# Amyotrophic Lateral Sclerosis (ALS) Fact Sheet

**What is amyotrophic lateral sclerosis?**

Amyotrophic lateral sclerosis (ALS) is a rare neurological disease that primarily affects the nerve cells (neurons) responsible for controlling voluntary muscle movement (those muscles we choose to move). Voluntary muscles produce movements like chewing, walking, and talking. The disease is progressive, meaning the symptoms get worse over time. Currently, there is no cure for ALS and no effective treatment to halt or reverse the progression of the disease.

ALS belongs to a wider group of disorders known as motor neuron diseases, which are caused by gradual deterioration (degeneration) and death of motor neurons. Motor neurons are nerve cells that extend from the brain to the spinal cord and to muscles throughout the body. As motor neurons degenerate, they stop sending messages to the muscles and the muscles gradually weaken, start to twitch, and waste away (atrophy). Eventually, the brain loses its ability to initiate and control voluntary movements.

Early symptoms of ALS usually include muscle weakness or stiffness. Gradually all voluntary muscles are affected, and individuals lose their strength and the ability to speak, eat, move, and even breathe. Most people with ALS die from respiratory failure, usually within 3 to 5 years from when the symptoms first appear. However, about 10 percent of people with ALS survive for 10 or more years.

ALS was once commonly known as Lou Gehrig’s disease, following the retirement of the famous ballplayer in the 1940s due to the disease.

**What are the symptoms?**

The onset of ALS can be so subtle that the symptoms are overlooked but gradually these symptoms develop into more obvious weakness or atrophy.

**Early symptoms** include:

- Muscle twitches in the arm, leg, shoulder, or tongue

- Muscle cramps
- Tight and stiff muscles (spasticity)
- Muscle weakness affecting an arm, a leg, the neck, or diaphragm
- Slurred and nasal speech
- Difficulty chewing or swallowing

The first sign of ALS usually appears in the hand or arm and can show as difficulty with simple tasks such as buttoning a shirt, writing, or turning a key in a lock. In other cases, symptoms initially affect one leg. People experience awkwardness when walking or running, or they may trip or stumble more often. When symptoms begin in the arms or legs, it is referred to as “limb onset” ALS, and when individuals first notice speech or swallowing problems, it is termed “bulbar onset” ALS.

**As the disease progresses**, muscle weakness and atrophy spread to other parts of the body. Individuals may develop **problems with moving, swallowing** (called dysphagia), **speaking or forming words** (dysarthria), **and breathing** (dyspnea). Although the sequence of emerging symptoms and the rate of disease progression can vary from person to person, eventually individuals will not be able to stand or walk, get in or out of bed on their own, or use their hands and arms.

Individuals with ALS usually have difficulty swallowing and chewing food, which makes it hard to eat. They also burn calories at a faster rate than most people without ALS. Due to these factors, people with ALS tend to lose weight rapidly and can become malnourished.

Because people with ALS usually can perform higher mental processes such as reasoning, remembering, understanding, and problem solving, they are aware of their progressive loss of function and may become anxious and depressed. A small percentage of individuals may experience problems with language or decision-making, and there is growing evidence that some may even develop a form of dementia over time.

Individuals with ALS eventually lose the ability to breathe on their own and must depend on a ventilator. Affected individuals also face an increased risk of pneumonia during later stages of the disease. Besides muscle cramps that may cause discomfort, some individuals with ALS may develop painful neuropathy (nerve disease or damage).

**Who gets ALS?**

ALS is a common neuromuscular disease worldwide. It affects people of all races and ethnic backgrounds.

**Risk factors for ALS include**:

- **Age**. Although the disease can strike at any age, symptoms most commonly develop between the ages of 55 and 75.
- **Gender**. Men are slightly more likely than women to develop ALS. However, as people age the difference between men and women disappears.
- **Race and ethnicity.** Caucasians and non-Hispanics are most likely to develop the disease.

Some studies suggest that military veterans are about 1.5 to 2 times more likely to develop ALS. Although the reason for this is unclear, possible risk factors for veterans include exposure to lead, pesticides, and other environmental toxins. ALS is recognized as a service-connected disease by the U.S. Department of Veterans Affairs.

**Sporadic ALS**

Nearly all cases of ALS are considered sporadic. This means the disease seems to occur at random with no clearly associated risk factors and no family history of the disease. Although family members of people with sporadic ALS are at an increased risk for the disease, the overall risk is very low and most will not develop ALS.

**Familial (Genetic) ALS**

About 5 to 10 percent of all ALS cases are familial, which means that an individual inherits the disease from a parent. The familial form of ALS usually only requires one parent to carry the disease-causing gene. Mutations in more than a dozen genes have been found to cause familial ALS.

- About 25 to 40 percent of all familial cases (and a small percentage of sporadic cases) are caused by a defect in the ***C9ORF72*** gene (which makes a protein that is found in motor neurons and nerve cells in the brain). In 2011, scientists found that a defect in the *C9ORF72* gene is not only present in a significant subset of individuals with ALS but also in some people with a type of frontotemporal dementia (FTD) that results from atrophy to the brain’s temporal and frontal lobes. This observation provides evidence for genetic ties between these two neurodegenerative disorders.

- Another 12 to 20 percent of familial cases result from mutations in the ***SOD1*** gene that is involved in the production of the enzyme copper-zinc superoxide dismutase 1.

On June 1, 2021, a team of scientists let by the NIH and the Uniformed Services University announced it had discovered a unique form of genetic ALS that affects children as early as age 4 years.  This childhood form of ALS is linked to the gene ***SPTLC1***, which is part of the body's fat production system, and may be caused by changes in the way the body metabolizes fatty materials called lipids.

**What causes ALS?**

The cause of ALS is not known, and scientists do not yet know why ALS strikes some people and not others. However, scientific evidence suggests that both genetics and environment play a role in motor neuron degeneration and the development of ALS.

**Genetics**

In 1993, scientists supported by the National Institute of Neurological Disorders and Stroke (NINDS) discovered that mutations in the *SOD1* gene were associated with some cases of familial ALS. Since then, more than a dozen additional genetic mutations have been identified, many through NINDS-supported research.

Research on certain gene mutations suggests that changes in the processing of RNA molecules may lead to ALS-related motor neuron degeneration. RNA molecules are involved with the production of molecules in the cell and with gene activity.

Other gene mutations indicate there may be defects in protein recycling—a naturally occurring process in which malfunctioning proteins are broken down and used to build new working ones. Still, others point to possible defects in the structure and shape of motor neurons, as well as increased susceptibility to environmental toxins.

**Environmental factors**

Researchers are studying the impact of environmental factors, such as exposure to toxic or infectious agents, viruses, physical trauma, diet, and behavioral and occupational factors. For example, exposure to toxins during warfare, or strenuous physical activity, are possible reasons for why some veterans and athletes may be at increased risk of developing ALS. Ongoing research may show that some factors are

involved in the development or progression of the disease.

**How is ALS diagnosed?**

There is no single test that provides a definitive diagnosis of ALS. It is primarily diagnosed based on a detailed history of the symptoms observed by a physician during physical examination, along with a review of the individual's full medical history and a series of tests to rule out other diseases. A neurologic examination at regular intervals can assess whether symptoms such as muscle weakness, muscle wasting, and spasticity are progressively getting worse.

**Muscle and imaging tests**

- **Electromyography (EMG)** is a recording technique that detects electrical activity of muscle fibers and can help diagnose ALS.
- A **nerve conduction study (NCS)** measures the electrical activity of the nerves and muscles by assessing the nerve's ability to send a signal along the nerve or to the muscle.
- **Magnetic resonance imaging (MRI)** is a noninvasive procedure that uses a magnetic field and radio waves to produce detailed images of the brain and spinal cord.
- **Blood and urine tests** may be performed based on the person's symptoms, test results, and findings from the examination. A physician may order these tests to eliminate the possibility of other diseases.
- A **muscle biopsy** may be performed to determine whether a physician believes an individual has a muscle disease other than ALS. Under local anesthesia, a small sample of muscle is removed and sent to the lab for analysis.

**How is ALS treated?**

There is no treatment to reverse damage to motor neurons or cure ALS. However, treatments can help control symptoms, prevent unnecessary complications, and make living with the disease easier.

Supportive health care is best provided by multidisciplinary teams of professionals such as physicians; pharmacists; physical, occupational, speech, and respiratory therapists; nutritionists; social workers; clinical psychologists; and home

care and hospice nurses. These teams can design an individualized treatment plan and provide special equipment aimed at keeping people as mobile, comfortable, and independent as possible.

**Medications**

The U.S. Food and Drug Administration (FDA) has approved drugs to treat ALS:

- **Riluzole** (Rilutek) is an oral medication believed to reduce damage to motor neurons by decreasing levels of glutamate, which transports messages between nerve cells and motor neurons. Clinical trials in people with ALS showed that riluzole prolongs survival by a few months, particularly in the bulbar form of the disease. Individuals with swallowing difficulties may prefer the thickened liquid form (Tiglutik) or the tablet (Exservan) that dissolves on the tongue.
- **Edaravone** (Radicava) is given by intravenous infusion and has been shown to slow the decline in clinical assessment of daily functioning in persons with ALS.

Physicians can also prescribe medications to help manage symptoms of ALS, including muscle cramps, stiffness, excess saliva and phlegm, and the pseudobulbar effect (involuntary or uncontrollable episodes of crying and/or laughing, or other emotional displays). Drugs also are available to help individuals with pain, depression, sleep disturbances, and constipation.

**Physical and occupational therapy**

Physical therapy and special equipment can enhance an individual’s independence and safety throughout the course of ALS. Gentle, low-impact aerobic exercise such as walking, swimming, and stationary bicycling can strengthen unaffected muscles and range of motion and stretching exercises can help prevent painful spasticity and shortening (contracture) of muscles. Physical therapists can recommend exercises that provide these benefits without overworking muscles. Occupational therapists can suggest devices such as ramps, braces, walkers, and wheelchairs that help individuals conserve energy and remain mobile.

**Communications support**

People with ALS who have difficulty speaking may benefit from working with a speech therapist, who can teach adaptive strategies to speak louder and more clearly. As ALS progresses, speech therapists can help people maintain the ability to

communicate.

Devices such as **computer-based speech synthesizers** use eye-tracking technology and can help people develop ways for responding to yes-or-no questions with their eyes or by other nonverbal means. Some people with ALS may choose to use **voice banking** while they are still able to speak as a process of storing their own voice for future use in computer-based speech synthesizers.

A **brain-computer interface (BCI)** is a system that allows individuals with ALS to communicate or control equipment such as a wheelchair using only brain activity. Researchers are developing more efficient, mobile, and even some auditory-based BCIs for those with severe paralysis and/or visual impairments.

**Nutritional support**

Nutritionists can teach individuals and caregivers how to plan and prepare small meals throughout the day that provide enough calories, fiber, and fluid and how to avoid foods that are difficult to swallow. People may begin using suction devices to remove excess fluids or saliva and prevent choking. When individuals can no longer eat, doctors may advise inserting a feeding tube, which reduces the risk of choking and pneumonia that can result from inhaling liquids into the lungs.

**Breathing support**

As the muscles responsible for breathing start to weaken, people may experience shortness of breath during physical activity and difficulty breathing at night or when lying down. **Noninvasive ventilation (NIV)** refers to breathing support that is usually delivered through a mask over the nose and/or mouth. Initially, NIV may only be necessary at night but may eventually be used full-time. NIV improves the quality of life and prolongs survival for many people with ALS.

Because the muscles that control breathing become weak, individuals with ALS may also have trouble generating a strong cough. There are several techniques to help people increase forceful coughing, including mechanical cough assistive devices.

As the disease progresses, individuals may need **mechanical ventilation (respirators)** 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). Although

ventilation support can ease breathing problems and prolong survival, it does not affect the progression of ALS.

**What research is being done?**

The National Institute of Neurological Disorders and Stroke (NINDS) is the primary federal funder of research on the brain and nervous system, including disorders such as ALS. NINDS is a component of the National Institutes of Health (NIH), the leading supporter of biomedical research in the world.

The goals of NINDS's ALS research are to understand the cellular mechanisms involved in the development and progression of the disease, investigate the influence of genetics and other potential risk factors, identify biomarkers, and develop new treatments.

**Cellular defects**. Ongoing studies seek to understand the mechanisms that selectively trigger motor neurons to degenerate in ALS, which may lead to effective approaches to halt this process. Research using cellular culture systems and animal models suggests that motor neuron death is caused by a variety of cellular defects, including those involved in protein recycling and gene regulation, as well as structural impairments of motor neurons. Increasing evidence also suggests that glial support cells and inflammation cells of the nervous system may play an important role in ALS.

**Stem cells**. Scientists are turning skin cells of people with ALS into stem cells that are capable of becoming any cell type, including motor neurons and other cells which may be involved in the disease. NINDS-funded scientists are using stem cells to grow human spinal cord sections on tissue chips to help better understand the function of neurons involved in ALS.

**Genetics and epigenetics.** Clinical research studies supported by NINDS are looking into how ALS symptoms change over time in people with *C9ORF72* mutations. Other studies are working to identify additional genes that may cause or put a person at risk for either familial or sporadic ALS.

A large-scale collaborative research effort supported by NINDS, other NIH institutes, and several public and private organizations is analyzing genetic data from thousands of individuals with ALS to discover new genes involved in the disease. By using novel gene editing tools, researchers are now able to rapidly identify new

genes in the human genome involved in ALS and other neurodegenerative diseases.

Additionally, researchers are looking at the potential role of epigenetics in ALS development. Epigenetic changes can switch genes on and off, which can greatly impact both health and disease. Although this research is exploratory, scientists hope that understanding epigenetics can offer new information about how ALS develops.

**Biomarkers**. NINDS supports research on the development of biomarkers—biological measures that help identify the presence or rate of progression of a disease or the effectiveness of a therapeutic intervention. Biomarkers can be molecules derived from a bodily fluid (blood or cerebrospinal fluid), an image of the brain or spinal cord, or a measure of the ability of a nerve or muscle to process electrical signals.

**New treatment options**. This work involves tests of drug-like compounds, gene therapy approaches, antibodies, and cell-based therapies in a range of disease models. Additionally, a number of exploratory treatments are being tested in people with ALS.

### How can I be involved in research?

### National ALS Registry

The National ALS Registry is a program to collect, manage, and analyze data about people with ALS in the United States. Developed by the Center for Disease Control and Prevention's Agency for Toxic Substances and Disease Registry (ATSDR), this registry establishes information about the number of ALS cases, collects demographic, occupational, and environmental exposure data from people with ALS to learn about potential risk factors for the disease, and notifies participants about research opportunities. The Registry includes data from national databases as well as de-identified information provided by individuals with ALS. All information is kept confidential. People with ALS can add their information to the Registry by visiting www.cdc.gov/als.

### Clinical trials

Many neurological disorders do not have effective treatment options. Clinical trials offer hope for many people and an opportunity to help researchers find better ways

to safely detect, treat, or prevent disease. For information about finding and participating in a clinical trial, visit NIH Clinical Research Trials and You at www.nih.gov/health/clinicaltrials. For more information about finding clinical trials on ALS, visit www.clinicaltrials.gov. Use the search terms “amyotrophic lateral sclerosis” or "ALS AND (your state)” to locate trials in your area.

**NIH NeuroBioBank**

The NINDS supports the NIH NeuroBioBank, a collaborative effort involving several brain banks across the U.S. that supply investigators with tissue from people with neurological and other disorders. Tissue from individuals with ALS is needed to enable scientists to study this disorder more intensely. The goal is to increase the availability of, and access to, high-quality specimens for research to understand the neurological basis of the disease. Prospective donors can begin the enrollment process by visiting www.neurobiobank.nih.gov/donors-how-become-donor.

**Where can I get more information?**

For more information on neurological disorders or research programs funded by the National Institute of Neurological Disorders and Stroke, contact the Institute’s Brain Resources and Information Network (BRAIN) at:

**BRAIN**
P.O. Box 5801
Bethesda, MD 20824
800-352-9424

Information also is available from the following organizations:

**The ALS Association**
275 K Street N.W., Suite 250
Washington, DC 20005
202-407-8580

**ALS Therapy Development Institute**
300 Technology Square, Suite 400
Cambridge, MA 02139
617-441-7200

**Les Turner ALS Foundation**
5550 West Touhy Avenue, Suite 302
Skokie, IL 60077-3254
847-679-3311

**Project ALS**
801 Riverside Drive, Suite 6G
New York, NY 10032
212-420-7382
855-900-2257

**Muscular Dystrophy Association**
222 S. Riverside Plaza, Suite 1500
Chicago, IL 60606
800-572-1717

**U.S. National Library of Medicine**
National Institutes of Health/DHHS
8600 Rockville Pike
Bethesda, MD 20894
301-594-5983
888-346-3656

Amyotrophic Lateral Sclerosis (ALS) Brochure

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