# Amyotrophic lateral sclerosis

**Amyotrophic lateral sclerosis** (also **ALS , Charcot's disease , Lou Gehrig's disease , motor neuron disease** ) is a disease characterized by progressive degeneration of motoneurons of the anterior horns of the spinal cord, motor cortex , motoneurons of the cranial nerves and degeneration of the corticospinal tract .

| Amyotrophic lateral sclerosis | |
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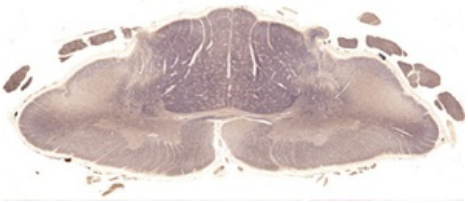
|  Degeneration of lateral cords | |
| **Risk factors** | male gender |
| **Incidence in the Czech Republic** | 1–2:100,000 |
| **Prevalence in the Czech Republic** | 4–6:100,000 |
| **Classification and references** | |
| **ICD-10** | G12.2 |
| **MeSH ID** | D000690 |
| **OMIM** | 105400 |
| **MedlinePlus** | 000688 |
| **Medscape** | 1170097 |

## Epidemiology

The incidence of ALS in the population worldwide is 1–2:100,000 (prevalence 4–6:100,000 ), and this is relatively uniform across nationalities. The disease usually affects individuals between the ages of 50 and 70. year of age, occurrence is rare before the age of 40. ALS is more common in men than in women by a ratio of 1.3:1. The disease occurs mostly sporadically, in 5–10% it occurs as a hereditary form (see Forms of ALS ).

**Risk factors** are age, male gender and genetic predisposition.

## Etiopathogenesis

Etiopathogenesis is not fully elucidated. Viruses , autoimmune mechanisms , and the toxic action of **glutamate** and **free oxygen radicals** are suspected( **ROS** ).

- In 20% of hereditary forms of ALS, there is a **defect in the SOD1 gene** on chromosome 21. The SOD1 147450 gene codes for *superoxide dismutase* , an enzyme involved in the conversion of superoxide anion into oxygen and hydrogen peroxide. In addition, superoxide dismutase also has the character of a peroxidase. A mutation in this gene will give rise to a structurally unstable product with low enzymatic activity and a short half-life. The cell is thus increasingly exposed to **oxidative stress,** which is toxic to the cell. This theory is supported by many studies, but it is not completely "bulletproof". This theory assumes the origin of ALS on the basis of reduced activity of the superoxide dismutase enzyme. An experiment was therefore carried out on mice in which the defective enzyme was overexpressed to compensate for its lower activity. However, the ALS picture developed the same way in mice. It was therefore concluded that the disease is not caused by insufficient enzyme activity, but by the very presence of a pathological enzyme that has **increased peroxidase activity** .
- **According to another hypothesis, the homeostasis of copper and zinc** is disturbed due to mutated SOD1 . These are metals known for their neurotoxicity. A sudden large release of these metals from SOD1 aggregates can lead to cell death.
- Another hypothesis refers to disruption of cellular transport due to **hyperphosphorylated neurofilaments** .[1]
- ALS can rarely be a paraneoplastic syndrome.[2]

# Histopathology

Microscopically, one can see **atrophy of neuron** bodies and **spherical formations** contained in their cytoplasm . These formations are formed by strongly argentophilic bundles of neurofilaments, which may also contain other cellular elements, e.g. mitochondria . **Small, round, eosinophilic bodies, so-called Bunina bodies** , and **eosinophilic inclusions similar to Lewy bodies** can also be seen in the cytoplasm of neurons .

# Clinical picture

A typical picture is a **combined paresis** of central and peripheral type. Muscular atrophy, fasciculation , but also tendon-bone hyperreflexia and spastic phenomena are present. Usually, the image is **asymmetrical** on one upper or lower limb, especially **acral** .  fine motor skills of the hand and its muscle strength are primarily affected, gradually the muscles of the forearm and arm are affected. The **disease progresses** relatively quickly , without remissions, and gradually affects more muscle groups of the limbs and trunk.  motoneurons of the cranial nerves are gradually affected, primarily the motoneurons located below in the brainstem are affected. Palsy of the oculomotor nerve is thus relatively rare, unlike damage to the hypoglossal nerve .  Disability IX.–XII. of the cranial nerve, the image of bulbar syndrome is created . However, bulbar syndrome can sometimes be the first symptom.

Sensitivity, sphincter activity and psyche are normal even in severe ALS.

ALS is a fatal, **incurable disease** , with an average survival time of 2–3 years.  There are also forms with slower progression. The cause of death is respiratory muscle failure or bulbar syndrome, in which the cough reflex is extinguished, aspiration and suffocation may occur.

# Forms of ALS

## Commonly recognized variants

- **SALS** – sporadic form of ALS (sporadic ALS).
- **FALS** – hereditary form of ALS (familial ALS).
- **Guam form of ALS** - **a rare form of ALS found in the Western Pacific (Guam) characterized by the presence of** parkinsonism , dementia , or both in addition to the ALS picture .

## According to isolated or predominant motoneuron involvement

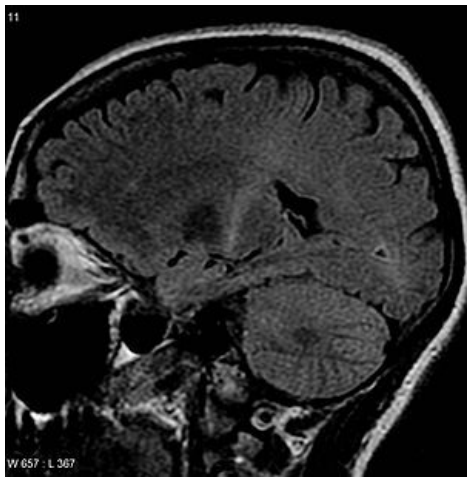
- **Progressive bulbar paralysis** – disability in the bulbar location (upper motor neuron of the cranial nerves and lower motor neuron of the cranial nerves).
- **Primary lateral sclerosis** - involvement only in the central region (upper motoneuron), is rare and relatively benign.
- **Progressive muscular atrophy** – disability in the spinal region (lower motoneuron).

# Diagnostics

In addition to the **anamnesis** and **neurological examination** , an EMG recording is examined , which will demonstrate the loss of motor units and denervation manifestations of multiple segments.  CSF proteinuria may be slightly elevated (less than 200 mg/dL). Similarly, muscle-type creatine kinase may be elevated .

In 1994, criteria ( **El Escorial criteria** ) were adopted to standardize the diagnosis of ALS. The criteria are based on clinical, electrophysiological and neuropathological signs of degeneration of the upper motoneuron (HM, central motoneuron of the cortex or trunk innervating the lower motoneuron) and lower motoneuron (DM, peripheral motoneuron innervating the muscle) and their progression over time.

- Suspected ALS
  - DM damage in at least two areas.
- Maybe ALS
  - both DM and HM damage in one area;
  - HM disability in at least two areas;
  - DM lesions are rostral to HM lesions.
- Probable ALS
  - HM disability in at least two areas, while they are above DM disability marks.
- Definitive ALS
  - damage to HM and DM in the bulbar region and simultaneous involvement of two spinal regions;
  - damage to HM and DM in three spinal regions.



MR - Increased signal of the inner posterior part of the capsula interna, which can be transmitted to the subcortical white matter of the motor cortex. Demarcation of the corticospinal tract is manifested by the clinical diagnosis of ALS.

# Differential diagnosis

- **Cervical myelopathy** – there is usually a peripheral or mixed motor deficit on the upper limbs, there is always a central spastic lesion on the lower limbs. There is no bulbar syndrome and, in addition, sensitivity disorders appear. CT , MRI , PMG will demonstrate the lesion.
- **Conditions after electric shock.**
- **Kennedy disease** - males only, very slow progression, lack of central motor neuron involvement.
- **Multifocal motor neuropathy** - mimics ALS very well, conduction block can be very difficult to find. Curable.
- **Chronic inflammatory demyelinating polyneuropathy (CIDP)**

- **Polyneuropathy and polyradiculopathy** - here, however, central motor symptoms are absent and sensitivity is often affected.
- **Spinal muscular atrophy** – occurs in younger people and the involvement is symmetrical.

# Therapy

Causal therapy is not known .

- Slowing down of disease progression was observed after administration of **riluzole** . Riluzole has a neuroprotective effect, however its effect on ALS is questionable and limited mainly to the early stages of the disease. Riluzole blocks voltage-gated sodium channels and is protective against glutamate toxicity.

- Symptomatic treatment can improve quality of life. **Baclofen , phenytoin and quinine** are used to relieve convulsions . **Anticholinergics** are used to suppress salivation . In some patients, amitriptyline may help to manage pseudobulbar symptoms.

- In the terminal phase, artificial pulmonary ventilation and nutritional care are used.

# Links

## Related Articles

- Bulbar syndrome

## External Links

- Amyotrophic lateal sclerosis, eng. Wikipedia (https://en.wikipedia.org/wiki/Amyotrophic_lateral_sclerosis)
- Amyotrofická laterální skleróza, prof. MUDr. Zdeněk Ambler, DrSc. (http://www.solen.cz/pdfs/neu/2006/01/02.pdf)
- http://www.alsa.org/

## References


1. NEVŠÍMALOVÁ, Soňa, Evžen RÚŽIČKA and Jiří TICHÝ. *Neurology.* 1st edition. Prague: Galén, 0000. 0 pp. ISBN 80-7262-160-2 .
2. ↑Jump up to:a b c d e f g h i j k l AMBLER, Zdeněk. *Basics of neurology.* 6th edition. Prague: Galén, 2006. 0 pp. ISBN 80-7262-433-4 .
3. ↑Jump up to:a b c GOETZ, Christopher, et al. *Textbook Of Clinical Neurology.* 3rd edition. 2007. ISBN 1-4160-3618-0 .
4. ↑Jump up to:a b c d e GOETZ, Christopher, et al. *Textbook Of Clinical Neurology.* 3rd edition. 2007. ISBN 1-4160-3618-0 .
5. ↑Jump up to:a b GOETZ, Christopher, et al. *Textbook Of Clinical Neurology.* 3rd edition. 2007. ISBN 1-4160-3618-0 .
6. ↑ Goetz, Christopher, et al. *Textbook Of Clinical Neurology.* 3rd edition. 2007. ISBN 1-4160-3618-0 .
7. ↑Jump up to:a b GOETZ, Christopher, et al. *Textbook Of Clinical Neurology.* 3rd edition. 2007. ISBN 1-4160-3618-0 .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2. **Cite error: Invalid <ref> tag; no text was provided for refs named `Ambler`**