Motor neurone disease

1. Motor neurone disease

This information comes from the NICE guidance on motor neurone disease (NICE NG42, 2019), a BMJ Practice Pointer article (BMJ 2022;379:e073857) and a joint document from the RCGP and the motor neurone disease association: Motor neurone disease: a guide for GPs and primary care teams, 2022.

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1.1. What is motor neurone disease?

Motor neurone disease (MND) is a neurodegenerative disease of the brain and spinal cord (NICE NG42, 2019). Motor neurones degenerate (NICE,

NG42, 2019), causing progressive motor weakness of limb or bulbar muscles (which control speech/swallowing) without significant sensory symptoms (BMJ 2022;379:e073857, Motor neurone disease: a guide for GPs and primary care teams, 2022).

1.2. Overview

Here is a quick overview (BMJ 2022;379:e073857):

- MND is rare, with a similar prevalence to glioblastoma multiforme, the commonest malignant brain tumour.
- Most commonly presents at age 50–60y; slightly commoner in males than females.
- Most cases are sporadic; 10–15% are genetic:
    - There is some evidence that those who engage with high levels of physical activity, especially if recurrent concussive or cervical trauma, are at an increased risk of MND.
    - In those with a family history of MND, neuropsychiatric and neurodevelopmental disorders are also more commonly seen.
- The interval between onset of symptoms and diagnosis can be many months (usually 10–16m). This is because symptoms or signs go unrecognised, or are misattributed to another diagnosis, or referrals are made to non-neurologists (often ENT or orthopaedics) (Motor neurone disease: a guide for GPs and primary care teams, 2022, BMJ 2022;379:e073857).

1.3. Why does early diagnosis matter?

Early diagnosis allows (Motor neurone disease: a guide for GPs and primary care teams, 2022 BMJ 2022;379:e073857, NICE NG42, 2019):

- Multidisciplinary team specialist support: this has been shown to prolong survival by about 8 months.
- Prompt and appropriate treatment and interventions.

So, what do we need to know in primary care to consider the diagnosis of motor neurone disease?

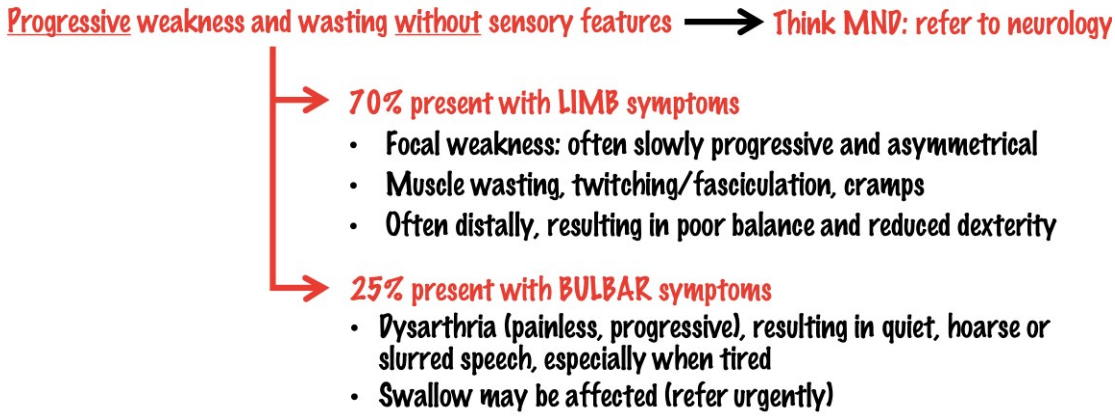
1.4. Initial presentation and diagnosis

Motor neurone disease (MND) causes progressive muscular weakness without significant sensory symptoms. Initial symptoms may be isolated and appear unexplained (NICE NG42, 2019, Motor neurone disease: a guide for GPs and primary care teams, 2022).

If MND is suspected: refer to neurology (NICE NG42, 2019):

- Specifically mention that you are querying a diagnosis of MND in the letter.
- Make direct contact with the consultant neurologist if you feel urgent review is needed.

Here are the key messages to take away to help spot MND (NICE NG42, 2019, NICE NG127, 2019, BMJ 2022;379:e073857, Motor neurone disease: a guide for GPs and primary care teams, 2022):



We cover this in more detail in the table below(NICE NG42, 2019, NICE NG127, 2019, BMJ 2022;379:e073857, Motor neurone disease: a guide for GPs and primary care teams, 2022):

There are two questions we should ask ourselves: • Firstly: does the patient have one or more of the symptoms below? • Secondly: are these symptoms progressive? If so, this could be MND: refer to neurology without delay and specifically query that diagnosis in the referral letter.	
Limb features *70% present with limb features*	No sensory features AND any/some of: • Focal weakness (painless with preserved sensation): often slowly progressive and asymmetrical. • Distal weakness: often results in poor balance (e.g. falls/trips from foot drop) and loss of dexterity (e.g. problems with zips and buttons). • Muscle wasting: often in hands and shoulders (typically asymmetrical). • Muscle twitching/fasciculation. • Cramps. On examination, there may be (BMJ 2022;379:e073857): • Muscle atrophy (focal but affecting >1 nerve root),

	slower gait, impaired hand movements, hyperreflexia, clonus, extensor plantars. • Split hand sign: wasting of the interosseous muscle between thumb and first finger and of the thenar eminence, but with preservation of the hypothenar eminence (95% specificity for ALS). Usually unilateral, at least initially. • Fasciculations: associated with weakness and more obvious proximally (fasciculations without weakness are common in healthy people).

Bulbar features
25% present with these (…before referring to ENT for puzzling symptoms, consider a bulbar presentation of MND!)
	• Dysarthria (painless, progressive dysarthria):
	  • Slurred or disrupted speech, often when tired.
	  • Quiet, hoarse or altered speech.
	• Dysphagia:
	  • More often liquids first, then solids (liquids may catch in the throat or choking may happen when drinking quickly).
	  • Choking sensation when lying flat.
	  • **Refer urgently if swallow affected** (NICE NG127, 2019).
	• Excessive saliva.
	• Tongue fasciculation.
	• Weak cough (often not noticed by the patient).
	• On examination, there may be a wasted tongue, brisk jaw jerk or high-pitched dysarthria (BMJ 2022;379:e073857).

Respiratory features *Rarely a presenting feature: usually occurs later*	• Hard-to-explain respiratory symptoms (not explained by pulmonary or cardiac causes). Happen due to reduced respiratory function: • Shortness of breath on exertion.

	• Orthopnoea: **refer immediately if breathless at rest/lying flat** (NICE NG127, 2019). • Sleep apnoea symptoms, e.g. excessive daytime sleepiness or early morning headache. • Frequent unexplained chest infections. • Weak cough and sniff.
Cognitive features	• Behavioural changes (apathy, lack of motivation). • Frontotemporal dementia. • Emotional lability (not caused by dementia). • Ask about a family history of similar features.
The following features do NOT support a diagnosis of MND: • Bladder or bowel involvement. • Prominent sensory symptoms. • Double vision/ptosis. • Symptoms that improve.	

1.5. Investigations

NICE does not suggest any specific primary care investigations, and is clear that we refer if MND is suspected (NICE NG42, 2019). The BMJ article suggested investigations which centre around ruling out differential diagnoses like peripheral neuropathies and MSK causes (BMJ 2022;379:e073857):

- Bloods:
    - FBC, U&Es, LFTs, bone profile, TFTs, B12, folate,

immunoglobulins/protein electrophoresis.

    - If immune/inflammatory myopathy is considered in the differential diagnosis, check a CK.

- Imaging: spinal neuroimaging to rule out cervical myeloradiculopathy (which can also give both upper and lower motor neurone symptoms).
- Secondary care may also consider nerve conduction studies and electromyography (EMG).

1.6. Subtypes

There are three main phenotypes of motor neurone disease (BMJ 2022;379:e073857), mentioned here for completeness. **But, in primary care, if we suspect any phenotype, the message is the same: refer** (BMJ 2022;379:e073857, Motor neurone disease: a guide for GPs and primary care teams, 2022):

Amyotrophic lateral sclerosis	Primary lateral sclerosis	Primary muscular atrophy
Commonest type: 85% of those with MND. Can have upper and lower motor neurone dysfunction: • 70% present with limb weakness (often starts in the dominant limb, then spreads to include the other side). • 50% present with shoulder girdle and intrinsic hand muscle weakness. • 30% present with dysphagia and dysarthria (bulbar symptoms). Classically has a rapid clinical decline. Survival is 3–4y from symptom onset.	Rare: <3% of those with MND. Upper motor neurone dysfunction and substantial spasticity. Best survival rates.	Lower motor neurone dysfunction with muscle atrophy and flaccid weakness. Survival longer than ALS but less than PLS.

And you may be thinking… *remind me of the difference between and upper and lower motor neurone…*

- Upper motor neurones: arise in the cerebral cortex and travel to the spinal cord/brainstem.
    - An upper motor neurone lesion causes spasticity, hypertonia and hyperreflexia.
- Lower motor neurones: arise in the spinal cord and travel to the muscle

it innervates.

- A lower motor neurone lesion causes flaccid paralysis, hypotonia and hyporeflexia.

1.7. Management

Information about the diagnosis, prognosis and management should be given by a consultant neurologist (NICE NG42, 2019). Secondary care MDT input is key and has been shown to improve survival by about 8 months (BMJ 2022;379:e073857)! The MDT input required will vary from patient to patient, but may include neurology, physiotherapy, occupational therapy, dietician support, speech and language therapy, respiratory medicine and palliative care (BMJ 2022;379:e073857).

There is no cure. Management focuses on alleviating symptoms, maintaining functional ability and advance care planning (NICE NG42, 2019).

This table covers the management of common symptoms of motor neurone disease (NICE NG42, 2019, BNF, accessed June 2023, and other sources as referenced directly in the table):

Problems	Management options
Muscles	**Muscle cramps** 1st line: consider quinine (off licence). 2nd line: consider baclofen (off licence). 3rd line: consider gabapentin, dantrolene (specialist use only), tizanidine (off licence).

	Spasticity, increased muscle tone or stiffness 1st line: consider baclofen, dantrolene, tizanidine or gabapentin (some off licence, see BNF). 2nd line: specialist referral. Note: medication for spasticity can inadvertently exacerbate weakness and cause drowsiness (Motor neurone disease: a guide for GPs and primary care teams, 2022).
	Orthoses should be provided without delay if needed. Exercise programmes can be considered to maintain joint range of motion, prevent contractures, reduce muscle stiffness and discomfort, optimise function and improve quality of life.
Saliva *Assess volume and viscosity, respiratory function, swallowing, diet, posture and oral care*	**Drooling** Advise on swallowing, diet, posture, positioning, oral care and suctioning. 1st line: consider antimuscarinic (off licence), or consider glycopyrronium (off licence) if the person has cognitive impairment as fewer CNS side-effects. 2nd line: refer to specialist for consideration of botulinum toxin A.
	Thick, tenacious saliva Review medications and advise on diet, posture, positioning, oral care, suctioning and hydration. Consider humidification, nebulisers and carbocisteine.
	Dry mouth (Motor neurone disease: a guide for GPs and primary care teams, 2022) Assess for any contributing medications (e.g. anticholinergics), consider artificial saliva sprays, advise about oral hygiene and increase fluid intake.
Speech and communication	Consider measures required for effective communication (and an effective consultation), e.g.

	gesture, symbols, communication boards and books, voice output communication aids. Consider how to communicate regarding care, e.g. face-to-face or remote consultation, written communication. Involve speech and language therapist and occupational therapist.
Respiratory *Weakness of respiratory muscles affects most people with MND as their disease progresses*	Identify and treat reversible causes (infection, respiratory secretions). **Respiratory physiotherapist** As part of the MDT, a respiratory physiotherapist can advise on interventions to improve cough effectiveness. **Non-invasive ventilation** An option for some based on symptoms, signs and respiratory function testing. Decision to offer made by multidisciplinary team and respiratory ventilation service. Careful consideration is required in people with frontotemporal dementia. **Medication** Consider opioids for relief of breathlessness. Consider benzodiazepines to manage breathlessness exacerbated by anxiety.
Nutrition *Arrange a clinical swallowing assessment if swallowing problems suspected*	Discuss gastrostomy at an early stage and at regular intervals as MND progresses. There are possible risks of late gastrostomy placement, including higher mortality and procedural complications. Careful consideration is required in people who have frontotemporal dementia.
Skin care	Pressure: depending on ability, positioning and turning may be required; consider aids, e.g. pressure-relieving mattress/cushions.

	Cold feet: advise warm socks. Itching skin: emollients or antihistamine. (Motor neurone disease: a guide for GPs and primary care teams, 2022)
Oedema	Usually dependent. Occupational therapy: posture and seating support. Compression stockings if not contraindicated. Light massage and reflexology may be beneficial. Do not use diuretics: rarely beneficial and cause urinary urgency and electrolyte imbalance. Lymphoedema service may be beneficial, depending on local provision. (Motor neurone disease: a guide for GPs and primary care teams, 2022)
Memory impairment and dementia	In those with established amyotrophic lateral sclerosis (BMJ 2022;379:e073857): • 50% have some cognitive impairment, and half of these will have frontotemporal dementia. • Apathy, disinhibition, emotional lability and executive dysfunction are seen. • 80% have anxiety. • 20% develop psychosis. Be aware of the association between MND, mental health and memory problems, and refer as required.
Hypermetabolism	Hypermetabolism can occur in up to 50% of those with MND (Motor neurone disease: a guide for GPs and primary care teams, 2022), and can result in (BMJ 2022;379:e073857): • Weight loss. • Sleep disturbance. • Autonomic dysfunction.

	Manage these symptoms accordingly; the MDT can be key here.

1.8. The needs of the carer

As well as the patient's needs, consider the needs of the carer (Motor neurone disease: a guide for GPs and primary care teams, 2022):

- If the carer is a patient at the surgery, are they coded as being 'a carer'?
- Have they had a carer's assessment?
- Are they aware of support available locally/nationally?
- Are there any children/young people in the household? Do they need additional support?

1.9. Driving and benefits

All with motor neurone disease must inform the DVLA (Motor neurone disease: a guide for GPs and primary care teams, 2022).

One-third of people with MND die within 1 year and over half within 2 years. Clinicians should consider completing a SR1 form (previously a DS1500) to enable fast-track benefit support (Motor neurone disease: a guide for GPs and primary care teams, 2022) if they believe (The Special Rules guidance, 2023):

- That the patient has a progressive condition AND
- As a consequence of that condition, the clinician wouldn't be surprised if that patient died in the next 12m.

1.10. Medication to treat motor neurone disease

- **Riluzole** is the only licensed drug in the UK for MND (NICE 2001, TA20, Motor neurone disease: a guide for GPs and primary care teams, 2022):
    - It doesn't improve muscle strength; instead, it slows decline of function. In trials, it extended survival by 3m on average over 18m.
    - It is licensed only for amyotrophic lateral sclerosis to extend life or time to mechanical ventilation.
    - It should be prescribed via a shared care protocol. Monitoring of LFTs is required during treatment.
- In the US in 2017, a new neuroprotective drug, edaravone, was licensed for the treatment of MND. Trials relating to this drug were short and included very small numbers of patients. It is not licensed in the UK (Lancet Neurology 2017;16:490).

1.11. Prognosis

Many people die within 2 –3y of diagnosis; 25% live at least 5y and 10% at least 10y. Certain factors are associated with a shorter survival if present at diagnosis (NICE NG42, 2019):

- Speech and swallowing problems.
- Weight loss.
- Poor respiratory function.
- Older age.

- Lower ALS functional rating scale score.
- Shorter time from first symptoms to diagnosis.

1.12. Palliative care

As the disease progresses, a predictable pattern is seen (NICE NG42, 2019):

- Increasing muscle weakness in arms and legs.
- Swallowing problems, communication difficulties and weakness of respiratory muscles.

End-of-life care for those with MND can be complex, and all should be offered referral to the palliative care team when appropriate (Motor neurone disease: a guide for GPs and primary care teams, 2022).

Advance care planning discussions should start early with the secondary care team, but we are also well placed in primary care to have these discussions. Patients may actively raise the topic of palliative care with us, or we may choose to start these conversations earlier, knowing that advanced MND can impact communication and cognition (NICE NG42, 2019).

NICE suggests offering the opportunity to discuss preferences and concerns at certain trigger points in the disease, for example: at diagnosis; if a significant decline in respiratory function occurs; or when considering interventions, e.g. non-invasive ventilation or gastrostomy (NICE NG42, 2019).

Consider discussing (NICE NG42, 2019):

- Advance care planning, including Do Not Attempt Resuscitation order, Lasting Power of Attorney and Advanced Decisions to Refuse

Treatment.

- How to ensure advance care plans are available when needed, e.g. in the Summary Care Record.
- When to involve specialist palliative care.
- What could happen at the end of life, and provision of anticipatory medications in the home.
- Aspects people may wish to plan for, for example: things they particularly do/do not want to happen with their care; what should happen if they develop an intercurrent illness, e.g. a chest infection; and who will represent their decision, if necessary?

If a patient on continuous non-invasive ventilation wishes to stop this, seek advice from a healthcare professional experienced in stopping non-invasive ventilation (NICE NG42, 2019). The Association for Palliative Medicine of Great Britain and Ireland has produced guidance on 'Withdrawal of ventilatory support at the request of a patient with motor neurone disease, 2015'; this provides lots of useful information, and highlights that if ventilatory support is withdrawn, acute respiratory symptoms and death may occur soon after. Patients should be aware of this, and anticipatory measures should be ready to minimise distress.

Motor neurone disease

- Look for progressive, asymmetrical muscular weakness, most commonly limb or bulbar features.
- Suspect MND if there is weakness and wasting without sensory symptoms.
- If you are considering MND as a diagnosis, refer directly to neurology, stating clearly that you are querying MND.
- Care should be provided by a specialist MND multidisciplinary team.
- Advance care planning is important.

Useful resources:

Websites (all resources are hyperlinked for ease of use in Red Whale Knowledge)

- Motor Neurone Disease Association - red flag diagnosis toolkit

Useful resources for patients:

- Motor Neurone Disease Association

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