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Motor neurone disease

Caring for the patient in general practice

Background
Motor neurone disease is a neurodegenerative disease that leads to progressive disability – and eventually death – within 2–3 years.

Objective
This article describes the role of the general practitioner in caring for patients with motor neurone disease.

Discussion
The diagnosis of motor neurone disease relies on the presence of upper and lower motor neurone features. There is currently no pathognomic test for motor neurone disease and it largely remains a diagnosis of exclusion following an accurate clinical history, combined with basic screening blood investigations and structural imaging of the brain and spinal cord. Neuro-physiological studies may be useful as an ancillary diagnostic tool. Riluzole, an anti-glutamate agent, is the only medication shown to have a survival benefit in motor neurone disease and results in a slowing of disease progression by an estimated 3–6 months. Noninvasive ventilation may relieve symptoms related to respiratory insufficiency and prolong survival by up to 12 months. A multidisciplinary approach to management has been shown to improve the quality of life for patients as well as survival. The GP is often the first point-of-contact when medical issues arise regarding management of disease related symptoms including sialorrhoea, dyspnoea, constipation and pain, through to percutaneous gastrostomy feeding tubes and maintenance of noninvasive ventilation. It is important to establish the patient's wishes for future care while they are still able to communicate easily.

Keywords: nervous system diseases; general practice

CPD

Motor neurone disease (MND) is a progressive neurodegenerative disease. It is characterised by motor systems failure that results in the death of nerves responsible for all voluntary movements, leading to limb paralysis, weakness of the muscles of speech and swallowing, and ultimately respiratory failure. Typically MND strikes patients at the prime of adult life, usually in the fifth to sixth decades, and has a short trajectory from diagnosis with an average life expectancy of less than 3 years.[1] Current estimates are that 1400 people are living with MND in Australia at any time, with 370 newly diagnosed patients each year.[2] More than one Australian dies every day from this most pernicious disease.

The cause of MND remains unknown but appears heterogeneous. Environmental factors may trigger an underlying susceptibility – toxins, chemicals, metals and trauma have all been proposed.[1] Most cases are sporadic with familial disease accounting for only 5–10% of cases. Recent studies have established that as many as 60% of patients will also display mild forms of cognitive impairment, often manifested by executive dysfunction, linking MND to other neurodegenerative processes, most commonly frontotemporal dementia.

When to suspect motor neurone disease

The diagnosis of MND relies on the presence of specific clinical criteria. A diagnosis of amyotropic lateral sclerosis (the most common form of MND) requires the presence of upper motor neurone features such as spasticity and hyper-reflexia, coexisting with lower motor neurone abnormalities such as fasciculation, wasting (*Figure 1*) and weakness; all in the same body region such as the arm or leg (*Table 1*).

Patients with upper limb onset MND will most commonly present with asymmetrical weakness,[3] reporting functional difficulties such as difficulty writing or opening bottles, or difficulty manipulating objects such as turning a key. On examination, there may be wasting of the intrinsic muscles of the hand.[4]

Early signs of lower limb weakness may include foot drop causing the patient to trip, difficulty climbing stairs, and patients may describe that their legs feel 'heavy'.[4] Patients with bulbar-onset MND typically present with slurring of the speech, which is sometimes mistaken for intoxication. Difficulties swallowing usually occur later. On examination, there may be weakness and wasting of the tongue and fasciculations (*Figure 2*). Rarely, weakness may begin in the respiratory muscles.

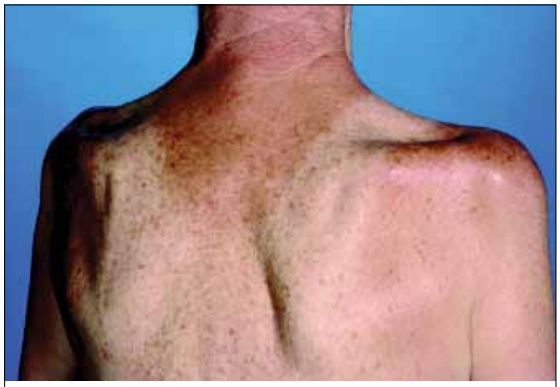


Figure 1. Prominent wasting of the shoulder girdle muscles in a patient presenting with upper limb-onset motor neurone disease

Table 1. Clinical signs of upper and lower motor neurone weakness

Upper weakness	Lower weakness
Muscle spasticity	Muscle wasting
Preserved reflexes in wasted muscles	Muscle weakness
Extensor plantar response	Fasciculations
Hyper-reflexia	Absent reflexes
Emotional lability	

Common clinical presentations

The most common clinical presentation of MND is amyotrophic lateral sclerosis, which presents with a combination of upper and lower motor neuron signs in the limbs and bulbar muscles. Othe conditions in the spectrum of MND include[5]:

- progressive muscle atrophy with only lower motor neuron signs initially; some patients develop later lower motor neurone signs
- primary lateral sclerosis, with predominantly upper motor neuron features, and
- progressive bulbar palsy, with degeneration of bulbar nuclei and preservation of anterior horn cell and upper motor neuron function.

Clinical examination aims to identify the presence of combined upper and lower motor neurone signs affecting the same region, essential for a diagnosis of amyotrophic lateral sclerosis. Either lower or upper MND may predominate in a patient and can vary between regions in the same patient, eg. one limb may be spastic with hyperactive reflexes while another limb has muscle atrophy and absent reflexes (*Table 2*).

Clinical investigations

There is currently no pathognomic test for MND and it largely remains a diagnosis of exclusion.[3] An accurate clinical history combined with basic screening blood investigations and structural imaging of the brain and spinal cord to exclude differential diagnoses remain the mainstay of investigations. Importantly, disorders that may mimic MND should be excluded (*Table 3*). However, a definitive diagnosis may not be possible initially and may only become clear over time with further evolution of signs and symptoms. Although confirmation of diagnosis takes an average of 14 months from the onset of symptoms,[4] it is important to reach a definitive diagnosis as soon as possible so that appropriate pharmacological and nonpharmacological therapies which address the emotional, social, psychological and spiritual needs of the patient may be implemented.

Neuro-physiological studies are the most critical ancillary tool in the investigation of MND and may be regarded as an extension of the physical examination. Routine studies include nerve conduction studies and electromyography. These provide information for:

- the support of a suspected clinical diagnosis
- identification of subclinical upper or lower motor neuron involvement
- determination of the extent and distribution of lower motor neuron loss
- the exclusion of disorders that may mimic MND (*Table 3*).[3]

Transcranial magnetic stimulation may be useful to establish upper motor neurone dysfunction.

Presently, the chief role of neuroimaging in the diagnostic work-up is to exclude the differential diagnoses. The most useful neuroimaging technique in MND is magnetic resonance imaging (MRI) of the brain and spinal cord. Structural lesions,[3] especially at the level of the spinal cord, and intrinsic parenchymal lesions, as seen in multiple sclerosis, can be effectively excluded with MRI. While most patients with MND will have a normal MRI scan, in some

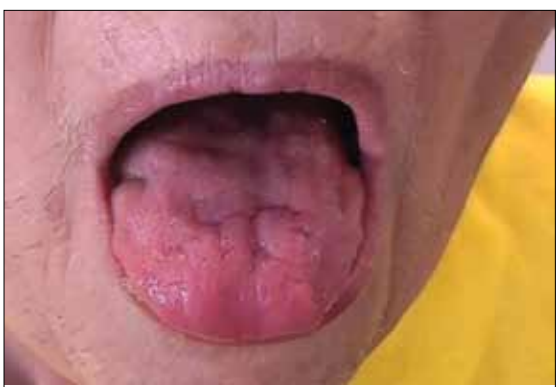


Figure 2. Bulbar features: the tongue is wasted and exhibits twitching/'worm-like' movements known as fasciculations

Table 2. Clinical findings suggestive of a diagnosis of motor neurone disease[5]

- Asymmetrical weakness in upper or lower limbs
- Brisk reflexes in a wasted limb
- Weakness in the absence of pain or prominent sensory symptoms
- Relentless progression of symptoms and signs

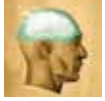


Table 3. Disorders that may mimic motor neurone disease[3]

Diagnosis	Investigations to confirm diagnosis
Multifocal motor neuropathy	Nerve conduction study (NCS), anti-ganglioside (GM1) antibodies
Chronic inflammatory demyelinating polyneuropathy	NCS, elevated cerebrospinal fluid (CSF) protein (lumbar puncture)
Post-polio syndrome	Clinical history, NCS/electromyography
Heavy metal poisoning (eg. lead)	Heavy metal urinary or blood screen
Myasthenia gravis	Repetitive nerve stimulation, single fibre-electromyography, antibodies for acetylcholine receptors
Inclusion body myositis, polymyositis, dermatomyositis	Serum creatine kinase, electromyography, muscle biopsy
Spinal cord compression	MRI spine
Vitamin B12 deficiency	Vitamin B12 levels
Multiple sclerosis	MRI brain, evoked potentials, CSF oligoclonal bands
Lyme disease	Lyme serology

patients, particularly those who are younger and have more prominent upper motor neuron signs, rounded foci of high signal intensity are evident along the corticospinal tract, reflecting axonal degeneration. However, these MRI changes lack sensitivity and specificity. With future refinement of techniques, MRI may play a more important role in the diagnosis of MND.

The diagnosis of MND is usually confirmed in the specialist setting. However, it is important for GPs to note that the news is invariably devastating for the patient and their family, and discussions must be handled sensitively. Patients must have ample time, including follow up appointments, to ask questions as they arise. Patients should be provided with information about support networks, particularly Motor Neurone Disease Australia (MNDA) (see *Resources*).

Role of the GP

Motor neurone disease is a relentlessly progressive disease without remission. As such, the needs of MND patients and their families change constantly. As the illness progresses, symptoms invariably escalate and patients will require more complex care. Managing these patients can be both challenging and demanding. The GP needs to be able to anticipate any problems that the patient may be facing and be proactive.

Australian figures indicate that 70% of people with MND are still living at home 4 weeks before death;[6] this will impact on the role of the GP, especially in geographic areas where palliative care in the home is not available. Specialist MND clinics and teams are available and can provide advice about specific patient care. Information about the location of these clinics and teams is available from MNDA (see *Resources*). Medicare rebates are available to GPs who coordinate or participate in case conferences and care planning through the Enhanced Primary Care Initiative (see *Resources*).

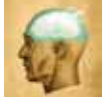
Multidisciplinary management

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.[7] Patients with bulbar-onset MND in particular, benefit from early advice about and early insertion of percutaneous endoscopic gastrostomy tubes to avoid surgical complications related to poor respiratory function.[7] Ideally, multidisciplinary teams should be coordinated by a specialist clinic in collaboration with the patient's GP.

Motor neurone clinics employ nurse specialists or allied health professionals as clinic coordinators, who can liaise with community teams and GPs. Clinics formally assess patients every 3 months, while the nurse coordinator manages daily care, facilitates care plans and makes recommendations to maximise patient quality of life. Importantly, while MND clinics exist in most Australian states and territories, patients in rural areas may find access difficult due to distance or deteriorating function. Seeing a neurologist with an interest in MND may be another option in these cases. If the patient is not under the care of an MND clinic, the GP may need to act in the role of case manager, liaising with the community health team and relevant physicians and coordinating the patient's care.

Pharmacological management

Riluzole, an inhibitor of glutamate release, is a neuroprotective agent that slows disease progression. Two large randomised trials established that riluzole had a modest effect in MND, increasing survival by 3–6 months,[7] although more recent analyses undertaken in multidisciplinary settings with respiratory intervention and nutritional support, suggest greater benefit. Riluzole is generally well tolerated by patients and is now available in Australia, approved by the Pharmaceutical Benefits Scheme for patients with MND. 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.



Effective treatments also exist for the relief of disease related symptoms including sialorrhoea, dyspnoea, constipation and pain (*Table 4*).

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.[4] 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,[8] in addition to improving quality of life.[4,9] A respiratory physician can determine patients suitable for noninvasive ventilation, taking into account factors such as bulbar weakness and disease progression. Patients experiencing symptoms such as claustrophobia and sialorrhoea may be assisted with medications (*Table 4*).

Other treatments

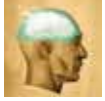
Patients newly diagnosed with MND often ask about the role of stem cell treatment. However, more critical experiments and clinical trials are needed before this becomes an option in MND. Some stem cell transplants have been reported to be safe and well tolerated in MND patients, although to date, no positive results have been reported.[10] There is a danger that patients will have false expectations if clinical trials are conducted prematurely. 'Stem cell centres' in the Ukraine and China lack published data and follow up, which prevents objective assessment of the effects of such approaches.[10] Some alternative therapies offer patients hope for a cure, however these are unproven, expensive and potentially harmful.[1]

The patient's wishes for future care

It is important to establish the patient's wishes for future care while they are still able to communicate easily. Ideally the patient's family will also be aware of the patient's wishes. This may be documented in the form of a letter for future care or an Advanced Care Directive

Table 4. Symptom management in motor neurone disease

Symptom	Drug management	Comment
Excess saliva	Amitryptyline, glycopyrrolate (oral or subcutaneous), atropine, hyoscine, botulinum toxin injection to salivary glands, irradiation of parotid gland	A portable suction machine may be helpful. Patient needs to be diligent with mouth care
Thick saliva	Normal saline nebulisers, mucolytics such as acetylcysteine nebulisers	Ensure the patient is adequately hydrated. Dark grape juice, pineapple juice or papaya may be helpful. A portable suction machine may assist
Dyspnoea	• Dyspnoea on exertion: short acting benzodiazepine (eg. lorazepam) • Dyspnoea at rest: long acting benzodiazepine (eg. diazepam and opioids)	A respiratory review will determine whether noninvasive ventilation will assist with respiratory symptoms
Constipation	• Coloxyl and senna • Movicol sachets	Ensure adequate hydration and dietary fibre
Muscle cramps	Magnesium, carbamazepine	• Physiotherapy – stretching • Tonic water
Muscle spasm/ spasticity	Baclofen, clonazepam	
Fasciculations	Carbamazepine, gabapentin	
Depression, emotional lability	Amitriptyline, selective serotonin reuptake inhibitors (SSRIs) (eg. citalopram) serotonin-noradrenaline reuptake inhibitors (SNRIs) (eg. venlafaxine)	Counselling may help
Choking sensation	• Lorazepam for short episodes • Oral morphine for longer episodes • Subcutaneous morphine and midazolam for severe and prolonged episodes	Patients (and their carers) need access to as-needed medications for use in a crisis (eg. morphine, midazolam, hyoscine). This can be done through the local palliative care team
Panic, claustrophobia	Lorazepam or clonazepam drops sublingually may assist (eg. if claustrophobic, taking clonazepam drops 20 minutes before mask fitting can help)	Deep breathing and meditation may help



(see *Resources*). This process can be initiated by the patient's GP, their neurologist or any other physician involved in their care. Discussions need to be documented in the patient's file and care plans must be shared with all members of the multidisciplinary team so that all are aware of the patient's wishes. Care plans may address the patient's wishes with regards to percutaneous endoscopic gastrostomy tubes, noninvasive ventilation, invasive ventilation and how actively they want their symptoms managed in the event of acute deterioration.[11]

Palliative care

At present, patients with MND are referred to palliative care at varying stages in the illness. Some clinicians argue that palliative care should start soon after diagnosis and form part of the continuum of care for the patient. However, a significant proportion of patients remain reticent to consider an early referral to palliative care services. Troublesome symptoms in patients approaching the terminal phase may include increased breathlessness at rest and worsening swallowing with increased risk of aspiration in the context of increased weakness. Appropriate medications should be made available in advance to these patients including[12]:

- morphine to relieve breathlessness and pain
- midazolam for agitation and distress, and
- glycopyorolate bromide or hyoscine sulfate to dry up distressing chesty secretions.

Having these medications available in the home may prevent a crisis situation from happening.

Summary of important points

- Motor neurone disease is a neurodegenerative disease resulting in limb paralysis, weakness of swallowing, and ultimately, respiratory failure.
- The diagnosis of MND relies on clinical criteria, specifically the presence of upper (eg. spasticity) and lower motor neurone features (eg. muscle wasting and weakness).
- There is no pathognomic test for MND; it largely remains a disease of exclusion.
- Riluzole is the only medication shown to slow disease progression (by an estimated 3–6 months).
- Noninvasive ventilation may relieve symptoms related to respiratory insufficiency and prolong survival by up to 12 months.
- A multidisciplinary approach to management has been shown to improve quality of life and survival. Ideally, multidisciplinary teams should be coordinated by a specialist MND clinic in collaboration with the patient's GP.
- It is important to establish the patient's wishes for future care while they are still able to communicate easily.
- Appropriate medications for relief of symptoms should be made available to patients approaching the terminal phase.

Resources

- Motor Neurone Disease Australia: www.mndaust.asn.au
- Enhanced Primary Care Program: www.health.gov.au/mbsprimarycareitems
- Advanced Care Directives: www.racgp.org.au/guidelines/advancecareplans.

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Conflict of interest: none declared.

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