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Condition: Motor Neuron Disease

Title: Motor Neuron Disease: An overview of epidemiology, genetics, symptomatology, investigations and Management

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Epidemiology

Motor Neuron Disease (MND) is an incurable but relatively uncommon neurodegenerative condition. Approximately 1 in 15,000 Australians are currently living with the disease[1]. Individuals often develop MND between the ages of 50 years and 70 years, although people from any age group can develop the disease. Males are more often affected than females.

Genetics Factors

The cause of MND remains to be confirmed and it seems likely that the underlying mechanisms are multifactorial with environmental and genetic factors playing a role. In some a minority of cases MND has been passed down the family line and we are now aware of a number of genes which can cause this disorder. In 2011 a gene abnormality on chromosome 9, known as the *C9ORF72* genetic mutation, was described[2,3]. This mutation explains at least one-third of cases of familial MND as well as a proportion of sporadic MND. Inheritance of this mutation remains to be fully elucidated so although a patient may not have a known family history of MND, genetic testing for this mutation may still be considered. Three other genetic causes of familial MND are the SOD-1, TDP-43 and FUS mutations[4,5]. These three mutations are known to be Autosomal Dominant with a 50% risk of passing on the mutation to offspring.

Symptoms and Signs

MND is a relentlessly progressive disorder usually resulting in death within 2 -3 years of symptom onset. However, as with many neurological conditions progress can vary markedly between individual sufferers[6].

Signs and symptoms in MND are due to either upper motor neuron or lower motor neuron involvement. Upper and lower motor neuron simply refers to the level of the nervous system affected and the resultant signs and symptoms which occur. As such, in upper motor neurone disease the problem is at the level of the spinal cord or brain, and in lower motor neuron disease the problem is at the peripheral nerve or muscle. Symptoms associated with upper motor neuron involvement include weakness, muscle tightness and spasms. Symptoms associated with lower motor neurone involvement include weakness, flaccid limbs, cramps and muscle twitching also known as fasciculations. Symptoms which affect the muscles of swallowing and eating are called bulbar symptoms and these can be due to either upper or lower motor neurone involvement as can the muscles of breathing. Additional symptoms include fatigue and weight loss.

In addition to motor problems, it has now widely recognised that patients with MND can also present with cognitive or behavioural issues[7]. Cognitive issues can manifest as difficulty planning and multi-tasking, memory and language problems. Behavioural symptoms include lack of motivation, poor judgement and control in social situations, a lack of sympathy or empathy for loved ones or changes in eating habits such as the development of a sweet tooth or overeating. These symptoms are similar to those found in a related neurodegenerative condition known as frontotemporal dementia, and the two diseases are now believed to be on the same spectrum with many patients exhibiting symptoms of both diseases.

There are a number of variants of MND: Amyotrophic Lateral Sclerosis (ALS) is the most common variant while another variant Primary Lateral Sclerosis (PLS) occurs much less frequently**.**

ALS is characterised by both upper and lower motor neuron involvement. Patients often complain initially of a combination of symptoms including muscle twitching, muscle weakness, cramps and spasms. The weakness is often focal initially, beginning in one arm or leg. Weakness in the arm can cause problems writing, dressing, eating and washing. When the foot is affected a foot drop can develop resulting in trips and falls. This weakness will often progress to involve other limbs as well as the muscles of breathing, eating, swallowing and speech.

Bulbar MND occurs in approximately 20% of MND patients, this variant initially affects the muscles involved in eating, swallowing and speech. Patients often complain of choking episodes, initially with liquids and slurred speech. Patients eventually require a feeding tube inserted into the stomach to help with nutrition. The speech difficulties eventually cause significant communication problems and in this instance assisted communication devices are extremely helpful. As the disease progresses, limb symptoms will eventually develop. This variant often progresses at the fastest rate of all the subtypes of MND.

Primary Lateral Sclerosis (PLS) occurs much less frequently and is characterised by upper motor neuron involvement only. This is much more likely to begin in the legs with weakness and spasms and as a result falls, it then progresses to involve the trunk, arms and bulbar muscles. It can be difficult to diagnose PLS as there are a number of neurological conditions which present in a similar way. PLS progresses gradually and patients can survive many years even up to a decade.

Progressive Muscular Atrophy (PMA) is anther rare variant of MND in which progression is typically slower than other forms with average life expectancy between 5 and 10 years. Symptoms in PMA occur as a result of lower motor neuron involvement only, with patients presenting with weakness, wasting, cramps and muscle twitching. Bibrachial amyotrophy , also known as flail arm is a type of PMA which affects the muscles of the arms initially.

Investigations

There is no specific test to diagnose MND, instead the neurologist will consider the presenting symptoms together with the signs found on examination to determine if the pattern is typical for MND. There are a number of tests which can support a diagnosis of MND which are entirely safe but can cause a minimal amount of discomfort. These include tests of the muscles and nerves which use small electrical currents to measure nerve function and a small needle into the muscle to check for abnormalities. Transcranial magnetic stimulation will also be used in some circumstances, particularly research settings[8]. In this test a small magnet is applied to the head to measure to measure how well the nerve cells conduct information. In addition, patients will usually undergo an MRI of brain and spinal cord to rule out other diagnoses which can cause similar symptoms.

Management

Unfortunately, there is no cure for MND and management is based around symptoms management, usually in the setting of a multidisciplinary clinic. Physiotherapists, occupational therapist and orthotists can address mobility issues, suggest pain management programmes, provide support braces and splints for weak areas. A social worker co-ordinates the complex care needs of patients and families, as well as providing practical support on issues such as social benefits and work. The MND nurse also co-ordinates care and is a point of contact for patients and their families. Speech and language therapists assess speech and swallowing and advice on dietary modifications, communication devices and eventually provide support when supplemental feeding via a gastrostomy tube is necessary. The dietician provides dietary advise to ensure adequate nutrition. Other important members of the team include psychologists, palliative care doctors, respiratory doctors and dementia specialists.

Rilutek is a drug, which has been shown to increase the life expectancy of MND patients[9]. This increase is modest, however, the effects are greatest if this medication is taken in the early stages of disease. And finally, there is hope on the horizon as all of the large MND research centres throughout the world are working together with patients and pharmaceutical companies towards finding a cure for this disease.