MOTOR NEURON DISEASE

Key Concepts
- Definition of Motor Neuron Disease
- Types of Motor Neuron Disease
- Causes of Motor Neuron Disease
- Treatment of Motor Neuron Disease

Abstract: The motor neuron diseases (MNDs) are a group of progressive neurological disorders that destroy motor neurons. It ranks as the third most common neurological degenerative disorder after Alzheimer’s and Parkinson’s disease. Motor Neuron Disease occur in adults and children. The pathogenic processes underlying MND are likely to be multifactorial. Over recent years, the management of MND has evolved toward a multidisciplinary approach involving medical specialists, physiotherapists, occupational therapists, speech pathologists, dieticians, social workers and palliative care teams.

Key Words: Motor Neuron Disease, Progressive Bulbar Palsy, Amyotrophic sclerosis.

Definition
The motor neuron diseases (MNDs) are a group of progressive neurological disorders that destroy motor neurons, the cells that control essential voluntary muscle activity such as speaking, walking, breathing, and swallowing.

Introduction
Normally, messages from nerve cells in the brain (called upper motor neurons) are transmitted to nerve cells in the brain stem and spinal cord (called lower motor neurons) and from them to particular muscles.

Upper motor neurons direct the lower motor neurons to produce movements such as walking or chewing. Lower motor neurons control movement in the arms, legs, chest, face, throat, and tongue. Spinal motor neurons are also called anterior horn cells. Upper motor neurons are also called corticospinal neurons.

When there are disruptions in the signals between the lowest motor neurons and the muscle, the muscles do not work properly; the muscles gradually weaken and may begin to waste away and develop uncontrollable twitching (called fasciculations). When there are disruptions in the signals between the upper motor neurons and the lower motor neurons, the limb muscles develop stiffness (called spasticity), movements become slow...
2 and effortful, and tendon reflexes such as knee and ankle jerks become overactive. Over time, the ability to control voluntary movement can be lost.

Epidemiology of motor neuron disease
The prevalence of MND is 4-6 per 100,000 in most parts of the world. However, its annual incidence is between 1.5 and 2/100,000 and males are more commonly affected than females (1.4:1). The incidence increases with age with a mean age of onset of 63 years. It ranks as the third most common neurological degenerative disorder after Alzheimer’s and Parkinson’s disease. The incidence of MND is said to be increasing, but this is probably the result of improved diagnosis, better awareness of the disease and an aging population. The incidence increases after the age of 40 years, peaks in the late 60s and early 70s, and declines rapidly after that.

Causes and Risk Factors
Motor Neuron Disease occur in adults and children. In children, particularly in inherited or familial forms of the disease, symptoms can be present at birth or appear before the child learns to walk. In adults, MNDs occur more commonly in men than in women, with symptoms appearing after age 40.

Some MNDs are inherited, but the causes of most MNDs are not known. In sporadic or non inherited MNDs, environmental, toxic, viral, or genetic factors may be implicated.

Mechanisms of motor neurone degeneration
The pathogenic processes underlying MND are likely to be multifactorial. Current evidence suggests interplay between several mechanisms including:

- Glutamate mediated excitotoxicity
- Oxidative stress
- Mitochondrial dysfunction
- Neurotrophic factor dysfunction
- Protein aggregation
- Glial cell dysfunction

Many future research investigations are likely to revolve around the TDP-43 and FUS genes. Deposits of the FUS product were found in spinal cells of all sporadic MND samples tested, except those where their MND was caused by a mutation to the SOD 1 gene. No FUS deposits were found in tissue samples from people not affected by MND.

Classification
- Amyotrophic Lateral Sclerosis
- Progressive Bulbar Palsy
- Progressive Muscular Atrophy
- Primary Lateral Sclerosis
- Multifocal Motor Neuropathy
- Spinal Muscular Atrophy
- Kennedy’s Disease
- Monomelic Amyotrophy
- Brachial Amyotrophic Diplegia

Amyotrophic Lateral Sclerosis (ALS)
Limb onset affects 62%, trunk or respiratory onset affects ~4% of all MND diagnoses. Both upper and lower motor neurones (UMN & LMN) may be involved. Characterised by:

- muscle weakness,
- spasticity,
- hyperactive reflexes,
- emotional lability,
- fasciculations,
- weight loss.

Usually progresses (80% of cases) to include progressive bulbar palsy symptoms. Average survival 2-5 years from onset of first symptoms.
Progressive Muscular Atrophy (PMA)
Affects about 10% of all MND diagnoses. Defined as a disease of purely LMN degeneration, however a significant number of cases develop sub-clinical and, eventually, overt UMN signs. Characterised by:
• muscle weakness,
• wasting,
• weight loss
• fasciculation.

Affects men 5 times more commonly than women. Younger age of onset: average survival five years plus.

Progressive Bulbar Palsy (PBP)
UMN & LMN may be involved. Typified by
• dysarthria and dysphagia.

LMN damage:
• nasal speech,
• regurgitation of fluids via nose,
• tongue atrophy
• fasciculation,
• pharyngeal weakness.

UMN damage:
• tongue spasticity,
• explosive dysarthria,
• emotional lability.

Slightly more women than men affected. Average survival 6 months to 3 years from onset of symptoms

Primary Lateral Sclerosis (PLS)
Approximately 2% of all MND diagnoses. Only upper motor neurones damaged.

Characterised by
• muscle weakness,
• stiffness of limbs
• increased reflex response.

Men are affected twice as often as women. Onset usually after 50 years of age: Survival similar to normal life span.

The demarcation between the different clinical groups is frequently blurred. As the disease progresses there may be a considerable overlap resulting in more generalised muscle wasting and weakness

Average Age of Onset:
Early symptoms may include: stumbling, foot drop, weakened grip, slurred speech, cramp, muscle wasting and/or tiredness.

Most common in middle years. Although familial cases tend, on average, to be younger middle aged while sporadic cases tend, on average, to be closer to retirement age, MND can strike in any decade of life.

Differential Diagnosis:
No diagnostic tests currently exist but neurological investigations normally include EMG, blood tests and investigations that sometimes include, Lumbar puncture, Myelogram, Muscle Biopsy, MRI and/or CT scan to exclude possibility of other neurological conditions.

Aetiology
• Sporadic MND
About 90-95% of MND cases occur in people with no known family history of the condition. Current research suggests that the sporadic form of MND may develop as a result of a combination of genetic susceptibility, lifestyle and environmental factors that occur throughout life. Epidemiological research has failed to identify any significant risk factors to date.
• Familial MND
Familial MND accounts for around 5 to 10% of MND cases. Approximately one-fifth of these have an autosomal dominant mutation in the copper zinc superoxide dismutase 1 (SOD 1) gene on chromosome 21. Several other genes have been implicated in familial inheritance. However, these known genes still account for only half of the familial cases. Research is ongoing to identify the causative genes in the remaining familial cases.

Familial MND almost always displays autosomal dominant patterns of inheritance, although penetrance is quoted as about 80%. Age and site of onset can vary between cases within the same family.

Clinically the sporadic and familial forms of MND are indistinguishable.

Multidisciplinary management
Over recent years, the management of MND has evolved toward a multidisciplinary approach involving medical specialists, physiotherapists, occupational therapists, speech pathologists, dieticians, social workers and palliative care teams. This approach has been shown to improve the quality of life for patients, and their families, as well as survival rates.

Pharmacological management
Riluzole, an inhibitor of glutamate release, is a neuroprotective agent that slows disease progression. Patients prescribed riluzole therapy need regular blood screening, including liver function tests and full blood count every month for the first 3 months on riluzole and then every 3 months after.

Noninvasive ventilatory support
A recent advance in the treatment of MND has been the discovery of the benefits of noninvasive ventilatory support, whereby MND patients use a mask system attached to a small ventilator, usually a bi-level positive airway pressure machine. Patients may begin by wearing a nose or face mask overnight, and in the later stages of disease use it periodically during the day to rest their respiratory muscles. Noninvasive ventilation may relieve symptoms related to respiratory insufficiency and prolong survival by up to 12 months, in addition to improving quality of life.

References


