Patients with motor neurone disease (MND) live in a world where time is crucial. The rapidly progressing neurodegenerative condition, which affects the brain and spinal cord, is usually fatal within just two to three years but its complexity and rarity make early diagnosis one of the greatest challenges in GP surgeries.

It has no cure but a concerted effort by the RCGP, the MND Association and NICE is helping clinicians identify and gear up treatments to slow the progression of MND and improve quality of life.

MND primarily causes degeneration of motor neurones, which control movement, leading to muscular weakness, wasting, cramps and stiffness as well as problems with speech, swallowing and, in the later stages, breathing. Sight, sound and feeling normally remain intact.

Statistics from the MND Association reveal that six people a day in the UK are diagnosed with MND and six people a day die from it. At any one time, there are up to 5000 adults in the UK being treated for the condition, making it a rarity. Many GPs see only one or two cases in a career.1

Improving diagnosis

MND’s bleak profile is being tackled by an innovative scheme launched in 2013 by the RCGP and the MND Association to guide diagnosis through a series of symptoms that can appear transitory when taken in isolation. The Red Flag diagnosis tool2 provides a clear and valuable prompt for GPs to consider MND as a possible diagnosis.

Developed by a steering group of neurologists, MND nurse co-ordinators, palliative care consultants and GPs, it is proving an anecdotal success, and the scheme has been taken up in the USA, Switzerland, New Zealand and Australia. It is supported by free online modules and an RCGP presentation featuring patients describing their condition, which are being used to cascade learning.

Clinical research into new disease-modifying therapies and ultimately a cure for MND is also more active now than at any other time, according to Martin Turner, professor of clinical neurology and neuroscience at Nuffield Department of Clinical Neurosciences, University of Oxford.

But despite the positive change and progress, the landscape remains challenging for patients and physicians and a recent study revealed that people are still waiting for long periods before they...
see a specialist. A report by the MND Association, based on responses from over 900 patients with a diagnosis of MND in England, Wales and Northern Ireland earlier this summer, found that one in five people waits more than a year to see a neurologist for help with diagnosis.

“Of these people, more than half (52 per cent) had been referred to other healthcare professionals first, most commonly physiotherapists, orthopaedic surgeons or ear nose and throat (ENT) specialists instead of straight to a neurologist – the professional best able to deliver an accurate, confirmed diagnosis of MND,” the report stated.

Karen Pearce, the MND Association’s director of care, commented: “The problem is there is still no single diagnostic test for MND and we appreciate that it is also challenging for GPs, who might only see one patient with MND in their whole career. Symptoms can be similar to other conditions, so people can spend months seeing various specialists and undergoing unsuccessful treatments until MND is suspected.”

MND was first recorded in 1874 and the term covers a group of related diseases affecting motor neurones. The most common subtype is amyotrophic lateral sclerosis (ALS). MND can affect adults of any age but most people diagnosed are over 40 years old with the highest incidence in the 50- to 70-year age group. The precise causes are not clear but a combination of genetic and environmental triggers, which vary individually, are in play.

Dr Steve Mowle, a GP in Clapham, south London and assistant honorary treasurer of the RCGP has only looked after one patient with MND in 23 years of practice. “GPs will very rarely diagnose it in their career and because of that, it tends to be diagnosed later owing to the nonspecific symptoms patients present with,” he says.

“People with MND have a shortened life expectancy, so what time they have is precious and they want to make the most of their last days. At a recent meeting with patients and specialists, it was clear that the early symptoms can be very minor and that patients may not even go to a GP. It could be as little as minor clumsiness, which a lot of us would put down to age alone.

“The symptoms can be quite subtle with emotional and behaviour change that can be very difficult to be objective about and pick up. Symptoms like difficulty swallowing and speech difficulties are red flags, full stop. Yet a loss of dexterity, cramps or fatigue could be pretty much anything or nothing, and there is no standard presentation. Progressive loss of dexterity with increasing cramps and fatigue identifies a pattern suggesting something rather serious that we can look at more closely as opposed to someone who has had nocturnal cramps for a week.”

**Red Flag diagnosis tool**

The Red Flag diagnosis tool focuses on the four area that can indicate MND – bulbar, limb, respiratory and cognitive features (see Figure 1). It subdivides these areas into symptoms such as dysphagia, dysarthria and tongue fasciculations (bulbar features); cramps, muscle wasting and loss of dexterity (limb features); and fatigue, shortness of breath and orthopnoea (respiratory features); with cognitive features such as behavioural change being much rarer in early presentations.

Further pointers are provided by the MND Association’s estimate that 75 per cent of patients present with limb features and 25 per cent with bulbar features while respiratory problems are usually a late feature of MND. The key Red Flag questions to GPs are: “Does the patient have one or more symptoms?” and “Is there progression?”

An evaluation of the Red Flag diagnosis tool is being carried out but anecdotal reports are promising, with the MND Association estimating that nearly half of patients are diagnosed by GPs within two visits.

“We are delighted with [the Red Flag tool’s] success and that it has been used at various regional and local training days and events because an early diagnosis is so important for patients,” says Jenny Bedford, partnership development manager at the MND Association.

“Prompt diagnosis removes uncertainty for the person experiencing symptoms and allows care and support to start as early as possible. This enables people with MND and their carers to consider and plan for their future. It also increases the window of opportunity to research into, and better understand, the condition.
“A delayed decision means that a person living with MND cannot discuss their options with professionals. It effectively compromises their quality of life when, sadly, they have relatively very little time left with family and loved ones.”

Dr Mowle believes the Red Flag tool has raised awareness among GPs, but a big barrier to early diagnosis continues to be time pressures on consultations. “We have to put up our hands and say we cannot look after someone with MND in 10 minutes. We need longer consultations full stop, but we certainly need to make more time for patients with complex conditions,” he says.

He also urges a balanced approach so that raised awareness does not lead to overdiagnosis. “There is always an issue of being careful of what you wish for as we have a limited number of neurologists and an even smaller number of MND specialists,” Dr Mowle notes. “If every GP in England sent just one patient with an MND query it would completely flood the system, which would mean the service was not there for people who have MND. There is a balance to reach on how much you push with limited resources.”

Optimising care
Dr Mowle stresses that GPs need to optimise the general health of MND patients and to ensure they have full social and care support. “Supporting the patient holistically – psychologically and socially as well as medically – and supporting the carers, is very important. It is often about having the right equipment, such as sophisticated wheelchairs, which allow people to leave their homes and have some independence,” he says. “It would be tragic if someone with a shortened lifespan spent 25 per cent of that time waiting for a wheelchair. It is also important to have a continuity of care. For example, looking after my patient’s wife when he died was essential. It is a bedrock of general practice.”

GPs currently have limited weaponry to treat MND directly. Riluzole, which can extend life expectancy by approximately three months, is the only licensed and NICE-approved drug (it is specifically licensed for ALS), and can only be prescribed by GPs under a shared-care arrangement. However, GPs are pivotal to high-quality care and ensuring co-ordination among the various specialist teams involved.

A multidisciplinary approach is important to tackle the sweep of physical and emotional challenges in MND, from communication difficulties, caused by a weakness in the tongue and vocal cords, to nutritional problems, caused by difficulty in chewing and swallowing food through weakening of muscles in the throat and mouth.

The NICE guideline on MND and its associated quality standard, both published this year, have established the need for clear information about the condition, its prognosis and management by a consultant neurologist with expertise in treating MND. They also emphasise the importance of access to tailored equipment, adaptations, consistency of care, and opportunities to discuss end-of-life care at diagnosis and key stages of disease progression. The five quality standard statements issued by NICE (see Table 1) were welcomed by the MND Association, who added that many aspects of care are already improving.

Research is also offering new hope with a plethora of genes linked to MND having been discovered in recent years. For example, a variant of the gene NEK1, which was identified thanks to the £88 million raised by the social media ‘Ice Bucket Challenge’ in 2014, appears to confer susceptibility to the disease.

Dr Brian Dickie, the MND Association’s director of research said: “While only around 10 per cent of cases of MND runs in families, indicating a genetic cause, we are aware that most cases will have a genetic component that predisposes an individual towards developing the disease later in life.

“We and others are supporting research to develop a panel of tests for known MND genes, which can be incorporated into the diagnostic process. This could help speed up diagnosis, allowing more time for care planning and, hopefully, also providing opportunities to conduct treatment trials earlier in the disease course.”

A cure or significant disease-modifying medication may be some distance away, which makes caring for patients, who rapidly become reliant on wheelchairs or assisted ventilation, a primary function.

“How we personalise care for individuals with rare conditions is our raison d’être as GPs,” explains Dr Mowle. “Making sure care is joined up is difficult as patients often have to travel miles to MND specialist centres. Co-ordination of care is crucial and specialist nurses are well placed to bridge the gaps between

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Table 1. NICE quality standard statements for motor neurone disease (MND)

| Statement 1 | Adults diagnosed with MND are given information about the diagnosis, prognosis and management of MND by a consultant neurologist with expertise in treating people with MND |
| Statement 2 | Adults with MND who have respiratory impairment are offered noninvasive ventilation based on regular assessments of respiratory function and symptoms |
| Statement 3 | Adults with MND receive tailored equipment and adaptations without delay, based on regular multidisciplinary team assessments |
| Statement 4 | Adults with MND receive personal care and support from a consistent team of workers who are familiar with their needs |
| Statement 5 | Adults with MND are given opportunities to discuss their preferences and concerns about end-of-life care at diagnosis and key stages of disease progression |

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“How we personalise care for individuals with rare conditions is our raison d’etre as GPs,” explains Dr Mowle. “Making sure care is joined up is difficult as patients often have to travel miles to MND specialist centres. Co-ordination of care is crucial and specialist nurses are well placed to bridge the gaps between
consultants and patients, their carers and families, and the GP. Good communication is the lynchpin of that relationship.

“The bottom line is that GPs are ever-vigilant for rare conditions and are focused on patient-centred care – doing our best in very difficult circumstances.”

Awareness is improving, according to the MND Association, with GPs explaining tests and answering questions clearly, while an increasing number of people have a named person co-ordinating their care. More people are having their breathing monitored regularly with increased access to noninvasive ventilation and machines, in line with the NICE guidance.

“The MND Association is working within a wide range of supportive and dedicated collaborations, including our MND Care Centres, Royal Colleges, professional bodies and universities, to raise awareness of MND and what constitutes excellent care,” concludes Jenny Bedford.

“We will continue to work together to improve the quality of life of people living with MND until a cure can be found.”

References
3. Motor Neurone Disease Association. 1 in 5 with MND have to wait a year or more for neurologist referral. www.mndassociation.org/news-and-events/latest-news/1-in-5-with-mnd-have-to-wait-a-year-or-more-for-neurologist-referral/

Declaration of interests
See http://www.mjauk.org/author/bucklandd/

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POEMs

Spironolactone most effective add-on for patients with resistant hypertension

Clinical question:
In patients with resistant hypertension (poor control despite the maximum dosages of three drugs), what is the most effective add-on medication?

Bottom line:
In the short term, spironolactone is most effective at lowering blood pressure in patients with resistant hypertension. Whether this will result in better long-term control or decrease the rate of clinically important outcomes – such as stroke, congestive heart failure, kidney failure, and so forth – is unknown. (LOE = 2b)

Reference:


Synopsis:
Many guidelines recommend the A+C+D approach to managing patients with hypertension: start with an ACE inhibitor or angiotensin II-receptor antagonist, add a calcium-channel blocker, then a diuretic.* Once patients are taking maximum dosages of all three drugs, then what? These authors enrolled 335 such patients in a randomised crossover trial to see which of the following was more effective in lowering blood pressure: spironolactone, doxazosin or bisoprolol. To be eligible, the patients had to be aged between 18 and 79 years, have systolic blood pressure (SBP) 140mmHg or greater in the office plus home SBP 130mmHg or greater in spite of maximum dosages of all three drugs. This was a 12-month study that began with all patients receiving a placebo during the first month followed by six weeks of low dosages of either spironolactone (25mg daily), doxazosin (4mg daily), or bisoprolol (5mg daily) followed by six weeks of double doses (if tolerated). In most crossover studies, there is a washout period between each treatment interval to minimise the potential for carryover effect of the previous treatment. These authors did not include washout intervals but tried to account for this by doing a sensitivity analysis comparing individual active treatment periods with the initial placebo period.

The primary outcome was the average of 18 home SBP readings ascertainment on four consecutive days. Unfortunately, 21 patients never “played at all” and only 234 patients completed all of the treatment cycles. However, the researchers reported having at least 274 patients for any single treatment period. Compared with the other drugs, the average reductions in SBP for spironolactone, doxazosin, and bisoprolol were 9mmHg, 4mmHg and 4mmHg respectively (p<0.001). Compared with placebo, the reductions were 13mmHg, 9mmHg and 8mmHg respectively. The rate of serious adverse events was comparable in each group (2–3 per cent) as was the rate of all adverse events (15–23 per cent).

*The Eighth Joint National Committee gives equal weight to each of three strategies: (1) push drugs to maximum dosage before adding an additional drug; (2) add a second agent before pushing initial agent to maximum dosage; and (3) start with two medications then titrate to maximum dosage. It also gives no preference to initial medication choice among “A, C or D”.

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