get my language, broken down into what? A single T3, single T4, single T4, T4, T4, T3, T4, may be reverse T3, whatever. And then they are, so and then they are taken into the cell.

But then this vacuole has remained. Occurrence of vacuole is an, is a histological indication that thyroid is very active. Are you with me? Of course one direct proof will be to take up gland and evaluate T3. That of course one proof is there. But other proof would be this indicates that the thyroid gland is active and under the stimulation of the TSH.

So T3 and T4 was formed after proteolytic leakage inside the cell. So how is the, how are the enzymes working outside of the cell? You are referring to this? One side before the This is the same. After the endocytosis, yeah, after endocytosis process proteolysis. Yeah this, this. You are talking about this, right? This, okay.

Actually it is not so hard and fast. It is the, this, this image does not really convey that. Or let me put it this way. The digestive enzymes will be released. T3, T4 will be broken down and then taken in, okay.

So, so it does not really matter. I mean the, the, you are asking whether it is broken down here, whether it is, you are asking whether it is broken down here or here. Okay. That does not matter.

That does not matter. What, what really happens is the, ignore this diagram, solve your problem. What is really happening is the enzyme is being released. That vacuole slide is correct, okay. This is diagrammatic. The, the, the message here is the molecule is, the molecule is being taken in.

Exactly where it is taking, what I am telling you is correct. It is happening in the colide, in the colide that is where broken in, that is where it is taken in and that is what it is released. Your question is, is the thyroglobulin molecule being taken in the cell as it is? No. No. What is being taken is? Get rid of whatever the image says.

What is taken in is what? No confusion. Good. Sir, does TSH also stimulate release of more thyroglobulin in the… Just say that again. Does TSH also stimulate release of more thyroglobulin inside the… Oh yeah, yeah, yeah, yeah, yeah, yeah. You are, you are asking does TSH promote the production of thyroglobulin within the thyrocyte? It promotes everything that is necessary for the formation of T3 and T4.

Okay. Okay. Now one mistake correction. I made a mistake. I told you what? Thyroglobulin, that is correct. The protein that is there for the transport is called as what? Read here for me.

Thyroid binding globin. I made a confusion there. So I am talking of two proteins. Two proteins. One protein is tyrosine, tyrosine, tyrosine, tyrosine 70.

Okay. What do you call it as? Thyroglobulin. Now T3 and T4 have come into the blood. Into the blood they combine with a protein molecule. That protein molecule is called as what? Please read for me here.

Thyrosine binding protein. Thyrosine binding protein. Okay. And actually we have seen this slide. So this is huge. Can you, this, this, the molecule is very large.

Can you see this tiny part? What is this tiny part? T4. What is it? The T4 is there. On entering the blood over 99 percent of the thyrosine combines immediately with the several other plasma proteins and one of them being and, and the moment it combines we actually know the reason for that. What would be the reason for that? To prolonging the half-life and, and the half-life of days.

Yeah, you are absolutely correct. Okay. Somebody had asked a question as to where, where is, is the T4 bound to the globulin molecule in the blood? The answer is somewhere here. Let us see. So this is a thyroid binding protein or thyroid binding globulin. Huge molecule we have seen in the previous slide.

It is bound to what? It is bound to what? T4. Okay. What about T3? Is it bound? It is not bound. It is free. Okay. The, the T3 can, the T3 can, because it is only T3, it can easily flow out of the capillary.

Can the, can that larger molecule flow out? No. It is bound to the protein. Okay. So, so T3 can easily come out or T4 can separate.

Okay. Okay. Under the influence of diazinase enzymes and then T4 can come. But once it comes T4 is again converted into what? T3. What are, what is the message we have here? The message is simple.

T4 is the storage part. Okay. It is availability. It is an available part. But what is really dynamically important is? T3. Is really T3. This is, yeah, look at this slide.

T4 half-life is about, half-life itself is 6.2 days. So it will, it actually, it will be for another 10-15 days. I do not know how long.

Half. Half. This is, yeah, yeah, yeah, yeah. Half-life, no, no. If you inject 100 micrograms, it will, it will be 50 by half-life is so much. Whereas the half-life of T3 is about how much? One day. One day. But, but if you give, if you inject radioactive what? T3 and T4, so much is then, it is, it is, you still get it in the blood for a very long time.

So you can, how much, how many days will it survive? Almost 10 to 11 days you will get. What is the aim of this slide? Just to tell you that these hormones are very slow acting. They remain for a very long time and out of the two again, the T4 has much more, much longer biological half-life as compared to, as compared to what? T3. Okay. Is there a mechanism for the kidney to re-absorb T3 because one day is like a very big, even though it is a very big.

No, no, no, no, no, no, no. T3 goes, it goes, it goes. It goes means it goes. There is no question of recovering it. See the point is the, at any given moment the amount of T3 being given is very little.

Okay. And what is given is one way traffic. Okay. It can be, there are deiodinases that can break down that iodine can be circulated. Iodine is circulated. Are you with me? Wait a minute. What let us take? Okay.

There is a cardiomyocyte in which the T3 has gone. In that, in that, in that cell iodine has been removed. Okay. That iodine can go back to the blood, it can go back to the thyroid and it can be re-circulated is the point well taken. So iodine can be, but that tyrosine will be metabolized whatever and the, it is a very slow, this, this hormone system is very slow acting. What do I mean by that? Is they say that you give an injection of a T3 or T4 to the rat and for about 12 hours or 24 hours nothing happens.

Okay. And then slowly the rate of metabolism will start going up and, oh I am sorry, I have not even, how many days we are talking about? The rate of metabolism will go up after how many days? Peek at about how many days? 10 days actually more than that. Okay. And then it will go down by about how much? By about, yeah, so it is a very slow acting system because it activates a huge amount of enzymes.

Okay. And they keep on generating the energy. The, your capability to withstand the cold will be greatly compromised without T3 and T4. Get this point loud and clear. So thyroid hormone increase transcription of large number of genes. Most of the thyroid secreted thyroid is T4, T4, basal metabolic rate goes up. Let us go here, let us go here, let us go here, basal metabolic rate goes up, let us go.

Okay. Just one impact on the heart, looking at the heart. I will draw your attention to the first image. Look at the heart and that is the ECG there, diagrammatic for us, that serves the purpose. Is it a normal one? Hypothyroidism, the thyroid has gone up.

Look at the ECG. Look at the hyperthyroid. Okay, where too much is thyroid? Look at the ECG area. Can you get a clear difference between, so this is just, this is just heart. You will, almost every organ, okay, you will find that it responds to the effect of, what is this? This is hypothyroidism.

The blood vessels stiffen there. Heart rate increases. This is not only the response in which every, this is the strength of the response, this is the frequency with which heart is beating. Almost everything goes up under the influence of T3 and T4. Skeletal system same hormone, temperature regulation is most important. This figure, does it tell you anything we have done it in the school? We are talking of frog, frog.

Okay, we have seen that the female frog will lay eggs in the pond. From the eggs within a matter of week or so, the eggs will hatch and the tadpole will come out and as we know, within a period of the tadpole will feed on the vegetation around, it will grow and it will, then what? Metamorphose and then become an adult. We have done it. Yes or no? Good, good. That entire metamorphosis depends on one hormone thyroid.

What did I say? Just one hormone. And our classic experiment in endocrinology that has been done long, long time back is you get tadpoles, we can do it even here, even on the campus we can do it. In June the month of July you can collect tadpoles from the pond. All you need to do is to add, add what? Injects. No, no, no.

Just in the, in the, in the bath, okay, in the jar you add thioria, thioria, okay. The thioria it, it binds with the iodine picking system and then the animal is chemically, the animal is chemically thyroidectomized, are you getting my language? Chemically. It is so small you cannot, you cannot surgically do it but you do not need to. And when you remove the thyroid obviously there is no T3, T4 and then as a result of that the tadpole becomes, tadpole remains a tadpole, becomes very big. It is still a tadpole, okay. And to that animal it is very, it is very, I mean it is actually becomes much larger, five times larger than a normal tadpole.

But it is not able to metamorphose. On the other hand if you take a tadpole and if you give it T3 or T4 which is available in a pharmacy, readily available, T3, T4 is very cheaply available. You will find that the tadpole will immediately metamorphose and you will get a tiny froglet. It is a frog, it is metamorphosed. It has lost its tail, its mouth parts are different, it can now feed an insect but it is very small, okay. So the classic, classic if you want to demonstrate the classic beauty of endocrinology you can just do it on the, on what? On the, on the process of metamorphosis, just one hormone is necessary for the process of metamorphosis, okay.

Okay, anyway let us to look at it. We have a, any cell, any cell, T4 comes in, T4, can you read there? T4 comes in, converted into T3. T3 can come in, that happens because of deiodinase and then it goes, okay, so there is a receptor, the big protein, it is generally, so there are two proteins, one is the different proteins, one is thyroid hormone receptor, it is with retinoid X receptor, the, the T3 will combine here, it will, it will trigger a number of enzymes and then as a result of that what do I have here, I can read. Many other systems, growth, CNS development, cardiovascular, metabolism, so everything, zodium potassium pump, oxygen consumption, glucose absorption, everything, almost everything, every biological action you can think of is accelerated by way of this enzyme. This is the, I will show you, we are looking at the, we have section through the pit-tory of rat, step number 1, okay and then I am going to show you staining with what? It is pit-tory, so TSH, we are going to take what? The antibodies against TSH, we are actually not going to take antibodies against TSH but I will show you something more interesting.

Listen to this, wait, wait, wait, wait, wait, I have to retain your interest. No, no, this is really interesting, look at this. I am talking of 4 different hormones. How many hormones? 4 different hormones, okay. Out of that 3 are from pit-tory gland, what is this hormone TSH? Okay, so far, what is the other hormone LH? We are going to talk about it, controls reproduction.

Are you okay so far? What is the third hormone? FSH. So FSH, LH and TSH, these are the 3 hormones, they are all secreted by what gland? Pit-tory gland. Are you okay so far? The fourth hormone author talks about is the HCG. HCG is for what? Human, very good.

Chorionic, it is a hormone for the placenta. Are you okay? All these 4 hormones are dimers. There is a protein chain, there is a protein chain, they come together and you make the hormone. Okay, now I am going to make a very interesting, look at the coding there in the image. Look at the coding there in the image. Across all the 4 hormones, alpha chain is same.

Alpha chain, alpha chain, alpha chain, alpha chain, alpha chain is same. What is different is what? Beta chain. Different is what? Beta chain. Okay, are you with me? So for the specific activity what is really important is, is the beta chain. Is what? Beta chain.

So what authors have done in the previous slide is, they have isolated the beta chain. Got the point? They have isolated the beta chain, generated antibodies against the beta chain and used those antibodies to stain. If you had done the entire, then what you will have? You will have the pitotory in which you have labeled LH, FSH and TSH. Got the point? Therefore you are not interested in making an antibody against alpha chain. You are interested in making antibody against? Beta chain.

Beta chain and therefore this is, therefore now you can appreciate the wording here. Can you read what is written here? TSH beta-minimetric cells in the pars distalis. Pars distalis is anti-reputery.

Pars distalis is what? Anti-reputery. You have done that. Anti-reputery. Anti-reputery is called as what? Pars distalis. Pars distalis. Okay, pustipitre is also called as pars narvosa. Very good. And these are the cells which are okay.