# NEUROSCIENCE PEARLS

## ALS - Amyotrophic Lateral Sclerosis

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Welcome to ***Neuroscience Pearls***: A publication from the **UW Medicine Neurosciences Institute**. Our goal is to provide useful information pertinent to your practice. Here we bring you key points related to **Amyotrophic Lateral Sclerosis - ALS**.

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### WHAT IS AMYOTROPHIC LATERAL SCLEROSIS?

Amyotrophic Lateral Sclerosis (ALS), also known as Lou Gehrig's disease, is a progressive neurodegenerative disorder affecting the motor neuron pathways in the spinal cord, brainstem and brain, leading to weakness and progressive muscle loss. Medical and supportive care improves quality of life and life expectancy, but individuals usually succumb to the disease within 5 years.

Amyotrophic refers to muscle loss from damage to the motor neurons; lateral indicates the area of the spinal cord affected; and sclerosis means hardening. ALS causes progressive loss of motor neurons, leading to weakness and muscle atrophy in arms, legs - and elsewhere adversely affecting all motor functions including swallowing, speaking and breathing. It is the most common motor neuron disorder. Absolute diagnosis of the disease relies on autopsy features of motor neuron loss and sclerosis. However, the findings on physical examination of upper motor and lower motor signs in multiple regions are pathognomonic of ALS (**Table 1**). These findings in combination with abnormalities in bulbar (the region of the brainstem controlling swallowing and speaking) muscles are highly associated with this particular disease. No laboratory or radiologic tests confirm the diagnosis. (Specific diagnostic criteria for research studies are included in **Table 2**).

The possible causes of ALS include genetic factors, inflammation, the environment, smoking, low body mass index and heavy metals. Other diseases which may present similarly to ALS include arthritic changes in the neck (spondylosis) causing spinal cord and nerve root compression, inclusion body myositis and rarely multifocal motor neuropathy and spinal muscular atrophy.

### EPIDEMIOLOGY AND PATHOPHYSIOLOGY:

The incidence of ALS is two cases per 100,000 per year. Men are slightly more often affected than women. The mean age of onset is 62 years. The cause of sporadic ALS is unknown. The familial forms make up ten percent of all ALS cases and include abnormalities in the following genes: C9ORF, SOD1, TARDBP, and FUS. The underlying pathology in ALS is motor neuron degeneration and death, and secondary gliosis, with a gradual and progressive loss of motor function. As the motor neuron undergoes apoptosis (cell death), the motor nerve axon degenerates, and neuromuscular junctions innervated by these dying motor axons are denervated and subsequently atrophy. As cortical motor neurons die, retrograde axonal loss in the corticospinal tract leads to spinal cord atrophy; with the loss of large myelinated fibers, the ventral roots atrophy.

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### TABLE 1: Lower Motor Neuron and Upper Motor Neuron Signs in Four CNS Regions

| | Brainstem | Cervical | Thoracic | Lumbosacral |
|---|---|---|---|---|
| **Lower Motor Neuron (LMN) Signs**:<br>• Weakness<br>• Atrophy<br>• Fasciculation | • Jaw, Face<br>• Palate<br>• Tongue<br>• Larynx | • Neck, arm, hand<br>• Diaphragm | • Back<br>• Abdomen | • Back, abdomen<br>• Leg, foot |
| **Upper Motor Neuron (UMN) Signs:**<br>• Pathologic spread of reflexes<br>• Clonus, etc. | • Clonic jaw jerk<br>• Increased gag reflex<br>• Exaggerated snout reflex<br>• Pseudobulbar features<br>• Forced yawning<br>• Pathologic DTRs<br>• Spastic tone | • Clonic DTRs<br>• Hoffman reflex<br>• Pathologic DTRs<br>• Spastic tone<br>• Preserved reflex in a weak wasted limb | • Loss of superficial abdominal reflexes<br>• Pathologic DTRs<br>• Spastic tone | • Clonic DTRs<br>• Extensor plantar response<br>• Pathologic DTRs<br>• Spastic tone<br>• Preserved reflex in a weak wasted limb |

**DTR =** deep tendon reflex

**CLINICAL PRESENTATION:**

The features of ALS comprise asymmetric weakness, muscle twitches (fasciculations), swallowing and speech difficulties and shortness of breath. Muscle cramps, cognitive changes and weight loss are also common. The initial presenting symptom is asymmetric limb weakness in 80% of people. The disease tends to spread to contiguous segments of the neuraxis. Swallowing difficulty typically presents as coughing or choking when eating solid foods, and are often accompanied by slurred speech. The muscles of respiratory function are compromised, particularly the diaphragm muscle, creating shortness of breath when lying supine. Involvement of the upper motor neurons manifests as stiffness and slowing of movements, such as finger tapping or rapid alternating tongue movements. Increased reflexes are seen on neurological examination, and carry particular significance if seen in a region of muscle atrophy - documenting both the upper and lower motor neuron features of the disease, respectively. Mild cognitive difficulties similar to those seen with frontal lobe disorders affect half of individuals with ALS, and include impaired organization, behavioral changes and lack of insight.

**TREATMENT:**

Supportive care, education and symptomatic medications are the main treatments in ALS. Addressing the complications of impaired swallowing with percutaneous endoscopic gastrostomy (PEG) placement, and respiratory impairment with non-invasive ventilation (BiPAP), are keys to improving quality of life and life expectancy. Riluzole is the only FDA-approved medication for ALS and slows progression of the disease by roughly 3 months. Many treatment trials to date have not shown efficacy in humans. Stem cell transplantation has gained attention as a possible treatment. The idea is that stem cells would be capable of slowing or stopping motor neuron death, possibly by modulating local inflammatory and immune reactions or by antagonizing toxic conditions throught to induce neuronal death..

## Table 2: Concensus Criteria for Clinical Studies (2000)

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| **Clinically Definite ALS** is defined on clinical evidence alone by the presence of UMN, as well as LMN signs, in the bulbar region and at least two spinal regions or the presence of UMN and LMN signs in three spinal regions. |
| **Clinically Probable ALS** is defined on clinical evidence alone by UMN and LMN signs in at least two regions with some UMN signs necessarily rostral to (above) the LMN signs. |
| **Clinically Probable ALS - Laboratory-Supported** is defined when clinical signs of UMN and LMN dysfunction are in only one region, or when UMN signs alone are present in one region, and LMN signs defined by EMG criteria are present in at least two regions, with proper application of neuroimaging and clinical laboratory protocols to exclude other causes. |
| **Clinically Possible ALS** is defined when clinical signs of UMN and LMN dysfunction are found together in only one region or UMN signs are found alone in two or more regions; or LMN signs are found rostral to UMN signs and the diagnosis of Clinically Probable ALS - Laboratory supported cannot be proven by evidence on clinical grounds in conjunction with electrodiagnostic, neurophysiologic, neuroimaging or clinical laboratory studies. Other diagnoses must have been excluded to accept a diagnosis of Clinically Possible ALS. |
| **Clinically Suspected ALS** may be suspected in many settings where the diagnosis of ALS could not be regarded as sufficiently certain to include the patient in a resesarch study. Hence, this category is deleted from the revised El Escorial Criteria for the Diagnosis of ALS. |

**Key References**


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