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# Amyotrophic Lateral Sclerosis (ALS) and Related Motor Neuron Diseases: An Overview

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**ABSTRACT.** *Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative motor neuron disease, resulting in the destruction and ultimate death of neurons that control muscles. ALS affects motor neurons in the brain, brainstem, and spinal cord (upper motor neurons, bulbar region of the brain, and lower motor neurons). ALS patients have an average life expectancy of 3-5 years, therefore, proper diagnosis, care, and treatment is essential in order to provide the best quality of life for these patients. A thorough understanding of the symptomatology, potential cause(s), progression, and treatment of ALS is essential to provide timely and high-quality patient care. Electrodiagnostic examination, specifically electromyography (EMG) and nerve conduction studies (NCS), is one of the key diagnostics of ALS.*

**KEY WORDS.** *Amyotrophic lateral sclerosis (ALS), electromyography/nerve conduction studies (EMG/NCS), Lou Gehrig, lower motor neuron, upper motor neuron.*

## INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a progressive disease of motor neurons in the brain and spinal cord that results in the destruction of nerve cells, which results in atrophy and degeneration of the muscles they supply. The name comes from the Greek word “amyotrophia,” which means “no muscle nourishment or sustenance” (Aebischer and Kato, 2007) (Figure 1). The word “lateral” refers to the area of the spinal cord that is damaged by the disease. The word “sclerosis” comes from the Greek word for “hard” and means hardening or scarring of the tissue. Since the late 1930s and early

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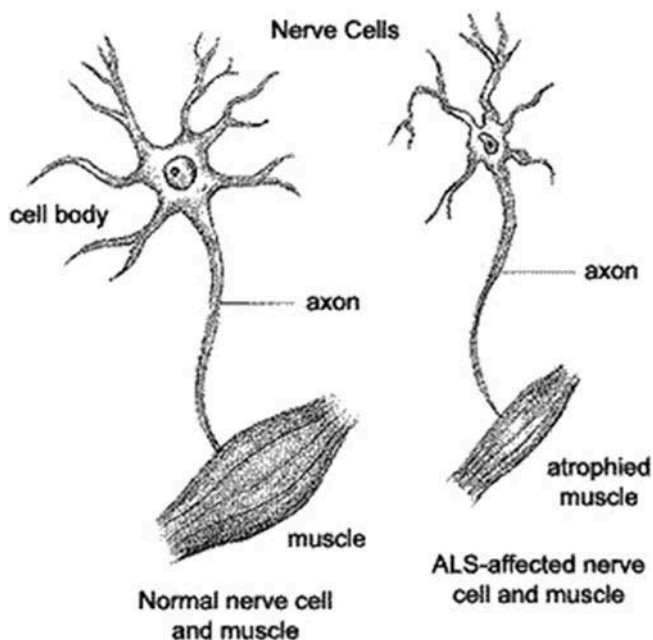


FIG. 1. Normal versus ALS nerve cell (Image courtesy of Pixgood).

1940s, ALS has also been called Lou Gehrig's disease, deriving its name from one of the most famous baseball players of all time (Aebischer and Kato, 2007). Gehrig succumbed to the disease that bears his name in June 1941.

Someone is diagnosed with or loses their life to ALS every 90 minutes (ALS Foundation 2014). This adds up to 16 people per day, every day, 112 people per week, and approximately 5,824 people per year. The incidence for ALS in the United States is approximately 1 in 100,000 people and the onset of the disease is usually between 55 and 66 years of age (Brashear and Elovic, 2011). Men are slightly more affected than women and the median survival range is 3 to 5 years in duration<sup>3</sup>.

## HISTORICAL SIGNIFICANCE

ALS was first described in 1824 by English anatomist, Sir Charles Bell (Rowland 2001). In the late 1860s, Dr. Jean-Martin Charcot correlated ALS symptoms with neuromuscular abnormality, and the disease was known as Charcot's disease until 1874, when Charcot officially identified and renamed the disease amyotrophic lateral sclerosis (Rowland 2001). For the next half-century, little was known regarding the disease. It would take a diagnosis of ALS for one of the most famous and legendary

sports heroes of all time to put ALS in the national spotlight, leading to increased awareness of the destructive effects of the disease.

Lou Gehrig was a Major League Baseball first baseman for the New York Yankees (Robinson 1990) (Figure 2). Gehrig's endurance and power were legendary, however by the middle of the 1938 season, Gehrig was experiencing a tiredness that he had never experienced before. By spring training in 1939, Gehrig's power had diminished greatly, along with his speed and coordination. Plays that were routine for him became more and more difficult. Finally, on May 2, 1939, Gehrig took himself out of the lineup, ending his consecutive game streak (Robinson 1990). Little did people know that Gehrig would never play baseball again. By the middle of June of the same year, Gehrig's condition had worsened so dramatically that his wife contacted the Mayo Clinic, where he was eventually diagnosed with ALS on his 36th birthday (Robinson 1990). His weakness



**FIG. 2.** Lou Gehrig (Harris & Ewing Collection at the US Library of Congress, copyright expired).

and swallowing difficulties were rapidly progressing, although his mind remained as sharp as ever. The Yankees announced his retirement in late June and on July 4th a day of appreciation was held at Yankee Stadium. Awards, trophies, and memorabilia were presented to Gehrig, who was too weak to hold many of them. During that celebration Gehrig delivered his “Luckiest Man on the Face of the Earth” speech, cruel irony in that he probably was one of the unluckiest men at the time (*Sports Illustrated* 2014). Gehrig’s outlook was remarkable for an athlete just struck down by such a devastating disease. He died June 2, 1941 at his home (Robinson 1990).

Since Gehrig’s death, ALS has been more closely followed and studied. The disease has struck people from all walks of life—the famous, the infamous, the ordinary, and the extraordinary. Perhaps the most recognized person with ALS alive today is astrophysicist Dr. Stephen Hawking (Aebischer and Kato, 2007). He was diagnosed with ALS in 1963 and has survived for over 50 years with ventilator support. He is completely dependent in all aspects of life, however his mind is still intact and he is able to continue making significant contributions to his field of study. With future research into ALS and the hope of a cure, people like Dr. Hawking may become the rule rather than the exception.

## UPPER AND LOWER MOTOR NEURON SIGNS AND SYMPTOMS

Motor neuron diseases are classified by pathogenesis and location of degeneration in upper motor neurons (UMNs), lower motor neurons (LMNs), or both. In ALS, the most common motor neuron disease, lesions occur in both, affecting the spinal cord, brainstem, and motor cortex (Brashear and Elovic, 2011). Classic characteristics of UMN lesions are as follows (Preston and Shapiro, 2005, Bertorini 2011):

1. Hyperreflexia: An increase, or over-responsiveness, in the deep tendon reflexes.
2. Presence of the Babinski reflex in the feet and toes: This reflex is dorsiflexion and fanning of the toes when an appropriate stimulation is given on the sole of the foot. It is normally present in children before the age of one, but if present later in life, it signifies an UMN lesion of some type.
3. Pyramidal weakness: Consisting of lower extremity flexor weakness in association with upper extremity extensor weakness.
4. Spasticity: The continuous contraction of muscles causes stiffness and tightness in the affected limb.
5. Clonus: A series of muscle movements that are rhythmic and involuntary; this also tends to present with the spasticity.
6. Dysphasia (the impairment of the ability to communicate) and agnosia (the inability to recognize sensory stimuli): These conditions may appear if the UMN lesion is in the cerebrum.

7. Dysarthria (poor articulation of speech) and dysphagia (difficulty in swallowing): These are likely to appear if the lesion is in the brain stem.

LMN originate in the anterior gray matter of the spinal cord and travel out distally to innervate muscles. Clinical findings of LMN lesions include (Preston and Shapiro, 2005, Bertorini 2011):

1. fasciculations (small involuntary, random muscle contractions);
2. muscle weakness;
3. muscle cramping both with and without exertion;
4. areflexia (absence of) or hyporeflexia (diminished) reflexes;
5. muscle hypotonia, atrophy, and/or flaccid paralysis.

Electromyography (EMG) findings of LMN lesions include:

1. fibrillation potentials, which appear when a muscle fires and its corresponding axons connect poorly or do not connect at all;
2. positive sharp waves;
3. polyphasic units, large or small.

One of the earliest symptoms of ALS may be the onset of distal weakness in the arms or legs, a lower motor neuron sign (Brashear and Elovic, 2011). The leg and foot weakness may manifest itself as weakness of the foot flexors and extensions. Walking may become difficult because of a mild to moderate foot drop. In the hands and fingers, the weakness presents as the inability to do fine motor skills. This weakness may be asymmetrical, affecting one arm and the opposite leg. It may also present as a one-sided weakness which then progresses to the opposite side. When muscles are not used due to weakness and affect the patient's ability to make voluntary movements, muscle atrophy then occurs in the limbs and even the tongue (Figure 3). In contrast to motor weakness, cognitive function and hearing and visual capabilities are spared in the early stages of the disease (Brashear and Elovic, 2011). As the disease progresses, bulbar problems may occur. The patient may choke and gag easily and have trouble swallowing. Respiratory failure occurs with chest and lung stiffness that results from ALS affecting the diaphragm and other muscles that affect breathing. This makes the use of a ventilator a must in many cases. In the late stages of ALS, decline of cognitive function involving the frontal and temporal lobes of the brain may occur, but generally the extra-ocular muscles are the last muscles to be affected. Patients at this stage often use eye movement as a means of communication (Aebischer and Kato, 2007). Patient essentially watch themselves die. The mind is fairly clear watching a disease ravage the rest of the body (Aebischer and Kato, 2007). In contrast, Alzheimer's patients have a relatively healthy body coping with a very diseased brain. There is no recovery, only progression of the disease until death.



**FIG. 3.** Patient with ALS. (A) The patient needs assistance from family members to stand. (B) Advanced atrophy of the tongue. (C) There is upper limb and truncal muscle atrophy with a positive Babinski sign. (D) Advanced thenar muscle atrophy (Open Access article from [openi.nlm.nih.gov](http://openi.nlm.nih.gov)).

### FORMS AND VARIANTS OF ALS

As described above, there are specific motor neuron disease symptoms based on the location of neurodegeneration. As such, there are several motor neuron diseases, described as ALS variant syndromes, which mimic ALS symptoms and must be ruled out before a diagnosis of ALS can be confirmed. Primary lateral sclerosis (PLS) is a rare, nonhereditary presentation of ALS that affects the upper motor neurons only (Bashear and Elovic, 2011). Symptoms of PLS include spasticity, stiffness, cramping and hyperreflexia, all signs of UMN involvement (Bashear and Elovic, 2011, Preston and Shapiro, 2005, Bertorini 2011). Onset of the disease is gradual and asymmetrical. This disease is seldom fatal and the life expectancy is normal, although patients with PLS can develop lower motor neuron presentation, even decades later (Bashear and Elovic, 2011, Bertorini 2011). Even though there is no known cure, treatment involves treating the symptoms with drugs like quinine and baclofen (Bashear and Elovic, 2011, Bertorini 2011).

Progressive muscular atrophy (PMA) is another motor neuron disease variant, and as the name implies, primary symptoms include muscle weakness and atrophy, and



fasciculations (Bashear and Elovic, 2011, Bertorini 2011, National Institute of Neurological Disorders and Stroke 2015). This disease affects only the LMNs and is also rare, typically with an earlier onset than other motor neuron diseases. PMA often develops into ALS (Bashear and Elovic, 2011, Bertorini 2011).

Progressive bulbar palsy (PBP) is a third variant of ALS. It attacks the brain stem, specifically the glossopharyngeal (9th), vagus (10th), and hypoglossal (12th) cranial nerves<sup>9</sup>. Symptoms include difficulty in swallowing, loss of speech as the disease progresses, and weakness and atrophy of facial and tongue muscles (Bashear and Elovic, 2011, Bertorini 2011). It has a very slow onset and generally affects patients over the age of 50. It is a slowly progressive disease and is often fatal, usually from complications of pneumonia, due to choking and aspiration (Bashear and Elovic, 2011, National Institute of Neurological Disorders and Stroke 2015).

### EL ESCORIAL AND ELECTRODIAGNOSTIC CRITERIA FOR ALS

ALS is a most serious, fatal disease, for which there currently is no definitive test available. In 1994, the World Federation of Neurology met in El Escorial, Spain, to establish guidelines for the diagnosis of ALS (Brooks et al. 2000). Because there are many conditions that mimic ALS and the range of disease progression is variable, diagnosis is very difficult, especially early in course of the disease. It is important that patients presenting with upper and/or lower motor neuron disease symptoms are referred for an extensive workup, such as electrodiagnostics and neuroimaging of the effected body part, blood work, HIV and genetic testing, and lumbar puncture to determine the degree of upper and/or lower motor neuron involvement and to exclude ALS mimics, such as myasthenia gravis, multiple sclerosis, Tay-Sachs disease, myopathies, and muscular dystrophies (Bashear and Elovic, 2011, Bertorini 2011). Once these determinations have been established, the El Escorial criteria described below, revised in 1998 and considered the gold standard of ALS diagnosis, provide a framework with which to establish a diagnosis (Bashear and Elovic, 2011, Bertorini 2011, Tan 2004):

- *Clinically definite ALS*: Presence of UMN and LMN signs in three body regions as defined by clinical evidence alone.
- *Clinically probable ALS*: Presence of UMN and LMN signs in two body regions. Clinical signs of UMN must be rostral to (above) the area of LMN signs.
- *Clinically probable, laboratory suspected ALS*: Presence of UMN and LMN signs demonstrated in one body segment OR UMN signs present in one body region and LMN abnormalities on EMG present in at least two segments.
- *Clinically possible ALS*: Clinical signs of both UMN and LMN in one body region OR UMN signs in two body regions OR LMN signs found in a segment above the UMN signs AND other diagnoses eliminated from consideration.



- *Clinically suspected ALS*: Clinical signs in at least one LMN region only or clinical signs in at least one UMN region only.

## EMG/NCS Examination

One of the most important diagnostic tools for ALS along with a thorough patient history and physical exam is the electrodiagnostic examination (Bashear and Elovic, 2011, Preston and Shapiro, 2005, Bertorini 2011, Kimura 2001). Clinical EMG testing characterizes motor unit action potentials during muscle contraction. A motor unit is the basic component of the peripheral nervous system, consisting of a single alpha motor neuron (LMN) and the muscle fibers it activates (Figure 1). Nerve conduction studies (NCS) are often performed with the EMG and help to assess demyelination (slow conduction velocities), axonal loss (drop in amplitudes), focal distal lesions (prolonged distal latencies), or combinations of the three. Repetitive stimulation studies are also done to study the neuromuscular junction.

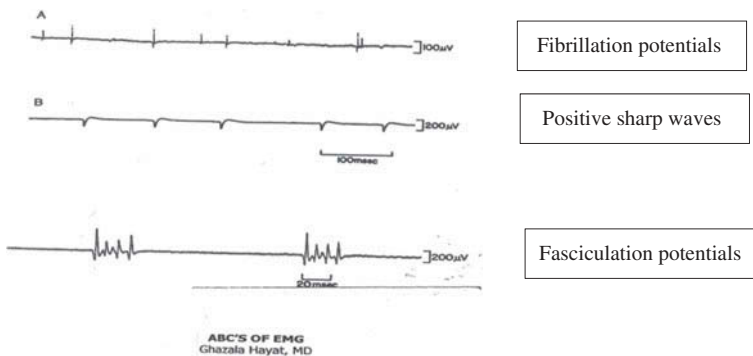
As discussed above, a set of electrodiagnostic criteria is used to ensure the correct diagnosis of ALS. These criteria include demonstrating the presence of fasciculations, fibrillation potentials, differences in motor conduction velocity (CV) between affected and unaffected nerves, and the excitability of the affected afferent nerve fibers (Preston and Shapiro, 2005, Kimura 2001). In the nerve conduction exam, the motor CVs may be scattered, but most result in normal values or values within 70% of the normal value for the patient's particular age group (Tan 2004). Motor distal latencies may well be normal. The only abnormality may consist of reduced motor amplitudes, resulting from axon loss (Tan 2004). It is important to keep in mind that axon loss may be present in neuropathies, plexopathies, and other radiculopathies, thereby mimicking ALS symptoms. In ALS, motor amplitudes may be decreased due to muscle atrophy along with a normal sensory studies. ALS may also be seen with other diseases like entrapment neuropathies that may make the motor latencies, motor CV, and sensory studies abnormal. Care must be taken to not confuse these diseases. Also remember that ALS may be seen in conjunction with neuropathies due to diabetes, alcohol, vitamin B12 deficiency, and other conditions, with those diseases causing an abnormal NCS exam. In almost 30% of ALS patients, a positive decrement (>12%) may occur on repetitive stimulation studies (Tan 2004). This is thought to be due to axonal branching and the formation of inefficient, immature neuromuscular junction sites in ALS patients and not due to diseases such as myasthenia gravis (Tan 2004). One of the diseases that may mimic ALS and may be confused with it is multifocal motor neuropathy with conduction block (MMNCB). This disease, like ALS, affects motor fibers with no sensory involvement. Patients with this disease experience the cramping and fasciculation that is common with ALS patients. Two very important factors make it different from an

ALS presentation (Preston and Shapiro, 2005, Bertorini 2011): First, the disease is primarily a disease of younger people rather than older ones. Second, and very important in distinguishing MMNCB from ALS, is that conduction block is the result of demyelination, not axonal loss. Unlike ALS, MMNCB is highly treatable and the outcome can be favorable, so it is very important that the two diseases be distinguished in the differential (Preston and Shapiro, 2005, Bertorini 2011).

### EMG FINDINGS

The EMG for ALS must be extensive and comprehensive, usually involving at least three extremities (LMN) and the tongue (UMN) (Preston and Shapiro, 2005). Findings for a definitive diagnosis of ALS are fibrillations and positive sharp waves in at least three extremities (Figure 4). These potentials signify that axonal loss has occurred and that denervation is present. Large polyphasic units with increased duration and a reduced recruitment pattern show that prior axonal loss and re-innervation has occurred.

While needle EMG is a sensitive indicator of axonal degeneration and loss, motor unit number estimates (MUNE) are more useful in assessing change over time and the progression of the disease (Tan 2004, Armon and Brandstater, 1999, Cudkowicz et al. 2004). MUNE is an electrophysiological technique used to determine approximately how many LMNs innervate a muscle or small group of muscles. Sequential decline in MUNE changes are required in order to properly assess degeneration and signs of progressive spread to other regions (Cudkowicz et al. 2004). MUNE typically decreases as much as 50% in each six-month period in the first year of the disease, but decreases more slowly after that (Tan 2004, Armon and Brandstater, 1999). Usually, the more that MUNE decreases in a shorter period of time, the poorer the



**FIG. 4.** EMG insertional potentials (image courtesy of Ghazala Hayat, M.D., “ABC’s of EMG,” presented at ASET Annual Conference, 2014).

prognosis for the patient. This presents the need for MUNE in earlier stages of the disease, to follow ALS patients over time, thus making the diagnosis of ALS more definitive (Cudkowicz et al. 2004).

## ELECTRODIAGNOSTIC FINDINGS THAT MIMIC ALS DISEASE

Many diseases and syndromes that are included in the differential diagnosis of ALS may mimic the electrodiagnostic findings of ALS. Some of these are very treatable and must be eliminated in order for a diagnosis of ALS to be confirmed.

As mentioned and discussed earlier, MMNCB is often confused with ALS during the electrodiagnostic exam. Since this is a motor entity, sensory studies will be normal. These patients have a far better prognosis than patients with ALS. Three characteristics of MMNCB help to differentiate it from ALS (Preston and Shapiro, 2005):

1. MMNCB has no UMN dysfunction.
2. In MMNCB, the weakness is out of proportion with the amount of muscle atrophy, therefore suggesting demyelination of the axon, not degeneration.
3. In MMNCB, distal weakness may spare individual nerves, making it a neuro-pathy rather than a motor neuron disease.

Inclusion body myositis (IBM), the most common inflammatory myopathy, is an autoimmune muscle disease (Bertorini 2011). It often presents as a slow, progressive weakness in the distal limbs, especially the foot extensors and deep finger flexors (Bertorini 2011). IBM can show an asymmetrical presentation, and most often patients display hyporeflexia or areflexia. Debilitating dysphagia also may occur with many IBM patients (Bertorini 2011). The EMG pattern is similar to that of ALS, however, IBM can be distinguished because cramps and fasciculations are not present in IBM, where as they usually are in ALS (Preston and Shapiro, 2005).

Another ALS mimic that should be ruled out in the differential diagnosis of ALS is lumbar and cervical stenosis (Preston and Shapiro, 2005). Gait disturbance and the combination of LMN signs in the upper extremities and UMN signs in the lower extremities present a picture similar to that of ALS. However, a good physical exam and history of the patient may help lead the examiner to the diagnosis of stenosis because it is usually stepwise in progression and may be associated with some related improvement (Preston and Shapiro, 2005). Back pain or neck pain is common in stenosis, depending upon its location. In addition, the pain may be exacerbated by walking and then relieved by sitting. None of these symptoms are common in ALS (Preston and Shapiro, 2005).

Fasciculations are found in many people and are considered normal, but too often the presence of fasciculations is a red flag for a diagnosis of ALS. If the number of fasciculations increase above what is normally seen and the patient has a normal EMG and neurologic examination, a diagnosis of benign fasciculation syndrome may be

made (Preston and Shapiro, 2005). It is important to note that fasciculations are not harmful nor do they present any proof of ALS.

There are several disease groups that affect the LMN and may be mistaken for ALS. One of these groups comprise the diseases known as spinal muscular atrophy (SMA) (Kimura 2001). This is an autosomal recessive disorder that causes progressive weakness. It is the second most common autosomal recessive disorder, just behind cystic fibrosis. It occurs in 1/10,000 live births and 1/24,000 chronic cases. SMA may be of four types:

- Acute infantile, known as Werdnig-Hoffman – birth to 6 months.
- Chronic infantile – 6 to 8 months.
- Chronic juvenile, known as Kugelberg-Welander – 18 months and older.
- Adult onset – This usually manifests around 30 years of age.

SMA shows weakness and muscle wasting with respiratory and bulbar problems as the disease progresses. There is no cerebral involvement. NCS usually affects motor studies with no sensory involvement, except in the Kennedy variant of SMA, where the sensory studies are abnormal. Motor studies may show decreased amplitudes if there is axon loss and, in some cases a slow CV of <44 m/sec in the arms and <41 m/sec in the legs if there is demyelination. EMG shows a myopathic picture with some fibrillations and pseudomyotonic discharge. Fasciculations are usually absent (Preston and Shapiro, 2005, Kimura 2001, Tan 2004).

Poliomyelitis is another strictly LMN disease that may be confused with ALS. It presents with fever, GI problems, aches and pains, and malaise and is caused by the poliovirus. The weakness is usually more prevalent in the legs than the arms (Preston and Shapiro, 2005, Kimura 2001). On NCS, motor amplitudes to atrophied muscles are decreased due to axon loss. On EMG, large motor units are present with decreased recruitment. Fibrillations, fasciculations, and positive sharp waves may also be present. Twenty-five to 30 years after the onset of polio, post-polio syndrome may occur. It is a chronic process, and muscles that were normal during the initial polio bout are now abnormal. It is a painful disease with fatigue as a common complaint.

Syringomyelia is another disease process that must be ruled out in diagnosing ALS. This is a cavity filled with spinal fluid that forms in the spinal cord and becomes a pseudocyst (Kimura 2001). This syrinx can expand and enlarge over time, destroying areas of the cord. The weakness seen on examination depends on the location of the cavity, either cervical, thoracic, or lumbar. Bladder dysfunction, muscle atrophy, and sensory loss may also occur. It is usually diagnosed radiographically by MRI. NCS may show decreased motor amplitudes due to axon loss. EMG findings include some fibrillation potentials and positive sharp waves with a reduced recruitment pattern. Somatosensory evoked potentials may be abnormal depending on the nerves studied.

## CAUSES OF ALS

There are three described causes of ALS, the most prevalent of which is the sporadic form, meaning unknown. Over 90% of all ALS cases in the United States fall into this category (Brashear and Elovic, 2011). The other two classifications are familial and Guamanian. Familial ALS comprises less than 10% of all ALS cases and is inherited as an autosomal dominant trait (Brashear and Elovic, 2011). In the 1940s and 1950s, an extremely high incidence of ALS was found in the Chamorro people of Guam and is thought to be associated with food and an environmental toxin (Brashear and Elovic, 2011, Plato et al. 2003). This form of ALS also includes symptoms of Parkinsonism and dementia and has also been described in patients from the Kii Peninsula of Japan, with findings suggestive of genetic pathogenesis due to environmental factors (Brashear and Elovic, 2011, Kuzuhara and Kokubu, 2005).

There have been many theories suggested and researched on how degeneration of motor neurons might occur in ALS patients (Aebischer and Kato, 2007) (Figure 5). Each theory suggests targeting different parts of the neuron or neighboring support cells, the glial cells. For example, one theory suggests that an over-activation of enzyme caspases, which function in cell death, inflammation, and necrosis, causes destruction of motor neuron cell bodies, thereby destroying the neuron (Aebischer and Kato, 2007). Another possibility is a buildup of damaging proteins in the cell body,

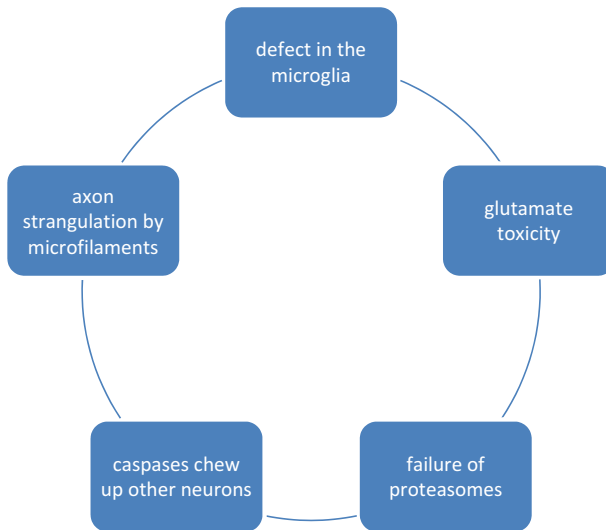


FIG. 5. Possible causes of ALS.

which is ultimately lethal to the neuron, due to the dysfunction of cell proteasomes. In normal cells, proteasomes act to break down these proteins to support the cell life cycle (Aebischer and Kato, 2007). “Axon strangulation” has also been proposed as a neurodegenerative mechanism in ALS patients (Aebischer and Kato, 2007). The shape of axons, especially long and wide axons, are supported by proteins called neurofilaments. Should neurofilaments accumulate abnormally in axons, they would interfere with the transport and flow of important nutrients and materials from the cell body, therefore “strangling” the axon. One proposed mechanism of both neurodegeneration and disease progression is an abnormality in the primary support cells of the central nervous system, microglia and astrocytes (Aebischer and Kato, 2007, Brashear and Elovic, 2011). Normally, microglia monitor nerve cells for damage and clear debris from damaged cells, and astrocytes act to clear excess glutamate from synaptic clefts. An abnormality in either of these glial cells causes a release or build-up of neurotoxins which harm the cell body (Aebischer and Kato, 2007, Brashear and Elovic, 2011). In fact, the only drug treatment approved by the U.S. Food and Drug Administration to slow the disease progression of ALS is Riluzole, which acts to inhibit glutamate release, thereby reducing glutamate build-up to decrease its deadly effects on motor neurons (Brashear and Elovic, 2011, Bertorini 2011).

## TREATMENT OF ALS

The spotlight on ALS began soon after Lou Gehrig died of the disease. In the 1950s the Muscular Dystrophy Association (MDA) was founded and began funding ALS research. Eleanor, Lou’s widow, served as the MDA’s National Campaign Chairman for more than a decade (Muscular Dystrophy Association 2015). By the 1980s, clinical trials of different drug treatments for ALS were begun. Dr. King Engel, a muscular dystrophy researcher at the University of Southern California, led the first clinical trial for a new ALS treatment using thyrotropin-releasing hormones to provide functional improvement in ALS patients (Engel et al. 1983). Interferons, a group of chemicals that attach to viruses, were also studied<sup>18</sup>. Another chemical trial used was to irradiate the lymph nodes of ALS patients (Muscular Dystrophy Association 2015). Amino acid trials were also used in a chemical study, as were growth hormones and cyclosporins. None of the above chemical trials were effective in the treatment of ALS.

By the 1990s, drugs such as myotrophin and gabapentin were shown to be ineffective in the treatment of ALS. Next, studies were begun on the neurotransmitters substance glutamate (Engel et al. 1983). Eventually, a drug that inhibits glutamate, Riluzole, was approved for use in ALS patients and found to extend life for a period of time. In 1991 a study was done that linked familial ALS to the super oxide dismutase (SOD1) gene on chromosome 21. Defects in this enzyme reduced the body’s motor neuron protection mechanism.

By the 2000s, other clinical trials also proved ineffective. Celebrex, an anti-inflammatory drug, coenzyme Q10, minocycline, and thalidomide all proved ineffective. Even drugs that blocked glutamate production or sped up its transport were not effective. Work with stem cell therapy is currently ongoing in ALS research.

For help in dealing with ALS, the ALS association provides certified centers of excellence, which provide individualized aspects of care and support during all phases of the disease, while at the same time being a liaison among the patient, the physicians, and the caregivers (ALS Association 2015). ALS, though not curable, is treatable. That treatment can be in many forms. One of the most important treatments is physical and occupational therapy. Mild to moderate exercise, such as bicycling and swimming, is a valuable tool, especially in the early stages of the disease (Bertorini 2011). Keeping ALS patients active is one of the best therapies available. As the disease progresses, patients must be able to use orthotics, walkers, and even wheelchairs. ALS patients need to keep their minds active, even as their bodies fail them, so mental exercise and well-being should be a priority. Supportive measures should also be used extensively (Bertorini 2011). A nutritionally sound diet is a must for those patients. If the problems affect the bulbar area, speech pathology and swallowing evaluations are needed to help preserve the patient's quality of life. Strong family support is necessary for patients with ALS. Counseling on what to do, where to do it, what's to come, how they can help, etc. should be a priority for each family member who is in close contact with the ALS patient. Medications to control pain and spasms and minimize infections should be readily available. As the disease progresses, ventilator support in the form of intermittent positive pressure ventilation or bilevel positive airway pressure may be necessary (Bertorini 2011). The goal is to help make these people as comfortable and independent as they can be under the circumstances. Remember, the mind is still working even though the body is not. End-of-life issues must be addressed with the patient and the family early in the course of the disease in order for quality decision making to be made.

## CONCLUSION

ALS is a motor neuron disease with a very poor prognosis. Therefore, it is essential to rule out other diseases that may mimic ALS. Knowledge of the symptoms and causes of ALS, a good physical exam, and an extensive electrodiagnostic examination all contribute to making the proper diagnosis of ALS.

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