

Neuroscience II

Pathology of CNS

Motor neuron diseases

Dr. Hani Ahmed Alanqar
Consultant of pathology



What Are Motor Neurons?

They are a type of nerve cell, and their job is to send messages around your body to move. Have two main kinds: **Upper motor neurons** are in your brain. They send messages from there to your spinal cord.

Lower motor neurons are in your spinal cord. They transmit the messages sent from your brain to your muscles.

As nerve cells die when you have a motor neuron disease, electrical messages can't get from your brain to your muscles. Over time, the muscles waste away "atrophy."

When this happens, the patient lose control over movements. It gets harder to walk, talk, swallow, and breathe.

Each kind of motor neuron disease affects different types of nerve cells or has a different cause. ALS is the most common of these diseases in adults.



Amyotrophic Lateral Sclerosis (ALS)

Amyotrophic lateral sclerosis targets upper and lower motor neurons (cranial nerves and spinal cord) and results in neuronal cell death and progressive loss of motor function.

Patients usually have lower extremity weakness that progresses to complete paralysis over the course of years. Genetic abnormalities in superoxide dismutase (SOD) 1 have been identified in rare cases of familial amyotrophic lateral sclerosis, suggesting that O₂-derived free radical damage may be responsible for neuronal damage.

Most of ALS are sporadic. This means anyone can get it. Only about 5% to 10% of cases in the United States run in families. ALS usually starts between the ages of 40 and 60. Most people with the disease live for 3 to 5 years after their symptoms start, yet some people can live for 10 years or longer.





Progressive Bulbar Palsy (PBP)

This is a form of ALS. Many people with this condition will eventually develop ALS.

PBP damages motor neurons in the brain stem, which is at the base of the brain.

The stem has motor neurons that help you chew, swallow, and speak. With PBP, the patient might slur the words and have trouble chewing and swallowing. It also makes it hard to control emotions. The patient may laugh or cry without meaning to



Primary Lateral Sclerosis (PLS)

PLS is similar to ALS, but it affects only upper motor neurons. It causes weakness and stiffness in the arms and legs, a slowed walk, and poor coordination and balance. Speech also becomes slow and slurred.

Like ALS, it usually starts in people 40 to 60 years old. The muscles get stiffer and weaker over time. But unlike ALS, people don't die from it.

Spinal and Bulbar Muscular Atrophy (Kennedy Disease)

This X-linked polyglutamine repeat-expansion disease is characterized by distal limb amyotrophy and bulbar signs, such as atrophy and fasciculations of the tongue and dysphagia, that are associated with degeneration of lower motor neurons in the spinal cord and brainstem. The expanded repeat occurs in the first exon of the androgen receptor and results in androgen insensitivity, gynecomastia, testicular atrophy, and oligospermia. The basis for the selective motor neuron involvement is unclear, but as in other polyglutamine expansion diseases such as HD and some forms of spinocerebellar atrophy, there are intranuclear inclusions that contain the involved protein. Progression of the disease is slow, and most affected individuals remain ambulatory until late in the disease course. Life span is normal.



Spinal Muscular Atrophy (SMA)

SMA includes a group of genetically linked disorders of childhood characterized by marked loss of lower motor neurons that results in progressive weakness. The most severe form (SMA type I, Werdnig-Hoffmann disease) has onset during the first year of life, and is usually fatal by the age of 2 years. Other forms, with later onset, have more gradual courses; in SMA type III (Kugelberg-Welander disease), motor disability usually emerges during later childhood and adolescence.

The severity of SMA is related to loss of a protein (termed SMN). Most SMN protein comes from mRNA transcripts derived from the SMN1 gene on chromosome 5q. All forms of SMA are caused by loss-of-function mutations in SMN1 (usually deletions), with the differences in clinical phenotype. A novel gene therapy for SMA is now available that uses an adenoassociated virus to express SMN in motor neurons, albeit at a cost of over \$2 million.

SMA comes in different types that are based on when symptoms first appear:

Type 1 (also called Werdnig-Hoffmann disease). It starts around age 6 months. Children with this type can't sit on their own or hold up their head. They have weak muscle tone, poor reflexes, and trouble swallowing and breathing.

Type 2. It starts between 6 and 12 months. Kids with this form can sit, but they can't stand or walk alone. They may also have trouble breathing.

Type 3 (also called Kugelberg-Welander disease). It starts between ages 2 and 17. It affects how a child can walk, run, stand up, and climb stairs. Kids with this type may also have a curved spine or shortened muscles or tendons around their joints.

Type 4. It usually starts after age 30. People with this type may have muscle weakness, shaking, twitching, or breathing problems. It mainly affects muscles in the upper arms and legs.

Pseudobulbar Palsy

This is similar to progressive bulbar palsy. It affects motor neurons that control the ability to talk, chew, and swallow. Pseudobulbar palsy causes people to laugh or cry with no control.

Progressive Muscular Atrophy

This form is much less common than ALS or PBP. It can be inherited or sporadic. Progressive muscular atrophy mainly affects your lower motor neurons. Weakness usually starts in hands and then spreads to other parts of the body. The muscles get weak and may cramp. This disease can turn into ALS.

Living With a Motor Neuron Disease

The outlook is different for each type of motor neuron disease. Some are milder and progress more slowly than others.

Although there is no cure for motor neuron diseases, medicines and therapy can ease symptoms and improve your quality of life.