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## Amyotrophic lateral sclerosis (ALS): A summary

Introduction   
Amyotrophic lateral sclerosis is a rapidly progressing neurodegenerative disease. It is also known as Lou Gehrig’s disease. It is a disease that targets the neurons (nerve cells) that control the voluntary muscles. ALS belongs to a class of neurological diseases known as the motor neuron diseases (MND). Motor neuron diseases involve the steady deterioration and death of motor neurons. Motor neurons function as the communication links between the voluntary muscles of the body and the nervous systems. These neurons are located in the brain and the spinal cord. Transmission of information and messages occurs from the motor neurons of the brain (known as upper motor neurons) to neurons in the spinal cord (known as the lower motor neurons) and to target muscles. ALS occurs when the upper and lower motor neurons degenerate and die and as a result, failure of signal transmission occurs. This death of motor neurons results in loss of function of the voluntary muscles. The muscles develop twitches and eventually become atrophic and die. The ability to initiate and control any voluntary movement is lost.   
Patients suffering from ALS lose their ability to move their arms, legs or move. The muscles that control breathing including the muscles of the diaphragm and chest wall do not function, and many patients die from respiratory failure, usually in 5 to 7 years from the commencement of the symptoms.

## Epidemiolgy of ALS

ALS is of the most commonly occurring degenerative neuromuscular diseases. 1-2 in 100, 000 people get affected by ALS. In the US approximately, 30000 patients have ALS, with 5000 or cases being diagnosed each year. It is mostly detected in patients 40-60 at years of age. ALS affects people of Caucasian origin more than other ethnic groups. However, three regions in the western pacific including Guam, western Papua demonstrate an increased occurrence of the disease (Gordon, 2013).

## Pathophysiology of ALS. What causes ALS?

The exact cause behind the disease is not well understood. The pathophysiology of ALS can be described by combination of molecular and genetic pathways. It has been demonstrated that 10% of ALS have a genetic link while 90% or so of cases occurs without genetic link and unknown cause. It has been demonstrated that a defect in the chromosome 21 that codes for the enzyme copper/ zinc superoxide dismutase (SOD) is responsible for 20% of ALS cases that occur due to genetic mutation or hereditary factors (Battistini et al. , 2010). SOD is an antioxidant enzyme that protects cells from free radicals such as superoxide formed in the mitochondria. It has been demonstrated that a mutant SOD1 protein can become toxic and cause neuronal cell death due to gain of function mutation. The mutant SOD also undergoes an aggregation that is a characteristic of both familial and sporadic ALS. A genetic abnormality known as the hexanucleotide repeat in a region known as C9orf72 has been shown to cause ALS in combination with dementia of fronto-temporal lobe and is responsible for 6-7% of all ALS cases in white Europeans (Majounie et al., 2012).   
While genetic mutations are responsible for a small percentage of ALS cases, most other ALS cases occur due to unknown reasons. Researchers have been looking at the role of environmental factors such as exposure to toxic agents’, occupational factors such as physical trauma suffered in wars and behavioral factors. The chemical messenger glutamate has also been demonstrated to be elevated in the serum and spinal fluid of patients with ALS. Glutamate is an excitatory neurotransmitter that binds to and activates postsynaptic receptors. Neurodegeneration can get triggered by over activation of the postsynaptic receptors by glutamate. A ‘ dying forward’ process has been suggested by which the UMN facilitate the degeneration of LMN by excitotoxic process (Kiernan et al., 2011). Other factors that contribute to ALS include abnormal functioning of the sodium/potassium pump, autophagy, mitochondrial structural abnormalities, etc. The neurotoxin -methyl amino L alanine that is found in cycad seeds consumed by native population in Guam has been demonstrated to cause neuronal cell death in ALS patients’.   
A few non-neuronal cells including the microglia and astrocytes can also contribute to neuronal damage by secreting neurotoxic molecules, insufficient neurotrophic factor release and increasing expression of glutamate receptors (Gordon, 2013).   
TDP-43 was recognized to play a role in neurodegeneration, in ALS by forming aggregates of ubiquitinated protein in the cytoplasm but not nucleus. Mutation in TARDBP gene that is responsible for the expression of TDP-43 that binds to both DNA and RNA. As a result, a mutation in TARDBP can lead to RNA processing regulation defect. FUS is another DNA binding protein that forms aggregates due to mutation in the gene FUS and is being demonstrated to be associated with ALS.

## ALS diagnosis

The presence of UMN and LMN symptoms suggest the presence of ALS, there is no conclusive test known for the disease. The diagnosis for the disease is carried out based on the number of symptoms that are observed by the physician and tests being carried out to rule out for other conditions. Neurological examination is routinely done to evaluate the progression of the disease symptoms such as muscular weakness and wasting, spasticity, etc. The symptoms of early stage of ALS resemble other disorders, as a result, tests such as electromyography (EMG), nerve conduction study (NCS), Magnetic resonance imaging (MRI), etc. can be utilized to rule out the diagnosis of ALS (Kiernan et al., 2011).

## Treatment and management of ALS

There has been no cure found for ALS as of yet. The medications and treatments used in ALS are used to improving the quality of life of the patients. A multidisciplinary team of physicians, physical and occupational therapists, nutritionists, nurses and therapists can provide supportive care for the ALS patient. The specialists can devise a plan aimed at keeping the patient active, mobile and comfortable. Exercise and physical therapy can help strengthen weak muscles and also reduce weakness and depression. Patients with ALS have trouble swallowing, therefore, nutritionists need to plan easy to prepare and swallow meals that provide enough nutrition. Riluzole is the first FDA approved drug for the treatment of ALS that reduces glutamate levels and prevents neuronal damage. It cannot reverse the damage already done to motor neurons. Non-invasive ventilators can be useful for respiratory insufficiency in ALS patients (Traub, Mitsumoto & Rowland, 2011).

## Future directions and ongoing research

ALS is a heterogeneous condition and treatments focused to induce neuroprotection are difficult to predict. Research is being done to identify good biomarkers to improve the diagnosis and progression of the disease (Otto et al. 2012). A number of ongoing studies are looking at use of physical therapy, exercise, and using a high fat diet to prevent energy depletion. The use of stem cell therapy has demonstrated efficacy in the mouse model of ALS and are now being investigated in patients. Antisense therapy targeted towards the genetic defects associated with ALS is also being evaluated (Miller et al., 2013). ALS is a rapidly progressing neurodegenerative disease. The disability causes by the disease can be overwhelming for the patient, their families and the health care team. A multidisciplinary focus on providing supplemental nutrition, respiratory support, and physical activity can improve the quality of life for the patient and extend survival modestly.

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