Human Physiology
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Lecture – 54
Thyroid gland - Part : 1

So, what were the two hormones we talked about that are being released by the posterior pituitary gland? Oxytocin and vasopressin. Oxytocin and vasopressin, they are actually synthesized where? In the hypothalamus, in the hypothalamus, different nuclei. And then we also talked briefly about the six different hormones which are secreted by what anterior or posterior? Anterior. Good, good, good. And out of those six hormones we focused on one particular, what was that? Growth hormone. That was the growth hormone.

Good, good, good, good. Now we will talk about the other hormones when we talk about the respective gland. So what we are going to do now is I am going to, let us, oh this is a very exciting organ. And I hope you are familiar with it because you remember we saw the slide.

Slide of what? Slide of what? Slide of what? So in the lab session when we saw these slides, we had a lab session. We are in sixth semester. We are doing animal physiology. We had a lab session. There we saw some slides.

The microscope, that apparatus that helps to magnify and see. And one of the slides that we looked at was what? Thyroid. What was it? Thyroid. Okay. So let us talk about this thyroid.

It is a very interesting gland. I will tell you why. In the humans it is situated right on your trachea. You know you have trachea, just outside the trachea. So this is your trachea.

Okay, this is your larynx at your sound box. And so can you see this butterfly shape? There are two lobes which are connected by a tiny isthmus. This is thyroid glands, one of the largest endocrine glands in the human body, weighing almost 15 to 20 grams. It is very large. And this gland is also interesting because it represents one of the most, one of the organs that has very high blood supply.

Okay, very high, very high. I think it is number 2, number 1 is adenocortex. Huge amount of blood keeps on flowing continuously through the thyroid, to this thyroid gland. Now this gland is important because let us appreciate the importance of the thyroid gland right in the beginning because it secretes two hormones called as T3 and T4. Why T3, T4? We will see.

These are the two hormones which are released. They have a profound influence on our metabolism. What do I mean by that? The rate at which oxygen is being used in every cell of your body. It is being used at a particular rate. It can go down, it can go up, whatever.

Depending on your biological need. And what are the factors which control the metabolism? Mitochondria, most important. Mitochondria could do it. The sodium potassium pumps everywhere, they are everywhere. The rate at which oxygen being used, all those factors and all the enzymes which are involved in that activity are under the control of T3 and T4.

So important. Okay, means if I just remove your thyroid gland, you will still live, you won't die. But the rate at which you are using oxygen may just fall to 50 percent. And accordingly every eat and every activity that you undertake, your brain would be as good as a vegetable. It is so important. It is so important.

And every mitochondria, no matter which tissue, it has such a profound effect on the metabolism. Rate at which we are using the oxygen. It all depends on the thyroid gland and the thyroid hub. So what we are looking at is a, so we take the thyroid gland of the rat, it is an experimental animal.

We fix it. And this is the slide that we saw in our end. We also observed something very interesting about this endocrine gland. We said that this is the only endocrine gland that stores the hormone extracellularly. Okay, you remember that? So here we have a follicle. What do you call this as? A follicle.

A follicle. Are you okay? So what we have here is a, there is a cell here, there is a cell here, there are several cells and they make a tiny follicle. Okay, and the diameter of the follicle is about 100 to 300 microns. Okay there is one cell may be 8 or 10 microns across and they create a human inside. And this human contains the secretion. And we call that secretion as the colloid.

So what is colloid? It is a secretion. What colloid contains, I will tell you a little. It is a secretion. Why all the cells? So there is lot of interaction happening between the cell and the colloid and the colloid serves as a storehouse.

Okay. So I will call these cells as the follicular cells. What will I call them as? Follicular cells. Call them as the follicular cells. Okay. Then there are certain cells which are also there but they do not actually communicate with the lumen.

You see these cells are they are all communicating with the lumen. And I will say that each cell will have an apical site. We have done this and a basal site. And on the basal site there will be a capillary here, a capillary here, there will be capillary here. A capillary will not go in the follicle.

Okay. So what is this? These are all what cells? They are all follicular cells, single layer cells, single, single, single. Actually we have seen this 100 times in a form of a tube. Is always a tube? The kidney, there is always a tube. Okay. And there is apical site, basal site.

Here it is not a tube, it is a follicle. Then there are some cells which are in this very gland, there are cells and cells and cells and those cells are, if you see this, I will draw your attention. So can you see this follicle clearly here? Each blue dot here represents a nucleus. Its hematoxylin strain, it represents nucleus. The cytoclasm is very weakly stained.

This is the collide. And then you get, you get to see these dark brown cells. And if you, if I draw your attention here, you will find that they are not directly committing a contact with the lumen of the follicle. Are you with me? Yes or no? I will call them as parafollicular cells. Follicular cells, parafollicular cells.

Got the name? Okay. You got it? So those cells which are directly making the wall of the follicle and directly coming in contact with the lumen, okay, which have an apical phase, I will call them follicular cells. Those extra cells which are also in between the two follicles, okay, we will call them as what? Parafollicular cells. We will call them as the parafollicular cells. Why are we talking about parafollicular cells? Remember, they are parafollicular, parafollicular. They are a source for yet another hormone.

That hormone is called as calcitonin. What did I say? Say that again. Calcitonin. It is a peptide hormone, very important and it plays an important role in lowering the calcium level in the blood. Okay, so thyroid is a source for thyroid hormones which are secreted by the follicular cells.

In addition to that, thyroid is a source for calcitonin and what is the actual source? The cells which are parafollicular, okay. And how did I label the cells here? I labeled the cells because I got a section of the red thyroid, okay, standard with antibodies against calcitonin, okay, and that is the immunoreaction I got and I know that I am looking at calcitonin secreting cells. That is all I am going to talk about calcitonin secreting cells and calcitonin. I will get back to our main story and our main story is to focus on what? T3 and T4. So this thyroid gland belongs to the thyroid hormone, belongs to the category, we had three categories, one was steroid, one was peptide, one was, second was steroid, right, and the third was tyrosine derived.

So T3, T4 belong to what category now? Tyrosine derived. Tyrosine derived, okay. So here I have at the top, we have, that is the structure of the tyrosine amino acid and there is a single 6-membrane ring there. Okay so far? Yes or no? Yes. And now this is, this is taken up in the, this is taken up in the thyroid follicular cells, follicular cells and there it is acted upon by an enzyme called as, what is the name of the enzyme? Iodinase.

Iodinase and then you can have, so you can introduce one iodine somewhere here. So can you see that iodine there? Okay. Now where are we? We are in the cells of thyroid gland. So thyroid gland has got an enormous capability, okay, of accumulating tyrosine and also iodine. How it accumulates that, I will show you a little later.

So the moment one, this molecule gets iodinated, we will call it as what? Monoiodotyrosine. Monoiodotyrosine makes sense. Monoiodotyrosine, just one iodine. If I add one more, I can call it as diiodo.

So here we have a diiodotyrosine. Okay. Now if I were to combine a monoiodotyrosine with a diiodotyrosine, now please remember each one has a single six membered ring. Single six membered ring, six membered ring. If I were to combine them, okay, then I might have a molecule in which there are two six membered rings and one, two, three iodine. If I were to combine one diode with another diode, I will have the similar molecule. Before iodine, are you with me? But since there are two rings, two six membered rings here and here, I will not call this as tyrosine anymore.

I will use the word thyronine. What will I call it as? Thyronine. So had they been single, it is tyrosine. There is no problem there. But since two of them come together, it becomes now what? Thyronine and, and. So if I have a molecule in which there are three of them, I will call it as what? 3, 5, 5 prime, read for me triiodothyronine.

If the four of them are there, I will call it as what? Tetraiodo. I can call it as tetraiodo. I can directly call it as what? Thyroxine. And those two of them who will take this big name, so when three are there, we will call it as T3. And when the four are there, four iodine are there, what will we call it as? So we are, this we are looking at the same time, tyrosine, iodination, monoiodotyrosine, diiodotyrosine coupling and then you will have the, you will have the.

Now, this is a interesting term there. Just see, very simple, we are looking at tyrosine, same thing, looking at the same thing. This is a tyrosine molecule and this is the four of them. So this is what? T4.

This T4. Done so far? Be with me. This T4. Okay. And if I remove this I from here, okay, or if I have one diado and one monoiodo, I will have this molecule. But please remember one thing. See, there is an amino group there. There is a benzene ring, six membered ring, near to that, it has two I I.

Be with me and then there is a single I. Okay, so far. Now, if I have a system in which this I does not sit on this but goes to next one. Does it happen? It happens. Okay. Such a molecule is called as reverse T3.

So get a clear difference between a T3 and reverse T3. Okay. It is just a question of I going from here to there. There are two rings, if it remains here, okay, and it is very important because whereas T3 is one of the most powerful hormones, reverse T3 is useless. It is wrong for me to call it useless but I am calling it useless because as on today we do not know what it really does.

But it is there in the blood. Okay. T3 is there in the blood. Okay. But what is the physiological significance of reverse T3? Okay. We are here to find out. So please remember very highly this is the T4, this is the T3, both of them are very meaningful and reverse T3 is relatively.

Sir. Are T3 and reverse T3 interconvertible? It is, they are not interconvertible but there are enzymes. Okay. There is, I will talk about it a little later, there is a deiodinase enzyme. Okay. That deiodinase enzyme can remove it, can remove it and there are also iodinase enzymes.

So you can remove, one enzyme can remove it, another enzyme can put it and then you can convert this into that. Okay. So there is a theory that reverse T3 also serve as a reserve for, for, that thought is there, I mean that it is, it is debated but it is, it is, the thought is there in the literature.

Okay. Then we will find that, okay, so let us see. So we take a blood, take blood sample and we evaluate how much of T3 and T4 are there. We generally find that of the total amount of the T3, T4 about 93 percent is T4 and 7 percent is what? T3. So they are not 50-50. Okay. So the most dominant, dominant hormone in terms of concentration, it is T4.

Now although T4 is a very predominant hormone, okay, the biological activity mainly resides with T3. Okay. Then how does it work? How does it work? Whenever T4 enters into the cell, it loses one iodine with the help of an enzyme called deiodinase, T4 is converted into T3 and it is actually, T3 does all the, does, all the biological activities are mainly carried out by what? By T3. Okay. So we need, so this is the only molecule in the body that requires iodine.

Okay. And without iodine we cannot really do and therefore we have iodized salt. Okay. So here we have, so our biological need is about, is about how much? Is about 50 milligram, 1 milligram per week.

We need, we need 1 milligram per week of what? Sodium iodide. Okay. Iodine salt we need it so as to, and our body has, thyroid has enormous capability of storing iodine. Okay. So even if I cut your total iodine intake, okay, you are still good for 2-3 months. Okay. But after that of course your iodine supply will go down and your rate of metabolism will certainly go down.

Alright. So let us see. So in the, so we are talking about a single cell. Just focus on single cell. We are looking at a single cell. And this single cell has a, an apical site and on the apical site this is the colloid and this is the basal site and there is a capillary somewhere here. So there is a capillary somewhere here, then there is a extracellular fluid and there is a, and there is a basal membrane.

Are you okay so far? In the basal membrane as usual there has to be a large number of sodium potassium pumps which are not so near but they are there, have to be there. As a result of that there is inside sodium, never forget inside sodium concentration may be 10 or 11 or whatever milliequivalents per liter and outside will be 142 or whatever that has always got to be there and as a result of that, as a result of that you have this simple system which is continuously working. What is this simple system? Look at the diagram and tell me.

Sodium ion. Sodium ion. So sodium goes in because there is a, there is gradient, okay and it pulls along, okay, a simple system it takes the iodine, okay. And therefore this molecule is called as iodine trapping system. Some people also call it as iodine pump but I am, we are little, we are little not happy with the phase because the moment you use a word to pump, ATPase comes in, there is no ATPase there, okay. The power is coming from sodium and the sodium, the power in the sodium is coming because of the sodium potassium pump which is a separate molecule, okay. So here we have the, so we have this sodium iodine simple system which is sitting in the and it is capable of any moment, at any given moment it is capable of accumulating iodine within the cell, that cell or within the follicle put together.

Iodine which is about 30, 40, 50 times more than in the blood. So if my whatever is, is iodine there in the blood, it is there. You see we are eating iodine, okay. We have to eat, okay. It is there and it is concentrated within the cell.

Why? Because of the, because of, because of simple system, okay. Now to the rat if you give an injection, even a single injection of TSH hormone, get the experiment. What am I doing? I have two groups of rats, okay. To this group I am injecting saline which is my control and to this group of rat I am injecting TSH hormone. Where do I get it? I can buy it from sigma, okay.

I will get that dose from the literature, okay. And then I will give the injection and wait for about 8 hours, 12 hours, 24 hours or so. And then I will try to evaluate the amount of iodine, iodine in the thyroid of this guy which is TSH injected versus the control. Are you with me? Experiment is good so far. I find that here the iodine concentration is about 250 times more as compared to the blood, as compared to the control where it is 30 to 40 times more than that of the blood. What is my take home message? That TSH has greatly stimulated the iodine trapping mechanism.

Actually what happens is that simple system, whatever is the number of molecule, that means that TSH has gone, it has influenced the entire, the necessary machinery of the cell so that you have far more number of copies of this import which go and sit in the plasma membrane and they start very aggressively taking the sodium ions. I made a mistake. Taking what ion? Iodide.

Good, good, good. And this is the, look at the huge molecule it is. What is this human sodium iodide importer? It goes up and down the plasma membrane. How many times does it go? 13 times, 13 times. This is the, NIS is what? 643 amino acid glycoprotein with 13 membrane spanning domains etc.

You can read about it. Just read this point. Families with congenital mutation of NIS gene are associated with what? Got the message here? Message is very clear there. Now this thyroid hormone, we spoke about this once, one of the earlier lectures also. It is carried along with the blood. It is bound to a very large protein molecule.

Since it binds to T4, to T4, it is called as thyroglobulin. It is a globulin molecule. We will call it as thyroglobulin. So what is it? It is a protein molecule that is in the blood and it can, so this is a huge protein molecule. I do not know how many amino acids are there. But the molecular weight is about how much? Can you read for me there? 335,000.

That is what? That is the molecular weight of a protein molecule. What is that protein molecule? It is, and where is it? It is in the blood. It is in the blood. So the T4 particularly the T4.

It binds to T4, it does not bind to T3. So T3 is what? T3 is free. T3 is free. Okay? And T4 and T3 are always in a ratio. 93 is to 7. Okay? And in the course of time, as the T3 is being used, used means what? It is getting the capillary, gets out the capillary, goes to the target organ and does its business.

Okay? So that 7% has gone to 6%. Now this T4 which is bound to thyroglobulin will release. We have done this point. Okay? So thyroglobulin serves as a reserve. Okay? To make sure, always make sure that the free hormone is always there in the right concentration available for every cell to regulate its metabolism. Got the idea now? Hello? Are you good so far? Yes.

There is also some T4 freely present in the blood. It is, there is, there is, there is, there is, not that every molecule is attached.

I have a slide on that. Okay. This is a very nice slide. Let us look at it. Focus on this slide if you understand this 90% of the job is done. At the left corner there is a single follicle there. Good. What author has done for us is he has picked up a cell, he has blown it up here.

So now we are looking at the cell here. What do you call the cell as? We will call it as a thyrocyte. Thyrocyte. Okay? It is a cell, thyroid cell. Okay? Good. This is the cell, this is the basal side. Okay? This is the blood capillary, the extracellular fluid, this is basal side and this is the apical side.

In the apical side you have this fluid which we call as colloid. What do you call it as? Colloid. Colloid. Good, good, good. And in the, as we have already seen, on the basal side we have this interesting protein system. We have already seen that in the 13 times going up and down.

Okay? That is this molecule, what do you call it as? Sodium iodine simple. Sodium iodine simple. We are okay so far? Now this sodium, this iodine as it gets in here, so we have now far more iodine in this as compared to blood. In the control at least 30 times, 30-40 times more. Now it is taken on the apical side, there is another protein. What is the aim? What is the aim? The aim is to take iodine from the blood into the cell and from the cell into the lumen of the follicle.

Why? Because that is where we are going to use it. Okay so far? For that, for the transport of the iodine here, we have this sodium simple system. On this side, we have another protein that transports the iodine ion from inside the cell to the lumen but it does not need sodium. It is called as sodium independent iodine transports protein. Are you with me? It is named, it has a specific name and that name is called as Pendrin.

So what is Pendrin? It is a protein. What is Pendin? It is a protein. It is sitting on, where is it? It is a thyrocyte. Where is it on thyrocyte? Apical, basal, lateral where? Apical side. Apical side. What does it do? It just takes iodine without the help of sodium.

Are you with me so far? And then it will take and this iodine will go and then iodine is oxidized. We will talk about it a little later. Now this cell is doing something else. So there is a nucleus in the thyroid cell and then whatever genes are activated and what it is really doing is it is synthesizing a thyroid cell.

It is synthesizing a molecule called as thyroglobulin. Let us talk about this now. Let us try to separate the two. There was a transport thing.

We will talk about it. I will come to that a little later. Let us talk about this molecule. So what we have here is a tyrosine. We have a polymer of tyrosine. Means what? Tyrosine, tyrosine, tyrosine, tyrosine, tyrosine.

That is what the amino acids do. It goes to about 60 or 70 amino acids. And then we will call it as the, what do you call it as? Thyroglobulin. Are you with me? Hello? What do you call it as? I made a mistake. What do you call it as? Thyroglobulin.

The transport protein, I will come back to that. We will call this as what? Thyroglobulin. Now this thyroglobulin is what? If you walk along the molecule, you will have 70 bits and this is a tyrosine. So far, now what the molecule does is, when the tyrosine is still a part of that bigger molecule, bigger polymer, it can get iodinated. Means you do not have a single tyrosine, single tyrosine, single tyrosine, iodinated, iodinated, iodinated, then link it up.

No. But why do you link up? Why do you link up? Because that is the way the molecule is stored. How is the molecule stored? It is stored as thyroglobulin. It is a 70, it is made up of 70 tyrosine molecules and then it is iodinated. It is still a part of the big molecule.

Am I getting the story right? So you have molecule, polymer, made up of how many tyrosines? 70. It is one molecule. It is one molecule. And then you can iodinate it. It is still a part of, it is still a part of. But then how do you release it at T3 and T4? You release it by, the cell will release an enzyme, it will break it up and then you will have T3 and T4.

Those T3 and T4 will be taken into the cell and then it will be taken. So let us see, let us see. I will draw your attention to this molecule and I will draw your attention to these two molecules. Can you tell me the difference between those two molecules? These are, these are, those, those. Can you see those purple dots there? What are those purple dots? The iodine, iodine, iodine, iodine, iodine, iodine. And if I, if you see here, there is a single six membered ring, single six membered ring, single six membered ring, there is still tyrosine.

And then I will draw your attention. This is the author calls it as conjugation and then what change you have gone from here to here? How many, how many rings are there? So what molecule is this? So this, this is, this may be, this may be diiodotyrosine, diiodotyrosine, diiodotyrosine, monoiodotyrosine, but these are now, these are all the thyroglobulins, may be dihydro. So this is the, this is not at all iodinated. Are you with me so far? This molecule has, how many amino acids, how many, this molecule is made of how many amino acids? 70.

70 amino acids. Okay. And then it combines, so this, this molecule comes from here and this iodine comes from here. The iodine is oxy, is, is, is, is, is, is, undergoes a process of oxidation and then it combines and you have iodine here, iodine here, iodine, but this monoiodotyrosine, diiodotyrosine and then this molecule will be taken up, it will be broken down into T3 and T4 and it will release back into the blood. That is the story in short. Hello, am I making sense? Okay, the cell will take iodine, the cell will synthesize the thyroglobulin and then it will go into the follicle, all that.

So lot of, lot of, lot of action is happening in the follicle. Okay. So this is the endocytosis and the follicle, most important, the iodine is going to combine with the tyrosine, okay, where in the, this is all going to happen in the follicle. But once it is done, it will be taken back. Okay, so I will call this process exocytosis, I will call this process as endocytosis and this is again, this is again, this is the release of the, of the vesicles which is again by the process of exocytosis.

Is pendant essentially a channel, like either channel or? No, it is not a channel. It goes ion by ion by ion. It is not a, it is not a channel, it is not a window. It is not a channel, it is not a channel. Okay. Okay. So this is the same image which has been magnified. Let us.