

# What's new in multiple sclerosis?

### BACKGROUND

The past 20 years have brought several important advances in the management of multiple sclerosis (MS). Magnetic resonance imaging (MRI) has given us a window into this disease and has transformed the diagnostic process, allowing it to be made much earlier. It has also been established that immunomodulation can prevent demyelinating events in relapsing remitting MS (RRMS). These developments impact on primary care because there is increasing evidence that early diagnosis and treatment of MS may delay, or even prevent the previously inevitable disability.<sup>1</sup> At the other end of the spectrum, people with MS with disability are increasingly being managed in the community away from secondary care. The National Institute for Health and Care Excellence (NICE) has recently published an updated guideline for MS patient care. This article highlights the new developments and NICE guidance.

### OVERVIEW OF MULTIPLE SCLEROSIS

MS is the most common cause of non-traumatic neurological disability in young adults with a prevalence of around 1 in 1000 and evidence that the incidence is increasing.<sup>2</sup> It is a chronic, progressive, demyelinating condition of the central nervous system (CNS) that typically presents during the ages of 20–40 years, occurring twice as frequently in females as in males. Typically, a large GP practice will have between 10–20 patients with MS.<sup>3</sup> Despite the highly heterogeneous course, a number of distinct subtypes have been identified. The most common is the relapsing remitting form (RRMS), which accounts for 80–90% of all cases. This is characterised by demyelinating events where there is loss-of-function, inter-spaced by periods of partial or complete recovery. After 10 years around 50% of those with RRMS will go on to develop secondary progressive MS (SPMS) with fewer relapses but a progressive worsening of disability. Around 10% of patients with MS have a progressive decline in disability from the outset, termed primary progressive MS (PPMS).

### CHANGES TO DIAGNOSIS

Dissemination in time and space has been central to diagnosis of MS. This was problematic in those with a history of a single clinically-evident episode of demyelination

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(Clinically Isolated Syndrome; CIS) as a diagnosis could not be made until a second clinical attack.<sup>4</sup> In 2001, the McDonald Criteria were developed enabling the use of MRI in the diagnosis of MS. In the latest revision in 2010,<sup>5</sup> the task of establishing dissemination in time and space has been further simplified allowing MS to be diagnosed at presentation, contrasting with the years of uncertainty previously faced by patients who presented with optic neuritis or myelitis before a clinically definite diagnosis could be made. Whether these changes will lead to an overdiagnosis and excess of intervention is one concern, but if, as some data suggest, early intervention with disease modifying therapies (DMTs) is beneficial, we may see a reduction in disability and health costs.<sup>6</sup>

Currently GPs can request MRI scans; directly demonstrating the importance of primary care early on in the disease. However, it is important to remember MS remains a clinical diagnosis and the updated NICE guidelines published in October 2014 stress that MRI findings cannot be the basis of diagnosis alone. The NICE guidelines also stress that the diagnosis of MS should only be made by a neurologist. Before specialist referral, a comprehensive set of bloods should be taken to rule out alternative diagnosis in the primary care setting.

### SYMPTOMATIC TREATMENTS

MS remains a potentially disabling condition and patients need support from the community and general practice. It is well documented that there is a positive correlation between MS disability and GP service use.<sup>7</sup> The mainstay of treatment remains symptom control, with steroids

used during acute relapses. The updated NICE guidelines for management of MS emphasise the importance of recognition and early treatment of symptoms for quality and efficiency of patient care.

Review of hospital data shows the most frequent reason for hospital admission for patients with MS is urinary tract infections (UTIs). UTIs could be avoided with simple primary care interventions such as lifestyle advice, pelvic floor exercises, continence advice, regular dipstick and early or prophylactic antibiotics.<sup>8</sup> Further work is required to establish best care in this area.

Gait disturbance is reported as the chief complaint in 85% of patients with MS. Encouraging physical activity is fundamental to dealing with this issue. Often problems in gait occur as a result of muscle weakness secondary to disuse. Referral to physiotherapy and encouraging the use of mobility aids has the potential to impact hugely on disability and improve quality of life. Exercise may also improve other symptoms, with a particular recommendation from NICE for the efficacy of aerobic, balance, and stretching exercises in the treatment of MS-related fatigue. Importantly, exercise should not just be encouraged, but delivered through a more formal approach, such as supervised exercise programmes, exercise referral schemes, or vestibular rehabilitation for those where fatigue and mobility issues are secondary to stability problems. Patients who have more moderate mobility problems, alongside fatigue, are also likely to benefit from cognitive-behavioural techniques.

Other major issues for patients with MS include depression, osteoporosis, falls, spasticity, pain, and sleep disorders.

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A shared care approach between primary and secondary care is necessary to tackle these problems, with NICE stressing the importance of a coordinated multidisciplinary strategy.

The range of services required for patients with MS can be extensive, involving speech and language therapists, occupational therapists, physiotherapists, and psychologists. It is on this basis that NICE recommends an individual to coordinate the care, often a nurse, but not necessarily so. In many areas MS nurses have been highly successful at coordinating patient care and this has been shown to improve patients with MS outcome and quality of life.<sup>9</sup> Indeed many patients say the greatest step forward in their care is the MS nurse.

There is evidence that flu vaccinations are beneficial for patients with MS and this is included in national guidelines. However it should be noted that live vaccines may be contraindicated in those who are on some of the new therapeutics discussed below. Therefore, an individualised approach is advocated based on a risk-benefit analysis.

### DISEASE-MODIFYING THERAPIES

There are now some new weapons in the physician's armoury that do not just seek to manage disability but can alter the course of the disease. Like their counterparts in rheumatology, they are known as DMTs.

The novelty of therapeutic choice is mainly reserved for those experiencing the earlier relapsing-remitting subtype. The original DMTs were the injectables; interferons (IFNs) and glatiramer acetate (GA). Although there is good evidence of their efficacy, it is recognised that the IFNs and GA are only partially effective.<sup>10</sup> The injection mode of delivery is also an obstacle for many patients.

NICE have now approved three oral DMTs (fingolimod, teriflunomide, and dimethyl fumarate). Aside from the obvious attraction of a 'pill' for MS therapy, the increase in the options of DMTs, with different mechanisms of action and ranges of efficacy, all help in the goal of successful MS disease suppression.

We can expect to see more patients with MS on these new medications coming through the GP surgery doors and awareness of these drugs will be important as they require monitoring to include regular

blood and urine tests and blood pressure checks which may ultimately be under the jurisdiction of the GP. Due to the underlying immunosuppressive mechanisms of action, GPs must also be vigilant for infections in these patients (be it newly acquired or reactivation of dormant infection), and avoid the use of live vaccines.

Again, like rheumatology, there has been the development of targeted monoclonal antibodies in RRMS. NICE have licensed natalizumab (Tysabri®, Biogen Idec Ltd) and alemtuzumab in response to their impressive relapse reduction and stabilising of disability.<sup>11-13</sup> This suppression of inflammatory disease activity comes at a cost, both financial and clinical. NICE obviously feel the £56 000 cost of alemtuzumab is justified, but there are concerns that 20% of patients develop thyroid disease, and have increased risk of other autoimmune conditions.<sup>13</sup> However if in 10 years time we no longer see the progression of disability in patients with MS treated with alemtuzumab then all those costs will have been fully justified.

### CONCLUSION

There have been significant advances in the management of MS, with early diagnosis and reducing relapse rates and accumulated disability. Current patients, and unfortunately it is likely some future patients, will develop disability and it is important to recognise that symptomatic therapies can produce significant benefits. As the new NICE guidance recognises, GPs play a significant role in the long-term management of MS and associated disabilities. The role does not end here however, with a greater responsibility falling onto general practice as MS is increasingly being managed in the community. The advent of new, sophisticated therapies, will involve the GP as well as the neurologist, as these therapies have ongoing side effects and require monitoring, which may often fall to the GP.

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