Amyotrophic Lateral Sclerosis (ALS) Point-of-Care Infographic

Due to its rarity and wide range of symptoms and progression rates, it is challenging to establish an ALS diagnosis based solely on clinical presentation. Additionally, ALS symptoms, particularly in the early stages, can overlap with those of other neurological and neuromuscular disorders. Furthermore, there is a lack of validated biomarkers that provide a clear diagnostic signal in ALS. As such, it is typically diagnosed through exclusionary testing. Adding to the diagnostic challenges, despite being present in ~30%-50% of patients with ALS, cognitive and behavioral symptoms are often overlooked during diagnostic assessment. This tool provides a framework for the recognition and evidence-based diagnosis of ALS.

Classification of ALS1-5

There are **two primary methods used to classify ALS**, one based on underlying cause, and the other on clinical onset.

Classification by Underlying Cause

ALS with no identified genetic mutation (~75% of all cases)

Exact etiology unknown
but thought to involve complex interplay of biological and environmental factors.

ALS with [name of specific] genetic mutation

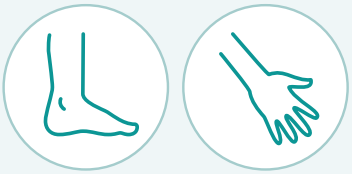
More than 40 ALS-associated genes have been identified.
Changes in known ALS genes are found in ~25% of ALS patients, of which ~5%-10% of cases are inherited. The presence of more than one variant is associated with earlier age of onset.

Classification by Clinical Onset

The early symptoms of ALS are usually relatively mild, initially impacting one part of the body before progressing to additional body regions. Depending on which part of the body is affected first, ALS is classified as limb-onset or bulbar-onset (or rarely respiratory).

Limb-onset ALS

Initial symptoms affect muscles in the **arms and hands or legs and feet**



Observed in **~two-thirds of all ALS cases**

Bulbar-onset ALS

Initial symptoms affect muscles in **head and neck**

Observed in **~one-third of all ALS cases; more common in women**

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ALS Risk Factors[3,6-8]

Older age (average age at diagnosis is 55)

Male sex

Family history and genetic factors

Environmental and lifestyle factors

More than 40 ALS-associated genes have been identified. Four account for most genetically based cases of ALS.

- ***C9orf72***
- ***SOD1***
- ***TARDBP***
- ***FUS***

Growing evidence suggests that several environmental and lifestyle factors may contribute to the onset of ALS.

- Military service
- Exposure to blue green algae
- Exposure to pesticides
- Exposure to electromagnetic fields
- Head trauma
- Smoking
- BMI and nutritional state

Common Signs and Symptoms of ALS[1-3,9]

ALS is characterized by **loss of upper and lower motor neurons, resulting in progressive weakness and atrophy of voluntary skeletal muscles** involved in movement, swallowing, speaking, and respiratory function.

Hallmark of ALS

Progressive, asymmetrical muscle weakness without pain or sensory loss

Motor and Extra-Motor Symptoms

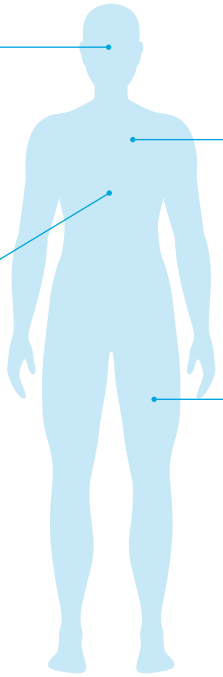
In addition to motor dysfunction, **cognitive and behavioral changes occur in ~50% of individuals with ALS**

Head and Neck (Bulbar-onset)

- ☐ **Fasciculations** (tongue/face)
- ☐ Dysarthria
- ☐ Dysphagia
- ☐ Hypersalivation

Upper Body (Limb-onset)

- ☐ **Fasciculations and cramps** (especially deltoid, scapula, triceps)
- ☐ Spasms
- ☐ Split hand sign
- ☐ Finger or proximal arm weakness
- ☐ Fine motor skill difficulties
- ☐ Limited range of motion



Respiratory

- ☐ Shortness of breath
- ☐ Restricted breathing
- ☐ Sleep disturbances

Lower Body (Limb-onset)

- ☐ **Fasciculations and cramps** (especially thighs)
- ☐ Ankle or proximal leg weakness
- ☐ Unsteady gait
- ☐ Frequent tripping
- ☐ Difficulty using stairs

Emotional, Cognitive, & Behavioral

- ☐ Emotional lability (pseudobulbar affect)
- ☐ Executive dysfunction
- ☐ Language deficits
- ☐ Verbal fluency difficulties
- ☐ Memory deficits
- ☐ Changes in social behavior
- ☐ Apathy
- ☐ Frontotemporal dementia (~15% of patients; more common in bulbar-onset)

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ALS Diagnostic Criteria and Common Diagnostic Tests[9-11]

The Gold Coast Criteria[10] was developed in 2019 to simplify and improve ALS diagnosis:

1 Progressive motor impairment documented by history of repeated clinical assessment, preceded by normal function

+

2 Presence of upper and lower motor neuron dysfunction in at least 1 body region

+

3 Investigations excluding other disease processes

Nerve conduction studies (motor and sensory)	• At least two sites tested, including one upper limb and one lower • Findings consistent with ALS: - Normal or compound muscle action potential (CMAP) - Prolongations of distal motor latency - Slowing of conduction velocity
Electromyography	• Often performed at same time as nerve conduction studies • Findings consistent with ALS: - Spontaneous electrical activity when muscle is at rest - Prolongations of distal motor latency - Slowing of conduction velocity
Magnetic resonance imaging	• Used to exclude brain and spine lesions that mimic ALS by producing upper motor neuron and lower motor neuron signs • Findings consistent with ALS: - Hyperintensity of the corticospinal tracts
Muscle and nerve biopsies	• Used to rule out mimic syndromes (eg, inclusion body myositis) • Can demonstrate lower motor neuron dysfunction in a body region when clinical or electrophysiological studies do not support • Findings consistent with ALS: - Loss of muscle fibers - Changes in muscle morphology and/or cell shape
Spinal tap	• Used to exclude mimic syndromes • Findings consistent with ALS: - cerebrospinal fluid (CSF) protein levels less than 100 mg/dl
Genetic testing	• Used to identify ALS-associated mutations
Neuropsychological evaluations	• Used to diagnose cognitive and behavioral impairment in ALS, including frontotemporal dementia (FTD)

Most common "ALS mimic syndromes":

cerebral lesions, skull base lesions, cervical spondylotic myelopathy, foramen magnum lesions, intrinsic and extrinsic tumors, conus lesions and lumbo-sacral radiculopathy, inclusion body myositis, cramp/fasciculation/myokymia syndromes, multifocal motor neuropathy, Kennedy's disease.

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