AMYOTROPHIC LATERAL SCLEROSIS

Amyotrophic lateral sclerosis (ALS) is a progressive neuromuscular disease that destroys muscle-controlling nerve cells called motor neurons.

In ALS, motor neurons in the **brain and spinal chord** are affected. As these nerve cells deteriorate and are lost, they stop sending signals to muscles. In the **absence of signals**, the muscles they control atrophy, becoming weak and then nonfunctional.

ALS is estimated to affect **7.7 out of every 100,000** people in the United States. Between **15,000 and 20,000 Americans** are estimated to be **living with ALS** in the U.S.[1]

Onset of ALS symptoms usually occurs in **late middle age or later**, although it also can occur in young adults, as well as in the elderly.

ALS affects persons of **all races and ethnicities**, and is 20% more common in men than women.

Some studies suggest that **military veterans and fire fighters** are about two times more likely to develop ALS. ALS is recognized as a **service-connected disease** by the U.S. Department of Veterans Affairs. [2]

Most ALS cases are sporadic, meaning there is no family history of the disease. About **5 to 10 percent of cases are familial**, meaning the disease runs in the family. Both familial and sporadic ALS can stem from genetic causes, and some people who have a diagnosis of sporadic ALS may carry ALS-causing genetic mutations that can be passed on to their children. **A genetic counselor** can help people with ALS understand inheritance and any associated risks for family members.

The **causes** of the vast majority of sporadic ALS cases are still **unknown**.

ALS affects many parts of the body, most notably the **skeletal and respiratory (breathing) muscles**.

1. Mehta, Paul, Jaime Raymond, Reshma Punjani, Moon Han, Theodore Larson, Wendy Kaye, Lorene M. Nelson, et al. 2022. "Prevalence of Amyotrophic Lateral Sclerosis in the United States Using Established and Novel Methodologies, 2017." Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, April, 1–9. https://doi.org/10.1080/21678421.2022.2059380.

2. Vanacore, Nicola, Pierluigi Cocco, Domenica Fadda, and Mustafa Dosemeci. 2010. "Job Strain, Hypoxia and Risk of Amyotrophic Lateral Sclerosis: Results from a Death Certificate Study." Amyotrophic Lateral Sclerosis 11 (5): 430–34. https://doi.org/10.3109/17482961003605796.

Each person's disease course is unique, but eventually most individuals with ALS will not be able to stand or walk, get in or out of bed on their own, use their hands and arms, or breathe without assistance.

ALS onset often occurs in one of the two distinct ways: Limb Onset ALS or Bulbar Onset ALS. If the symptoms initially appear in the limbs of the body, ie. arms and legs, it is defined as **Limb Onset ALS**. The common initial symptoms include muscle cramps or stiffness, muscle twitching,weakness in the hands or legs and loss of grip strength.[3]

ALS is defined as Bulbar Onset when the first symptoms occur in the face or neck. Slurred speech, difficulty chewing and swallowing, weakness in the face muscles, jaw and throat are early symptoms.[4]

The latest studies show that approximately 75% of ALS cases are reported as limb onset.

The **involuntary muscles**, such as those that control the heartbeat, gastrointestinal tract and bowel, bladder and sexual functions are not directly affected in ALS. **Sensations**, such as vision, hearing and touch, are also unaffected.

In many cases, ALS does not affect a person's thinking ability. However, as many as 50% of people with ALS develop some degree of **cognitive** (thinking) or **behavioral** abnormalities. [5]

Life expectancy after an ALS diagnosis typically is **3 to 5 years**.

Currently, there is no cure for ALS and no effective treatment to halt or reverse the progression of the disease. However, there are treatments that may modify or slow the disease course, as well as therapies that can help control symptoms, prevent unnecessary complications, and make living with the disease easier.

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3. Walhout, Renée, Esther Verstraete, Martijn P. van den Heuvel, Jan H. Veldink, and Leonard H. van den Berg. 2017. "Patterns of Symptom Development in Patients with Motor Neuron Disease." Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration 19 (1-2): 21–28. https://doi.org/10.1080/21678421.2017.1386688.

4. Williams, James R, David Fitzhenry, Lauren Grant, Derek Martyn, and Douglas A Kerr. 2013. "Diagnosis Pathway for Patients with Amyotrophic Lateral Sclerosis: Retrospective Analysis of the US Medicare Longitudinal Claims Database." BMC Neurology 13 (1). https://doi.org/10.1186/1471-2377-13-160.

5. Crockford, Christopher, Judith Newton, Katie Lonergan, Theresa Chiwera, Tom Booth, Siddharthan Chandran, Shuna Colville, et al. 2018. "ALS-Specific Cognitive and Behavior Changes Associated with Advancing Disease Stage in ALS." Neurology 91 (15): e1370–80. https://doi.org/10.1212/WNL.0000000000006317.

WHAT SHOULD I KNOW ABOUT ALS?

1 There is no test that can provide a definitive ALS diagnosis. Diagnosis is based on a detailed history of symptoms and signs observed by a physician during physical examination, along with a series of tests meant to rule out other diseases that can mimic ALS.

2 For many individuals the first sign of ALS may appear in a hand or arm, as they experience difficulty with simple tasks such as buttoning a shirt, writing, or turning a key in a lock. In other cases, symptoms initially affect one of the legs, and people experience awkwardness when walking or running or they notice that they are tripping or stumbling a lot.

3 When symptoms begin in the arms or legs, it is referred to as limb-onset ALS. In bulbar-onset ALS individuals first notice speech or swallowing problems.

4 In the early stages of ALS, muscles may become weak and soft or stiff, tight and spastic. Muscle cramping and twitching (fasciculations) occurs, as does loss of muscle bulk. Symptoms may be limited to a single body region or may affect more than one region. The person may experience fatigue, poor balance, slurred words, a weak grip, tripping when walking or other minor symptoms.

5 Symptoms become more widespread in the middle stages of ALS. Some muscles are paralyzed, while others are weakened or unaffected. Fasciculations may continue. Unused muscles may lead to contractures, in which the joints become rigid, painful and sometimes deformed. If a person falls, he or she may not be able to stand back up without help. Weakness in swallowing muscles may cause choking and greater difficulty eating and managing saliva. Weakness in breathing muscles can cause respiratory insufficiency. Some people experience bouts of uncontrollable and inappropriate laughing or crying (pseudobulbar affect).

6 In the late stages of ALS, most voluntary muscles are paralyzed. The muscles that help move air in and out of the lungs are severely compromised. Mobility is extremely limited, and help is needed in caring for most personal needs. Poor respiration may cause fatigue, fuzzy thinking, headaches and susceptibility to pneumonia. Speech, or eating and drinking by mouth may not be possible.

In ALS, death typically results from respiratory failure.

HOW IS ALS TREATED?

The U.S. Food and Drug Administration (FDA) has approved the drugs Rilutek, Radicava, Tiglutik, Exservan, Radicava ORS, Relyvrio, and Qalsody to treat ALS.

- **Rilutek** is believed to protect motor neurons by decreasing levels of the neurotransmitter glutamate. Clinical trials in people with ALS showed that Rilutek prolongs survival by a few months, but does not reverse the damage already done to motor neurons.
- **Tiglutik** is an oral suspension liquid formulation of riluzole. **Exservan** is an oral film formulation of riluzole. Developing new formulations of riluzole allows the drug to be easier to take for individuals who have difficulty swallowing.
- **Radicava** is thought to work by relieving the effects of oxidative stress, which has been suspected to play a role in the death of nerve cells in people with ALS. Radicava has been shown to slow the decline in clinical assesment of daily functioning in persons with ALS. The oral formulation of Radicava, **Radicava ORS**, provides more flexibility by allowing people to take the drug by mouth or via feeding tube, rather than requiring an IV.
- The affected people treated with **Relyvrio** experienced a slower rate of decline on an assessment of daily functioning compared to those receiving placebo. Longer overall survival was also observed in a long-term analysis of trial participants who received Relyvrio versus those who received placebo.
- **Qalsody** received accelerated approval from the FDA for the treatment of ALS associated with mutation in the superoxide dismutase 1 (SOD1) gene (SOD1-ALS). Qalsody is the fourth approved therapy to treat a form of ALS and the first therapy to target a genetic cause of ALS.

Speech therapy can help with difficulties speaking or swallowing. Other useful technology can help with writing, art projects, using a computer or cellphone, and electronically controlling the environment. Computer-based speech synthesizers that use eye-tracking technology can help with nonverbal communication, and voice banking allows patients to store their own voice for future use.

Nutritional support is an important part of care. Nutritionists can teach individuals and caregivers how to plan and prepare small meals throughout the day that provide enough calories, fiber, and fluids, and how to avoid foods that are difficult to swallow. Suction devices may be used to remove excess fluids or saliva and prevent choking.

Muscle relaxants may reduce spasticity. Botulinum toxin may be used to treat jaw spasms or drooling, and there are medications that can be used to reduce excessive saliva. Nuedexta can be prescribed to help control pseudobulbar affect. Antidepressants and anxiolytics may be helpful in treating depression and anxiety, and other drugs may help with pain, sleep disturbances and constipation.

A machine called the cough assist can help to remove secretions from lungs.

A gastrostomy tube (sometimes called a g-tube or feeding tube) allows liquid nutrition to enter the stomach directly, bypassing the mouth, throat and esophagus, when weakness in the muscles of the throat makes chewing or swallowing difficult and prevents individuals from being able to get enough nourishment from eating.

Physical therapy helps to restore and maintain muscle strength and function through exercise, as well as to maintain range of motion through stretching. Occupational therapy can help people with ALS conserve energy and remain mobile.

Respiratory devices such as BiPAP (bilevel positive airway pressure) can assist the movement of air in and out of the lungs. This support, delivered through a mask over the nose and/ or mouth, is called noninvasive ventilation (NIV). As ALS progresses and muscles weaken further, individuals may consider forms of mechanical ventilation, in which a machine inflates and deflates the lungs. Doctors may place a breathing tube through the mouth or may surgically create a hole at the front of the neck and insert a tube leading to the windpipe (tracheostomy). The tube is connected to a respirator.

An array of assistive technology products can help maintain mobility and independence even when muscles become very weak. Standers, walkers, various kinds of powered and manual wheeled vehicles and wheelchairs can help people with ALS stand and move around.

WHAT ARE THE SIGNS AND SYMPTOMS OF ALS?

Nervous system
- Impaired motor function
- Pseudobulbar affect

Cognition
- Impaired decision-making

Behavioral
- Anxiety
- Depression

Skeleton and muscle
- Muscle weakness
- Fatigue
- Cramps
- Fasciculations
- Spasticity
- Contractures
- Dysarthria

Gastrointestinal
- Dysphagia
- Constipation
- Malnutrition

Respiratory system
- Breathing difficulties
- Chest infections
- Respiratory failure

To learn more about ALS, visit mda.org or contact the MDA Resource Center at 800-572-1717.

Or visit cdc.gov/als/WhatisAmyotrophiclateralsclerosis.html

MDA GLOSSARY

Aspiration
When food or liquid accidentally enters the windpipe instead of the stomach

Atrophy
A decrease in the size and mass of muscle tissue

Contracture
A shortening of muscles or tendons around joints that can limit mobility

Dysarthria
Difficulty speaking or forming words

Dysphagia
Difficulty swallowing

Dyspnea
Difficulty breathing

Fasciculations
Muscle twitching

Mutation
A flaw in the DNA code

Oxidative stress
An imbalance between the production of free radicals (highly reactive oxygen-containing molecules) and the ability of the body to counteract or detoxify their harmful effects through neutralization
by antioxidants

Progressive
Describes a disease in which the symptoms get worse over time

Pseudobulbar affect
Bouts of uncontrollable and inappropriate laughing or crying

Sialorrhea
Excessive saliva

Spasticity
An unusual tightness or stiffness of muscles

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Designated a Top-Rated Charity by the American Institute of Philanthropy, MDA is the first nonprofit to receive a **Lifetime Achievement Award from the American Medical Association** for "significant and lasting contributions to the health and welfare of humanity."

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