

Human Physiology
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Hello everyone, welcome to another brand-new class of human physiology. Let us recall what we did in our last class; we thoroughly discussed various endocrine glands. We saw how the pituitary, hypothalamus, pancreas, and gonads are different types of endocrine glands that secrete hormones and play an important role in maintaining various physiological functions of our body. In this class, we will discuss glucose homeostasis, and we will also see what conditions can develop in our body if glucose homeostasis is disturbed, which is called diabetes. So, let us start. So, what would the contents for this class be? So, first we will see what glucose homeostasis is, then we will also discuss the importance of glucose homeostasis in the body.

Then we will see about the regulation of blood glucose and the factors maintaining the regulation of blood glucose. Then we will find out what the different hormones are that play an important role in regulation, and after that, we will see what will happen if any disruption occurs in glucose homeostasis. The disease that will develop after the glucose disturbance will be called diabetes mellitus, and the different categories of diabetes, for example, type 1 and type 2, will be thoroughly covered. So, what is glucose homeostasis? Glucose homeostasis is nothing but maintaining blood glucose levels in our body.

And as you know, glucose is the foremost and most important component for producing energy in our body, and without a constant supply of glucose to our cells and tissues, the cells will be unable to generate the energy that is so necessary to maintain our healthy body functions. So, for this reason, the glucose needs to be maintained in our blood, and a proper supply of blood glucose should always be there to transport from blood to the cells and the organs. And to maintain this glucose balance, an important organ, which is the pancreas, is primarily involved. As you remember, in the last class, we also mentioned that the pancreas has two types of different cells: one is beta cells, which are also known for secreting the insulin hormone. And then the other type of cells that we have in our pancreas is the alpha cells.

Alpha cells are important for secreting the glucagon hormone in the body. So, as you remember, insulin generally carries blood glucose and distributes it to various parts of the cells, and also, glucagon helps convert glycogen, which is present in the liver, back to glucose whenever the glucose level is low in our body and maintain glucose homeostasis. So, that is why the liver is also very important for glucose storage and release. As you can see, the liver acts as a glucose reservoir, right? So, if there is optimum glucose present in the blood, then, of course, that would be utilized by all the cells and tissues. But if we ate too much food, then what will happen? Then we will have excess glucose, and excess glucose is never good for the body because if it is always a high glucose condition in the body, the glucose can disturb cellular homeostasis.

So, the body needs to convert this excess glucose. So, in that case, what insulin does is generally convert this excess glucose to glycogen and store it in the liver. So, what it is, is that the insulin will convert the glucose and store it in the liver as glycogen. And this glycogen can be stored for future use in case we need any glucose during a fasting condition; this glycogen

can then be converted by alpha glucagon back to glucose. So, this is the way the liver can act as a glucose reservoir, and this process of conversion of glucose to glycogen is called glycogenesis.

So, this process by which glucose is converted by the beta cell insulin secretion is called glycogenesis. In the same way, when glycogen is converted back to glucose by the mechanism of glucagon, it is called glycogenolysis. So, when the stored glycogen during the first condition can be converted back to glucose, this is called glycogenolysis. And you also need to know this term, gluconeogenesis. In this case, glucose generally forms from non-carbohydrate-based sources.

For example, it can be amino acids, lactate, or glycerol. So, there are certain situations where glucose can be produced from sources other than carbohydrate-based molecules in cases of a lack of glucose supply to the body or even if there is a lack of glycogen storage. So, for example, amino acids and lactate can also develop glucose and maintain the glucose balance in our body through the process of gluconeogenesis. The same way, liver in our skeletal muscle and adipose tissues also has a role to play in glucose homeostasis. As you can see, muscle can store glucose in the form of glycogen, and this glucose can act for ATP production.

In the same way, adipose tissues can also store excess glucose in the form of triglyceride. And this triglyceride can release free fatty acids during fasting conditions. So, the liver, skeletal muscles, and also the central nervous system and hypothalamus, all these organs along with primarily the pancreas are involved in maintaining glucose homeostasis. Then what are the important reasons that blood glucose homeostasis needs to be maintained? Glucose is a metabolic fuel for our tissues. So, this basically produces ATP or energy, and if glucose levels are not maintained, our body can have very low glucose, which is also called hypoglycemia.

A lack of glucose or a hypoglycemic condition can cause severe seizures, as it can cut off the glucose supply to our brain, and we can also become unconscious or even go into a coma. So, maintaining glucose levels and delivering glucose to all the organs, especially to the brain, is very critical because without an adequate supply of glucose, some of the organs may immediately shut down. Chronic hyperglycemia leads to diabetes mellitus. So, if the glucose level is high, and if the glucose level is too high, then we can see a situation called chronic hyperglycemia, which can lead to diabetes or diabetes mellitus. And so, hypoglycemia is when the glucose level is low, and if there is a condition where the glucose level is always persistently high, that is called hyperglycemia.

And as you know, a high level of glucose can damage the cells and tissue. So, they can cause retinopathy, nephropathy, and neuropathy, resulting in damage to the nephron cells, damage to the retinal cells, and damage to the neuronal cells. So, these sorts of different diseases can also happen. So, as you can see, to maintain or regulate blood glucose, we really need to have a normal blood glucose level all the time in our body, and for that, food can be a supplier. So, we can consume the food, and the carbohydrates can break down into glucose, fructose, or sucrose.

So, this glucose mainly comes from the food supply. What are the different processes apart from diet? Apart from diet, glycogenolysis can also happen, which, as you remember, is the conversion of glycogen to glucose, and this is done by the glucagon hormone, right? Gluconeogenesis can also convert amino acids or lactate into glucose. So, all this way, glucose will be nicely maintained. But if the glucose level, for example, goes high, then what will happen? Then glucose can be stored for future use, for example, inside the liver by the process

of glycolysis, like glycogenesis. So, glucose can be stored in the liver by the process of glycogenesis, and it can be converted to glycogen.

And regular glucose in the process of glycolysis generally forms energy. So, in the process of glycolysis, glucose is being utilized in the cells and tissues to maintain normal cellular and physiological functions. It can also be converted to lipid in the process of lipogenesis. So, glucose can be not only stored as glycogen, but it can also be stored as lipid for future use by the process of lipogenesis. So, as you can see, factors that cause the entry of glucose into the blood can include absorption from the intestines, glycogenolysis, gluconeogenesis, or hyperglycemic hormones.

And what are the different factors leading to the depletion of glucose in the blood? It can be utilized by tissues through the process of glycolysis; it can be glycogen synthesis or glycogenesis; it can be the conversion of glucose into fat; or it can even be the role of hypoglycemic hormones. So, these are various factors that can either increase or decrease the glucose level in our body naturally. So, let us see the hormonal regulation of glucose homeostasis. As we said, the pancreas releases two important hormones. The first one is insulin, which we can also call the hypoglycemic hormone.

Why? Because beta cells that secrete insulin in response to high blood glucose and insulin have two roles to play. First of all, it increases glucose uptake by the GLUT4 transporter. So, for example, if I consider that we have cells and that cell has a transporter which is GLUT4. Whenever insulin activity occurs, the glucose that is free-floating in the blood is taken up into the cell by the process of the GLUT4 transporter. And then it can also enhance glycogenesis and store excess glucose in the liver.

Insulin also inhibits processes like gluconeogenesis and lipolysis. So, these are some of the functions of the insulin hormone, and then, oppositely, during the fasting condition, as you know, glucagon, which is also called the hyperglycemic hormone, gets secreted from the alpha cells. So, insulin is secreted from beta cells, and glucagon is secreted from the alpha cells. So, during fasting, in a fasted condition, what you will observe is low blood glucose, and at that time, the stored glycogen will get converted back to glucose in a process called glycogenolysis, and that way, glucose can be maintained in the blood, right? And it also promotes lipolysis, or fat breakdown, to provide alternative energy. So, this is a very important and crucial hormone that plays a role in glucose homeostasis in the body, and in many cases, due to either beta cell destruction or insulin resistance, we observe a prolonged hyperglycemic condition, which is also called diabetes.

We will discuss in a couple of minutes. What are the other different hormones that can also affect glucose homeostasis, such as epinephrine, or adrenaline, which is generally released during stress? It can also promote glycogen breakdown to glucose; in this way, epinephrine can also help control glucose homeostasis. Then cortisol generally stimulates gluconeogenesis and also promotes insulin resistance. Next is like the growth hormone; growth hormone reduces glucose uptake by the muscles to prioritize fat metabolism, okay. And finally, like GLP-1 and GLP, which are incretins, these also enhance insulin secretion from the beta cells and inhibit glucagon release after meals.

So, these are a few other kinds of hormones that also have a role not as important as the alpha cells and beta cells, which can directly control blood glucose levels all the time, but in a slower manner or at a lower level, these other hormones can also have a massive impact on maintaining

the regulation of glucose in our blood. That you can see this nice figure of the pancreatic cells where you can see that we have beta cells. These are the beta cells which produce insulin, and you can also see that there are alpha cells which produce glucagon. And these are like some other acinar cells and delta cells. They are also very important for maintaining overall glucose homeostasis, but primarily it is the insulin that gets secreted by the beta cells and the glucagon that gets secreted by the alpha cells.

And this is the same homeostasis that we have discussed. So, you can go through this figure that whenever the glucose level is high in the body, insulin will be secreted from the beta cells, and that insulin promotes two things: one is the glucose supply to the tissue, and the second is that it can store the excess glucose inside the liver by converting the glucose to glycogen. In the same way, when there is a low blood sugar level or the glucose level is low, the body, specifically the alpha cells of the pancreas, secretes the glucagon hormone, which can convert glycogen back to glucose. So, this glucagon hormone can convert glycogen back to glucose, and in this way, glucose can enter the bloodstream to maintain the glucose level in the body, right? So, what will happen in case the disruption of glucose homeostasis occurs, and what different types of disorders can we experience? So, first of all, we have to understand that whenever there is high blood glucose, we call this situation hyperglycemia. What are the different causes of hyperglycemia? It can be, as we said, due to insulin resistance, or it can be due to the loss of pancreatic beta cells in the pancreas.

These are mainly the two reasons why hyperglycemic conditions are observed. Now, this is like saying that the condition of hyperglycemia is also called diabetes, right? So, the continuous or persistent hyperglycemic condition can lead to a disease called diabetes. And what are the different types of diabetes? You can see there can be type 1 diabetes mellitus or type 2 diabetes mellitus. In cases of type 1, as you can see, this is a very typical type of disease, which can also be called a genetic disorder, where our own immune cells can detect the beta islet cells as harmful cells, and due to autoimmune activity, those beta islet cells can be destroyed pretty early in life. Genetic factors have been observed in children aged 4 to 10.

Many of the kids or children can experience this autoimmune destruction of the beta-cell, and due to that, the pancreas would not have any more beta-cells to secrete insulin, which will severely hamper the glucose homeostasis of the body. In cases of type 2 diabetes, what can be seen is a lack of insulin secretion efficiency, which can happen due to beta cell dysfunction; along with that, insulin resistance is also observed. So, insulin will not be able to properly bind with the receptor and with the glucose molecule, and this can lead to improper delivery of glucose to the cells and tissues, causing high blood glucose levels and resulting in diabetes. Apart from that, a lot of metabolic syndrome, for example, such as obesity, hypertension, and similar conditions, can also cause higher blood glucose levels in the body. And next, when there is a low amount of blood glucose, we generally call this condition hypoglycemia.

What are the different causes? For example, if excess insulin activity is observed in the body, it can lead to a decrease in glucose in the blood because, as you know, insulin distributes glucose and also stores that additional glucose. So, overactive insulin activity in the body can reduce the blood glucose level, which can cause a hypoglycemic situation. Prolonged fasting can also cause hypoglycemic situations; intense exercise and alcohol intake can also lead to hypoglycemia. What are the different symptoms? We can have symptoms like dizziness, and prolonged hypoglycemia can cause unconsciousness, which could even lead to a brain coma. This can be a very severe case, and if it is not treated properly, the glucose level may not be restored immediately, which could lead to death.

So, as we said, diabetes mellitus is a chronic metabolic disorder in which a persistent hyperglycemic condition is attained in the body. Globally, you can see that almost 537 million adults aged 20 to 80 years are affected by this deadly disease called diabetes. And this figure is ever rising; by 2045, WHO expects that the number of patients could go as high as 783 million. And as you see, there are mostly two types of diabetes mellitus. One is like type 1 diabetes; the second is type 2 diabetes.

Apart from that, there can be gestational diabetes during pregnancy. Mostly, these are different forms of diabetes that can be observed at different times in life. And this is just a brief cartoon example; you can see that in healthy cases, our pancreas, especially the pancreatic beta cells and alpha cells, will work and function in a properly controlled way. Whenever there is a high glucose level in the body, these beta cells will secrete insulin, and this insulin will eventually transport the glucose with it. Eventually, this insulin will bind with the insulin receptors of the cells, promoting the glucose channels inside the cell.

For example, there are different glucose receptors or glucose channels like GLUT-4; it can be GLUT1, GLUT2, or GLUT3. So, by increasing the expression of these GLUT receptors or glucose receptors, glucose will eventually be taken up into the cells, and the cells can utilize the glucose for energy production. But in cases of type 1 diabetes, what we described as the autoimmune activity, like the autoimmune destruction of these pancreatic beta cells, is that all the beta cells will eventually die. And if all the beta-cell cells eventually get destroyed, there would be a lack of insulin production or there would not be any insulin production, basically. And if there is no insulin production, there will not be any binding with the insulin receptor, which will cause the glucose channels to stay closed or to remain less active.

And for that reason, the blood glucose will not be able to come inside, right? So, this is very important; this happens during type 1 diabetes, and for type 2 diabetes, we will observe either a lack of insulin secretion, for example, maybe we will see only a few molecules of insulin secretion. That would not be sufficient to deliver the glucose to the cell, or you may observe something like insulin resistance. So, what will happen due to insulin resistance is that the secreted insulin will not be able to bind with the insulin receptor, and that can eventually cause an inactive condition of the glucose receptor, leading to a lack of glucose uptake inside the cells, which means the glucose level in the blood will stay high. So, for both of these cases, the glucose level in the blood will stay very high, and that is called hyperglycemia, or it can cause both type 1 and type 2 diabetes. See, like type 1 diabetes, we already discussed.

So, we are not discussing this again; you can go through it, and in case you have further questions, please ask us during the live session. We will be happy to answer. So, what are the different risk factors for type 1 diabetes, such as autoimmune destruction, which we have already mentioned, and this autoimmune destruction is mostly triggered by the T cells, right? So, mostly the T cells generally attack our pancreatic beta cells to destroy all those pancreatic cells, and it can also be a genetic factor, as there is a strong association with this HLA type of gene. Apart from that, there are environmental factors; for example, viral infections and family history can have an impact, and rarely has it been seen that, in response to some vaccines, it can also create an autoimmune reaction. For example, I know of a few cases where the patient has been bitten by either a monkey or a dog and they need a rabies vaccine, and due to having the rabies vaccine within a few months to a year, the patient experiences hyperglycemic conditions, and when they have been tested for the cause of hyperglycemia, it has been found that due to the overactive autoimmune activity, all their beta cells were destroyed.

So, these are very peculiar; it is very difficult to predict when the autoimmune reactions will be overactive in our body, but it can happen mostly at younger ages. And we also talked about type 2 diabetes, where most patients experience insulin resistance, causing a lack of glucose delivery to the cells, right? Mostly, it happens in the peripheral blood tissues that cause increased blood glucose and compensatory hyperinsulinemia; it can lead to excess insulin production initially to prevent hyperglycemia. It can happen that the remaining beta islet cells will try to overperform and secrete more and more insulin to initially compensate for the condition of hyperglycemia. But during this process, many of those beta islet cells eventually die due to overperformance or stress conditions, and slowly, there is a loss of beta islet cell function and a lot of beta islet cell viability as well. So, all of these can eventually cause diabetes, which can damage the tissues and the existing organs.

So, what are the various risk factors you can see, like obesity, insulin resistance, family history, age, and lack of exercise? All these can cause type 2 diabetes, and mostly type 2 diabetes, but they can also contribute to some extent to type 1. But type 1, as you know, is mostly due to autoimmune destruction. But type 2 diabetes can be prevented if you maintain a healthy lifestyle with a proper diet and regular exercise; we can kind of maintain the physiological condition even if type 2 diabetes occurs. Type 1 diabetes is mostly a chronic disorder. And if the insulin level cannot be maintained or the glucose level cannot be maintained in the body, even after insulin therapy, then the patient may die.

But with type 2 diabetes, generally, the lifespan is much longer. They can easily control their blood glucose levels with different interventions, which can improve their lifespan. So, these are some situations you can see, like during the fasting state, and if we intake food, what will happen is that blood glucose levels will be high, and as blood glucose levels go high, the beta cells will secrete insulin. So, insulin levels will also go high, and then you can see that the ketone levels can go down, and the metabolic rate generally goes down. In cases of fasting, to maintain the balance, the blood glucose level goes down, the insulin level also goes down, ketones may go up, and the metabolic rate generally goes up to compensate for the low blood glucose condition.

So, think about how prolonged fasting affects glucose homeostasis and what metabolic pathways are activated to maintain the energy supply. And next, why is glucose homeostasis crucial for brain function? What happens when blood glucose levels become too low or too high? What role does the liver play in terms of glucose homeostasis, and how do processes like glycogenesis, glycogenolysis, and gluconeogenesis contribute to this? So, hopefully, you liked our blood glucose homeostasis and diabetes class. If you have any questions, please drop us those questions during live sessions or in the comment section. We hope to answer all of your questions. If you want to read further, you can read a medical physiology textbook, right? You can read all of these, or you can also consult web content.

So, thank you again for attending this class. Let us hope to meet with you very soon for another new class of human physiology. Thank you.