

**Human Physiology**  
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**Week - 12**  
**Lecture - 05**

Hello everyone, welcome to another new class on human physiology. We are almost in our last class of human physiology. So, this was a long journey with you. So, today you will be the last class, and we will discuss the neurological disorder. So, we will see what different types of diseases can occur in our nervous system. And then let us see how their physiology is.

So, let us stay with it. So, what different concepts will be covered in today's class? We will discuss different neurological disorders, what neurological disorders are, what their different physiological changes are, and we will see what their symptoms are. Then we will focus on a few diseases, for example, Alzheimer's, Parkinson's, stroke, multiple sclerosis, epilepsy, amyotrophic lateral sclerosis, and cerebral palsy. So, let us go one by one and see exactly what happens in cases of this disorder.

So, to start with, in terms of the neurological disorder, these are a group of conditions that affect our brain, spinal cord, and nerves. And when it affects, it can disrupt the functions of the nervous system, leading to a wide range of different types of symptoms, mainly the abnormal symptom. These disorders can be caused by different factors. It can be a genetic factor. It can be like various sorts of bacterial and viral infections.

It can happen due to different types of injuries, environmental toxins, or factors. And it can affect all age groups. and why it is important to kind of understand different types of neurological disorders for developing treatments related to these types of diseases. So, unless you understand the physiology and general details of this neurological disorder, the treatments cannot be developed specifically for this disease. So, it is very important to have at least a basic knowledge of this neurological disorder.

So, what common symptoms are associated with neurological disorders? For example, in cases of motor symptoms, we will observe things like muscle weakness or paralysis. Apart from that, we can see tremors or involuntary movements; stiffness or rigidity can also be seen; seizures can also be observed. In cases of sensory symptoms, we can observe numbness or tingling, mainly sometimes at the top of the fingers and toes. There can be a response to pain; it can be an acute or chronic pain symptom. Apart from those changes in vision, hearing, taste, or smell can also be seen.

In cases of cognitive and psychological symptoms, memory loss or confusion can be seen. Apart from that, difficulties with speech or language can be observed. Other than that, changes in mood and behavior, as well as impaired cognitive function, can also be observed. So, these are all different types of motor symptoms, sensory symptoms, along with cognitive and psychological symptoms that can be seen. So, the first one, the very important one we will discuss, is about Alzheimer's disease.

And what is the reason for Alzheimer's disease? Because it is caused by the abnormal buildup of protein. Mostly the amyloid protein, amyloid plaques, and tau tangles are a group of

aggregated types of protein. If these proteins are aggregated in the brain, they can damage and destroy the nerve cells. Genetic relations are present with Alzheimer's disease, but apart from that, lifestyle, environmental factors, and food habits can also affect it. Mostly it affects primarily the cerebral cortex, particularly the area where memory and cognitive functions are performed.

Symptoms can be associated with memory loss, especially short-term memory loss. It can also have symptoms like confusion and disorientation. Apart from that, difficulties with language, communication, impaired judgment, and decision-making can also be a challenge. Basically, there is no proper or complete treatment for Alzheimer's, but there are different drugs and medications that can manage the further progression and condition of Alzheimer's disease. So, as we said, the main reason behind Alzheimer's is the formation of amyloid plaques and tau tangles.

So, basically, the amyloid plaques are primarily made of the beta-amyloid fragment, and these fragments are produced when a larger protein, which is called APP or the amyloid precursor protein, is cut by different enzymes, for example, beta-secretase and gamma-secretase. These are normal kinds of functions, like generally this type of protein, this APP protein during the process of enzyme degradation, which forms the beta amyloid fragment. But we also have a natural process in the body to basically destroy, eliminate, or remove these beta amyloid fragments. so that it does not create any neurological disturbances. But in cases of disease conditions, for example, Alzheimer's disease, this cleavage process or elimination process is altered.

This basically leads to the overproduction of the stickier forms of amyloid beta. And now, this stickier form of amyloid beta is more prone to clumping together. So, basically, what happens is a cleavage process that is cut from the APP by the enzymes called beta-secretase and gamma-secretase. This gets altered, and during the alteration of this cleavage, it starts to form more and more amyloid beta, and these amyloid beta then become much stickier, creating a lot of neurological issues because it also has impaired clearance. As we already said, the brain normally has a mechanism to clear the amyloid beta fragments, but in the case of Alzheimer's, it is unable to remove those clustered or stickier amyloid beta fragments.

and it can also be associated with tau protein abnormality. So, basically, in cases of Alzheimer's, tau undergoes abnormal chemical changes; for example, excessive phosphorylation or hyperphosphorylation. This can cause tau to detach from the microtubules and clump together. Generally forming the neurofibrillary tangles inside the neuron. So, these are like different situations; mostly, you can see how the amyloid beta fragments or the plaque can form.

Apart from that, the tau tangle formation can also cause Alzheimer's. Next, we will discuss what a stroke is, and as you know, it can happen if the blood flow to the brain is interrupted. So, basically, a stroke can be of two types: it can be ischemic stroke or it can be hemorrhagic stroke, right? So, in case proper blood flow gets obstructed in the brain, It can build up the pressure and it can create a brain stroke, further causing damage to local tissues and the nerves. And what we just said is that it has two types of basically conditions: one is the ischemic stroke, where there is a presence of a blood clot. So, you can see that in the case of ischemic stroke, there is a presence of a blood clot, and this can basically prevent proper blood flow.

There can also be a hemorrhagic type of stroke, where you can see a rupture of the blood vessel causing a lot of bleeding inside the brain, and due to that, there can be challenges in terms of proper blood flow in the brain, causing a stroke. What would the symptoms be if a stroke happens? Basically, sudden numbness or weakness of the face, arm, or leg can be observed, and it can also cause dizziness, trouble speaking, sudden vision changes, and imbalance. In severe cases, the patient can become completely senseless, with the possibility of coma. Treatment can be like emergency medical care that should be immediately obtained. In cases of ischemic-related stroke, clot-dissolving drugs, for example, tissue plasminogen activator or TPA, are used.

So, basically, tissue plasminogen activator can be used; different types of thrombus dissolution reagents can also be used. In case of hemorrhagic stroke, we can prescribe certain drugs to control the bleeding and further consider surgical removal of the clots. Surgical repair of those bleeding areas can also be done. But to get back to the normal speech, normal response, and sensory rehabilitation type of therapy, including physical therapies, speech therapy can be recommended by the doctor. The next condition is called migraine, which is basically a complex neurological condition that involves different changes in brain activity, blood flow, and nerve signaling.

Its triggers can include stress, hormonal changes, certain foods, and environmental factors. What would be different symptoms you can see? It can be a very intense and throbbing type of headache, including nausea and vomiting. Apart from that, sensitivity to light and sound can also be observed. Treatments can be given in the form of pain relievers; apart from that, preventive medication, for example, beta blockers, can also be given. The next disease we will discuss is epilepsy.

Mostly, epilepsy has been seen as being characterized by recurrent seizures. Generally, it is caused by abnormal electrical activity inside our brain. It can be caused by either genetic factors, environmental factors, or different types of developmental abnormalities. Apart from that injury, infections can also cause epilepsy. Frequent seizures can be seen along with loss of consciousness, and convulsions can also be observed.

Treatment can be given in the form of anticonvulsant medication; apart from that, surgery can sometimes be helpful. The next disease we will discuss is Parkinson's disease. So, basically, in the case of Parkinson's disease, which is a progressive disorder, it has been seen that there is a relation to the loss of dopamine-producing nerve cells. So, dopamine, as we know, is a neurotransmitter, and it plays a significant role in the body. Dopamine is also a hormone, of course.

So, in the case of Parkinson's, dopamine-producing nerve cells get destroyed. And where it affects, if you see, primarily it affects the basal ganglia, a brain region involved in movement control. So, what would be a different type of symptom? You will often see tremors at rest. So, these are like tremors in the body without any stimulation; you can see them during rest. Muscle rigidity and slowed movement can be seen.

Treatment basically has no cure; however, certain medications like dopamine agonists can be given to manage the condition. And also, recently, deep brain stimulation, or DBS, can also be tried. So, you can see that in the case of Parkinson's, there can be challenges in terms of voluntary movement production, as well as challenges with cognition, memory, learning, motivation, emotion, and perception, right? And there can also be challenges in cases such as

sensory processing, hormonal regulation, and maternal nurturing. So, there are so many issues that can be associated with Parkinson's disease. And how this disease basically progresses is that alpha-synuclein, which is a protein that normally exists in a soluble unfolded state, is involved.

So, basically, alpha-synuclein generally exists in a soluble state, but what happens in the case of Parkinson's disease, due to genetic mutation, oxidative stress, and other unknown triggers, is that these proteins become misfolded and adopt an abnormal shape. So, basically due to the reason of alpha-synuclein, which becomes misfolded, along with that it adopts an abnormal shape, and what happens after the misfolding? The misfolded alpha-synuclein proteins have a tendency to aggregate. So, basically, this protein, although it was initially soluble due to the abnormality, can misfold due to genetic changes and oxidative stress, and now it is more in an aggregated form. And in this aggregated form, they eventually become like a cluster, which is called a Lewy body. Dopaminergic neurons, particularly those present in the substantia nigra, have a high firing rate and metabolic demand.

This makes them more susceptible to the oxidative stress, which can promote the alpha-synuclein misfolding and aggregation. So, this basically dopaminergic neuron can be highly susceptible to reactive oxygen species or oxidative stress, causing a risk of alpha-synuclein aggregation. Apart from that, neuromelanin, which is also like a pigment in neurons, can also react with alpha-synuclein to promote Parkinson's disease. So, basically, as you can see, due to this aggregation of alpha-synuclein, it starts to damage the dopamine receptor-based neurons, causing a lot of challenges, mostly in motor-related activities.

Then the next disease we will discuss is traumatic brain injury, or TBI. Basically, it is caused by a sudden impact or jolt to the head. It may be due to some injury. Mainly, the cause can be cases of car accidents or falls, such as sport-related injuries. The symptoms can be a headache, dizziness, confusion, and convulsion.

Treatment can be given in terms of emergency medical care, surgery, and rehabilitation. Then the next one we'll discuss is about multiple sclerosis. In these cases, autoimmune-related activation happens in the brain. So you can see that due to many reasons, autoimmune diseases can be caused by various factors, and it's very difficult to predict why autoimmune diseases are triggered. But you can see that in these cases, both T cells and B cells penetrate the BBB, and the T cells and B cells can react to produce antibodies.

T cells and microglia can also react to produce antibodies, and these antibodies, along with the cytokines, are mostly related to pro-inflammatory cytokines that start to destroy the filaments. As you can see, T cells and B cells can produce antibodies, and T cells and microglia can also produce antibodies and cytokines. And these are mostly like the inflammatory type of molecules, and these inflammatory molecules can destroy the myelin sheath along with the neurons. So, basically, it degenerates the myelin sheath and the neuron. In this way, we can observe symptoms such as fatigue, numbness, or tingling.

We can also observe muscle weakness, as well as difficulty with balance and coordination. So, basically, if the myelin sheaths are degenerated, what will we observe? The conduction speed will decrease. So, basically, the speed of electrical conduction will decrease. The next one we will discuss is a condition called amyotrophic lateral sclerosis or ALS. This is basically a progressive neurodegenerative disease that affects motor neurons, leading to muscle weakness and paralysis.

Where it affects, if you see, it mostly affects the motor neurons in the brain and spinal cord. In terms of symptoms, we will see muscle weakness in the limbs that slowly starts to spread. Apart from that, muscle twitching and muscle cramps can also be seen. Along with that, slurred speech, difficulty in swallowing, and breathing can also be observed. Basically, until now, there has been no treatment because many cases of ALS are caused by a genetic disease that leads to misfolded protein production or non-functional protein production, which progresses this disease, and unless those genetic corrections can be made.

This disease is very difficult to control, but some medications like Riluzole can be given to manage the condition rather than prevent it; apart from that, supportive care can be provided, and very recently, there has been a lot of interest in genetic therapy. So, like a lot of modern therapy, such as genetic therapy and cell-based therapy. These therapies can be adopted, but none of them are clinically approved to date. So, none of them are clinically approved so far, but with gene therapy, for example, like CRISPR, we can remove the faulty genes. With the cell therapy, we can create a functional protein from external cells so that this functional protein can restore functions in the case of ALS.

And as you can see, ALS is a group of diseases that can be affected by various genes. So, for example, the SOD gene or superoxide dismutase gene can get altered, which can affect the astrocyte. Superoxide dismutase gene alteration can also affect microglial function. It can also affect oligodendrocyte function. Apart from that, you can see C9ORF72, which is another important genetic mutation that has been very frequently seen in cases of ALS and also hampers glial function.

There are a lot of other related genes, for example, SPG11, TUB, TUBA4A, PFN1, DCTN1, PRPH, and NEFH. So many genes are basically affected during ALS, and certain genes can either affect astrocytes; for example, the mutation of SOD1. that creates an environment of neuronal hyper excitability. So, neurons are always in an excited condition, and it is potentially due to impaired glutamate regulation. So, in this case, if the SOD1 mutation happens, astrocytes will create a condition of hyperexcitability of the neuron.

Then in cases of SOD1 or the C9ORF72 gene mutation, we can see microglial dysfunction, where activated microglia can contribute to neuroinflammation and neurodegeneration. Apart from that mutation in several genes, for example, SOD1 and others, abnormalities can occur in oligodendrocytes. It can also cause axonal degeneration or a condition called axonopathy. So, you can see that so many genes and so many conditions are correlated with amyotrophic lateral sclerosis. And Stephen Hawking, you have heard of Stephen Hawking; he suffered for a long time with this disease, which is ALS, or amyotrophic lateral sclerosis.

So, now we will discuss Huntington's disease, which is basically an inherited genetic disorder that occurs due to mutations in the HTT gene, which provides instructions for making a protein called Huntingtin. And you know what the role of Huntingtin is; it is very important in terms of neuronal development and neuronal transport. So, basically, whenever there is a mutation in the HTT gene, the huntingtin protein, which has an important role in neuron development and neural transport, will not be properly formed, and its function will be severely impaired, causing involuntary movements and cognitive decline. Basically, there is no treatment, but in the same way as gene therapy, cell-based therapy can be employed. These are modern approaches to the therapy, but none of them are yet clinically approved.

Lastly, we will discuss cerebral palsy, which is basically a group of disorders caused by abnormal brain development or damage. It can occur before, during, or shortly after the birth. Symptoms can include muscle weakness or stiffness, lack of coordination, involuntary movements, and difficulties with walking, and there is basically no cure, but different therapies can be provided to improve brain function and quality of life. Apart from that, occupational and speech therapy can also be given. So, do you know that stroke is a leading cause of death and disability worldwide? Like, one in four people will be affected by the disease.

Stroke, like every day, has been continuously arising in so many cases. Do you know that Alzheimer's disease is the most common cause of dementia? Dementia is a broader term for the decline in cognitive function. So, in cases where a patient is suffering from a stroke, Alzheimer's, or Parkinson's, cognitive function may decrease. And dementia is basically associated with the broader term if a patient is suffering from a decline in cognitive function. So, the activity question is, what do you think about the brain disease that has limited treatment and therapy? Can you tell that because we discussed various organs in our body for the last 12 weeks, we are discussing different diseases and treatment options? We saw how these affect those organs, but we also discussed that there are many therapies available for all those organs.

But in the case of the brain, the therapies are so limited; you know, like all these last few slides we discussed, one thing I was kind of continuously saying is that there is no treatment or cure, and even if there are certain treatments, they are just for improving the condition in a limited way; there are no complete cures for many of these neurological disorders. So, can you tell me what the main reason for it is? So, thank you again. Thank you again for attending today's class on human physiology. If you have further questions, please send us your question by email, or you can also discuss it during the live sessions. So, we are at the end of today, like the whole 12 weeks of class.

Hopefully, you enjoyed the entire syllabus of human physiology. We thoroughly covered various organs and parts of our body. We try to start from the brain, heart, lungs, and defined endocrine glands. Our overall discussion included neurological systems, the skeletal system, and a thorough discussion of the reproductive systems of males and females. We also discussed the excretory pathways.

So, hopefully it will be helpful for all of you. And if you go through this 12-week class, I hope that you will be able to learn many things that will be useful for you throughout your life. Thank you again for staying with us. Thank you again. Let's, like, thank you, and we will end our, like, course here.