Definition of Motor Neurone Disease

The motor neurone diseases (MNDs) are a group of progressive neurological disorders that destroy motor neurones, the cells that control essential voluntary muscle activity such as speaking, walking, breathing, and swallowing. Some MNDs are inherited, but the causes of most cases of MND are not known. In sporadic or non-inherited MNDs, environmental, toxic, viral, or genetic factors may be implicated. MNDs are classified according to whether they are inherited or sporadic, and to whether degeneration affects upper motor neurones, lower motor neurones, or both.

Motor Neurone Disease Research Australia recognises the following forms of motor neurone disease:

1. Amyotrophic lateral sclerosis (ALS) is a progressive, ultimately fatal disorder that disrupts signals to all voluntary muscles. Both upper and lower motor neurones are affected. Approximately 75 percent of people with ALS will develop weakness and wasting of the bulbar muscles (muscles that control speech, swallowing, and chewing). Muscle weakness and atrophy occur on both sides of the body. Men are affected more often than women and ALS most commonly strikes people between 40 and 60 years of age. Several recent studies suggest that some people with ALS may develop cognitive problems involving word fluency, decision-making, and memory. Most cases of ALS occur sporadically, and family members of those individuals are not considered to be at increased risk for developing the disease. Familial forms of ALS account for 10 percent or less of cases of ALS.

2*. Progressive bulbar palsy*, also called progressive bulbar atrophy, involves the brain stem—the bulb-shaped region containing lower motor neurones needed for swallowing, speaking, chewing, and other functions. Symptoms include pharyngeal muscle weakness (involved with swallowing), weak jaw and facial muscles, progressive loss of speech, and tongue muscle atrophy. Limb weakness with both lower and upper motor neurone signs is almost always evident but less prominent. Affected persons have outbursts of laughing or crying (called *emotional lability*). In about 25 percent of individuals with ALS, early symptoms begin with bulbar involvement. Some 75 percent of individuals with classic ALS eventually show some bulbar involvement.

3. Pseudobulbar palsy, which shares many symptoms of progressive bulbar palsy, is characterised by degeneration of upper motor neurones that transmit signals to the lower motor neurones in the brain stem. Affected individuals have progressive loss of the ability to speak, chew, and swallow. Progressive weakness in facial muscles leads to an expressionless face. Individuals may develop a gravelly voice and an increased gag reflex. The tongue may become immobile and unable to protrude from the mouth. Individuals may have outbursts of laughing or crying.

4. Primary lateral sclerosis (PLS) affects the upper motor neurones of the arms, legs, and face. It occurs when specific nerve cells in the motor regions of the cerebral cortex gradually degenerate, causing the movements to be slow and effortful. The disorder often affects the legs first, followed by the body trunk, arms and hands, and, finally, the bulbar muscles. Speech may become slowed and slurred. When affected, the legs and arms become stiff, clumsy, slow and weak, leading to an inability to walk or carry out tasks requiring fine hand coordination. Difficulty with balance may lead to falls. Affected individuals commonly experience pseudobulbar affect and an overactive startle response. PLS is more common in men than in women, with a very gradual onset that generally occurs between ages 40 and 60. The cause is unknown.

5. Progressive muscular atrophy is marked by slow but progressive degeneration of only the lower motor neurones. It largely affects men, with onset earlier than in other MNDs. Weakness is typically seen first in the hands and then spreads into the lower body, where it can be severe. Other symptoms may include muscle wasting, clumsy hand movements, fasciculations, and muscle cramps. The trunk muscles and respiration may become affected. The disease develops into ALS in many instances.

The forms of motor neurone disease outlined in numbers 1 to 5 are the classical forms of motor neurone diseases (MND).

(Additional reference for considering the forms of MND for the purpose of MNDRA funding provision: MND Association, Guidelines for Submitting Summary Applications)

The following forms of motor neurone diseases will only be considered for MNDRA funding if a case for the potential benefit to the classical forms can be demonstrated.

6. Spinal muscular atrophy (SMA) is a hereditary disease affecting the lower motor neurones. It is an autosomal recessive disorder caused by defects in the SMN1 gene, which makes a protein important for the survival of motor neurones. SMA in children is classified into three types, based on ages of onset, severity, and progression of symptoms.

7. Kennedy's disease, also known as *progressive spinobulbar muscular atrophy*, is an X-linked recessive disease caused by mutations in the gene for the androgen receptor. The onset of symptoms is variable and the disease may first be recognised between 15 and 60 years of age.

Developed from the National Institute of Neurological Disorders and Stroke, Motor Neuron Diseases Fact Sheet at
www.ninds.nih.gov/disorders/motor_neuron_diseases/detail_motor_neuron_diseases.htm