Although agents that have a partial benefit on relapses in multiple sclerosis (MS) are available, there is little to suggest that we are able to influence disease progression in any meaningful way—thus the need to manage the accumulating impairments and disability that accompany progression actively. Attempting to evaluate and treat the wide range of fluctuating and interacting symptoms associated with MS can be frustrating and at times demoralising for patient and physician alike. Additionally, available drug treatment is limited both in its efficacy and in the evidence available to guide its use. Many agents are poorly tolerated, often because they will exacerbate co-existing symptoms.

Given the limitations of drug treatment both for symptom management and disease progression, it is essential that the neurologist is aware of other approaches to management, knows when and how to refer to other disciplines, and is able to explain the reasons for the referral. Equally, it is important that the patient leaves the consultation with a clear management strategy and not with the old adage ringing in their ears “it is because of your MS and there is nothing to be done.” A key element in symptomatic treatment is the involvement of the patient in their management. This requires that they have an understanding of their symptoms (for example, spasticity) and are taught how to minimise their impact (for example, positioning, standing programme, etc).

In approaching the patient with established MS, a detailed assessment of their symptoms—their character, severity, and particularly their impact on the patient’s day-to-day life—is essential. The first question to ask is: “Does this symptom relate to MS or is there an entirely different explanation?” This may not always be straightforward. Patients and their general practitioners usually ascribe any new symptoms to MS and patients are usually worried about the possibility of another relapse. This may be reasonably straightforward for characteristic symptoms such as Lhermitte’s phenomenon, paroxysmal ataxia, and dysarthria, but is more difficult for sensory disturbance or discomfort in the lumbar area, which may well be secondary to other MS symptoms such as weakness and spasticity but may also result from nerve root compression. Clinical examination may be helpful but it may also be necessary to carry out further investigations to exclude other pathologies.

Next, ask whether the symptom is having a major impact on day-to-day living and to establish what additional symptoms co-exist. The responses to these questions may determine whether or not drug treatment is appropriate and will influence the choice of approach. For example, an element of stiffness in the lower limbs may not warrant drug intervention unless it is affecting mobility. Physiotherapy assessment may help determine this. The use of anti-spasticity agents may be limited because of their side effects if, for example, the patient also suffers from severe fatigue.

It is important to consider all therapeutic options—not just drug treatment but also input from disciplines with particular expertise, such as physiotherapist, uroneurologist, etc. Consider a multidisciplinary assessment if the situation is particularly complex or there have been notable changes in a number of areas. This should not be restricted to patients with very severe disability but should also be directed to those with potential to improve, even if only for the short to medium term. Involvement of other disciplines needs to be coordinated. The goal of every treatment approach should be to encourage self management and to provide the patient with a sense of control over their disease. Thus a sensible management strategy for the majority of symptoms should include:

- education
- therapy input
- drug treatment.

Finally, it is important to remember that this is a progressive condition, and the patient will need periodic reassessment; treatments that were inappropriate or considered excessive (for example, baclofen for spasticity) may need to be reconsidered.

INDIVIDUAL SYMPTOMS

A detailed discussion of symptom management in MS may be found in a number of texts and review articles. It is appropriate to consider them from the patient’s perspective and although surveys vary in their results, fatigue and bladder dysfunction are usually regarded as having the...
greatest impact on the patient. Mobility is another key concern and results from a range of motor disturbances (weakness, spasticity, and ataxia), sensory impairment, fatigue, visual dysfunction, and lack of confidence. Two symptoms which were not well recognised in the past (or even denied), and which can be very troublesome, particularly if not identified and managed well, are cognitive dysfunction and pain. Others, which will be mentioned briefly, include visual disturbance, psychiatric disturbance, and brainstem symptoms including dysarthria, dysphagia, vertigo, and respiratory difficulties.

### Symptoms in multiple sclerosis

- Cognitive dysfunction, mood disturbance
- Reduced mobility, weakness, spasticity, ataxia
- Fatigue, heat intolerance
- Reduced dexterity
- Pain, sensory disturbance
- Bladder, bowel, and sexual dysfunction
- Visual disturbance
- Dysarthria, dysphagia, vertigo, respiratory dysfunction

### Patient priorities

**Fatigue**

Fatigue is considered by many patients to be their most disabling symptom from MS. This overwhelming feeling of exhaustion must be distinguished from depression, which may co-exist. Common, practical issues such as a poor sleep pattern, resulting from painful spasms or nocturia, must be identified and addressed. Fatigue management programmes are the cornerstones of treatment though drug treatment may be useful in a minority of patients. Amanitane has been shown to be effective while pemoline has not.

More recently, promising results have been presented in a preliminary study of the “wake promoting” agent modafinil given at a dose of 200 mg daily. The theoretical potential for the potassium channel blockers, 4-aminopyridene and 3,4-diaminopyridene, to improve fatigue has never been realised.

**Bladder, bowel, and sexual dysfunction**

These symptoms, which often occur in tandem as a result of spinal cord disease, have a major impact on the patient. Active management is crucial.

**Bladder disturbance**—Pelvic floor exercises may have a useful role, particularly in women. The combination of clean, intermittent self catheterisation (CISC) and an anticholinergic agent such as oxybutynin (tolterodene tartrate is a useful alternative) is usually sufficient to address the incomplete emptying and hyperreflexia so commonly seen in this condition. A relatively simple approach to bladder management incorporating these interventions is shown in fig 1. This does not involve urodynamic investigations but does emphasise the need to be able to measure residual volumes ideally with an ultrasound machine. For patients reluctant to consider CISC, a bladder stimulator may improve emptying but has only been shown to be useful in mobile patients. The synthetic antidiuretic hormone desmopressin (DDAVP), given by nasal spray, is useful in the management of nocturia. The anticipated side effect of symptomatic hypotraemia is rare though is more common in elderly patients. Finally, in very severe disease, the intravesical instillation of the neurotoxic agent capsaicin may reduce detrusor hyperreflexia. The potential benefits of an ultrapotent capsinoid substance, resiniferotoxin, and a sublingual cannabinoid preparation are currently being evaluated. Permanent catheterisation may eventually be necessary and suprapubic placement is then usually the preferred option.

**Bowel disturbance**—The most common bowel symptoms are constipation and faecal incontinence, which may coexist. There is little evidence to support particular interventions. However, establishing a bowel programme is usually advocated and increasing dietary fibre, together with bulk laxatives such as lactulose, may be helpful in mild constipation; when more severe, stimulant laxatives, such as senna and bisacodyl, may have a role. The iso-osmotic laxative polyethylene glycol (Movicol) has been found to be particularly useful and possibly more effective than lactulose.

**Sexual dysfunction**—This is now acknowledged to be a frequent symptom in MS and the underlying mechanisms are better understood. The recent licensing of sildenafil (Viagra) represents a major breakthrough in the management of erectile dysfunction in men and its potential role in women is currently being investigated. In a recent randomised, placebo controlled trial involving 217 men with MS, the ability to achieve and maintain erections was significantly better in the treated group, with 92% reporting an improvement in sexual activity. Adverse events were mild in nature with headache and flushing the most common (23% and 13.5%, respectively), and there were no cardiac events in the treated group. In relation to intracorporeal pharmacotherapy, papaverine has been replaced by prostaglandin E1 (alprostadil) which may now be given as a pellet into the urethra via a small applicator.
Mobility related symptoms (motor, sensory, and visual disturbance)

Spasticity

This common symptom is poorly understood and usually poorly managed. The aims of management should be to improve function, relieve pain and/or ease care and not the removal of spasticity per se. The management of spasticity is an excellent example of the need to combine patient education, therapy, and judicious drug treatment. Patients need to have an understanding of the symptom: awareness that noxious stimuli, such as urinary tract infections, bowel impaction, and ingrown toenails may worsen spasticity; an understanding of the importance of the correct positioning in lying and sitting; and the value of a standing programme. Physiotherapists have a vital educational role, but there should also be a focus on avoiding postures that encourage spasticity and facilitating a normal pattern of movement. Drugs are a useful adjunct to these interventions and may be given orally or by injection (intramuscular, intraneural or intrathecal).

It is preferable to manage spasticity with a single agent and baclofen is the most effective, though not always best tolerated. This γ amino butyric acid (GABA) β agonist acts on both pre- and post-synaptic terminals. Appropriately for MS, it is thought to be particularly effective for spasticity of spinal origin and for flexor spasms. It should be commenced at a low dose (5 mg three times daily) and increased gradually to between 60–80 mg. Patients should be monitored carefully by the physiotherapist to avoid problems with low tone, particularly in relation to the trunk muscles, and to identify side effects which, along with hypotonia and weakness, include drowsiness and fatigue. Abrupt discontinuation may result in severe withdrawal symptoms including hallucinations and seizures.

Of the alternatives, it has been suggested that tizanidine may not cause so much weakness, though this is not so obvious in clinical practice. It acts by stimulating β₂ adrenergic receptors and has been evaluated in two randomised, placebo controlled trials. It should also be started at a low dose (2 mg three times daily) and increased slowly up to a maximum of between 24–32 mg. It may cause fatigue and a dry mouth, and liver function tests should be checked before starting and at monthly intervals for three months as transient hepatotoxicity may occur. Other agents include diazepam and clonazepam, which may be particularly useful for nocturnal spasms. Dantrolene sodium has the potential advantage of acting peripherally and therefore might be usefully combined with the any of the agents discussed earlier in more resistant cases. However, it is poorly tolerated and causes hepatotoxicity, which is not always reversible. Other agents, including gabapentin, memantine, and vigabatrin, have undergone small uncontrolled studies. The use of cannabis has been widely advocated, most vociferously by patients themselves, and a large randomised placebo controlled trial is underway in the UK comparing tetrahydrocannabinol, cannabis oil, and placebo.

For more severe spasticity, the choice of intervention will depend on whether it is focal or generalised. For the former, intramuscular botulinum toxin or intraneural injection with either alcohol or phenol may be appropriate. A recent study has shown particular benefit from botulinum toxin in adductor spasticity, though little functional benefit was seen. However, focal spasticity is relatively uncommon in MS, and for more generalised spasticity, intrathecal baclofen administered via an externally programmable pump may be useful in carefully selected patients. Because the drug is infused directly into the spinal fluid, only very small quantities are required, thus providing a powerful effect without systemic side effects. Notable reductions in tone and spasm frequency have been reported, though the process is not without complications. If patients are very severely disabled and are not suitable for a pump, intrathecal phenol could be considered provided the patient no longer has effective bladder and bowel control. Serial injections are usually required as the effect tends to wear off.

This overall approach to spasticity management is shown in fig 2.

Ataxia

Ataxia and incoordination are among the most complex, frustrating, and resistant symptoms in MS. They usually occur in patients with other disabilities. Intention tremor is one of the most disabling manifestations. Truncal ataxia, which interferes with standing and sitting balance, can be both distressing and incapacitating. Physical therapy has some limited effect, focusing on improving posture and proximal stabilisation and occasionally applying weights. Drug treatment is equally ineffective. A number of agents have been assessed in small studies including isoniazid (with pyridoxine), clonazepam, primidone, propranolol and, more recently, gabapentin and the 5H3 antagonist ondansetron. The latter appeared useful when given intravenously, but this was not convincingly demonstrated in a subsequent study when it was given orally.

Surgical intervention, either by thalamotomy or thalamic stimulation, has also been used in MS with variable success—certainly not as effective as in Parkinson’s disease.

There have been no controlled studies of thalamotomy of the ventral intermediate nucleus (VIM) and functional benefit is variable. Serious complications occur in up to 10% of patients and include hemiparesis, dysphasia, and dysphagia. Thalamic stimulation may be more effective and appears to have a lower incidence of side effects, but again there are few controlled studies. Further work is underway to identify more effective targets for this procedure.
**Recently acknowledged symptoms**

**Pain and other paroxysmal symptoms**

Pain is common in MS and can have a major impact on both activity and participation (disability and handicap). It is chronic in nature in about 85% of cases and acute or paroxysmal in the remainder. Trigeminal neuralgia is the most common of the paroxysmal pain syndromes and carbamazepine is the drug of choice. If this is ineffective or poorly tolerated, other anticonvulsants including phenytoin, lamotrigine, and gabapentin may be considered. Recent small studies have suggested that the prostaglandin E1 analogue misoprostol may be helpful. In a small proportion of patients, a percutaneous procedure may be necessary and rarely microvascular surgery may be helpful. Other paroxysmal symptoms include paroxysmal dysarthria and ataxia, tonic spasms, and sensory symptoms including Lhermitte’s symptom. Again, carbamazepine is the most useful treatment and gabapentin may also have a role. Finally, epilepsy occurs in 5% of patients with MS and may in some cases relate to corticor subcortical plaques. Treatment with anticonvulsants need not be indefinite and can be withdrawn after an appropriate period of seizure remission.

Chronic pain is common, usually multifactorial, and refractory to treatment. Amitriptyline may be useful in chronic dysesthetic pain. Physiotherapy to improve posture in sitting and standing is the cornerstone of management of chronic lumbar pain. Non-steroidal anti-inflammatory drugs, transcutaneous electrical nerve stimulation (TENS), and heat may all play a role. However, referral to a specialised pain clinic may be necessary in more resistant cases.

**Cognitive dysfunction**

Cognitive deficits occur in up to 60% of patients. To date, there is little evidence to support cognitive rehabilitation but a computer based retraining programme for specific attentional deficits may be beneficial.

**Visual and brainstem symptoms**

Severe reduction in visual acuity may follow serial episodes of optic neuritis or result from progressive visual loss, which may occur late in the condition and requires referral to a “low vision” clinic. Involuntary eye movement disorders, such as pendular nystagmus, oscillopsia, and opsoclonus, may also cause debilitating visual dysfunction. Treatment with prisms or occasionally medications such as baclofen, gabapentin, isoniazid and, most recently, memantine may be useful.\(^1\)

Vertigo, another disabling symptom, may be eased by prochlorperazine or cinnarizine, while physiotherapy, including Cawthorne-Cooksey exercises, is useful if the situation becomes chronic. Dysphagia may occur in up to 45% of patients and symptoms such as coughing when eating, choking, and change in swallowing function should alert the clinician to this. Mild dysphagia can usually be managed by assessment and advice from the speech therapist. If severe, videoflouroscopy is indicated and percutaneous gastrostomy required if swallowing is unsafe or intake is inadequate. Dysarthria is common and again requires assessment and active management from a speech and language therapist. Finally, respiratory insufficiency may occur in advanced MS but may also complicate acute episodes, usually resulting from respiratory muscle weakness and aspiration.

**Psychiatric and psychological dysfunction**

Diagnosis of psychiatric disturbances is important as symptoms such as depression may worsen fatigue and cognitive function. Depressive symptoms are usually quite mild and often do not require antidepressant medication. Finally, many patients have great difficulty coping with both the diagnosis and subsequent disability in MS. This may, in part, be abated by education and support but some patients may require counselling or psychotherapy.

**Neurological rehabilitation**

Patients with MS require comprehensive management that incorporates the expertise appropriate to their symptoms and is sufficiently flexible to respond rapidly to their changing pattern of need. They require information and support to facilitate their involvement in the management of their own condition, retain a sense of control, and maximise their independence.\(^1\) The philosophy of rehabilitation, which emphasises education and self management, is ideally suited to meet the needs of people with this fluctuating, unpredictable, and incurable condition. This philosophy must be based on a thorough understanding of the mechanisms underlying disability and recovery in MS.\(^1\) It is translated into practice by carrying out goal orientated rehabilitation programmes which are based on expert multidisciplinary assessment and evaluated through appropriate clinical outcome measures\(^1\) and monitoring of goal achievement through the use of integrated care pathways.\(^2\)

There have been a number of studies in recent years that have evaluated rehabilitation. These can be divided into those assessing components of process and those assessing the rehabilitation package itself (for example, inpatient rehabilitation). Tentative evidence now exists to support the use of components of the rehabilitation process including physiotherapy\(^3\) and aerobic exercise.\(^4\) The physiotherapy study was randomised, controlled, and crossover in design and evaluated hospital and home based therapy in 40 patients using a wide range of outcome measures. Benefit from physiotherapy compared to no therapy was seen (irrespective of location) in the primary outcome measure (the Rivermead mobility index) and was cheaper if carried out in the hospital. Attempts to evaluate the potential benefit of the full rehabilitation package have focused primarily on the inpatient setting and have attempted to identify which areas are likely to improve and whether that improvement is maintained following discharge into the community. Although recent studies have methodological limitations, they are an improvement on earlier work and, perhaps most importantly, demonstrate that such studies are feasible.\(^5\) Despite small numbers, inpatient rehabilitation resulted in a significant benefit in disability and handicap in a UK study of patients with progressive MS, and benefit in disability and aspects of quality of life in a less disabled Italian cohort.\(^6\) The duration of benefit has not been looked at in a randomised controlled trial, but a single group study suggested that benefits in disability and handicap persist for approximately six months while the positive effect on quality of life and emotional well being may continue for longer.\(^7\)
When to refer for rehabilitation?

The majority of patients tend to be referred after they have lost important function(s). This usually relates to the ability to walk but is equally applicable to transfers, loss of upper-limb function or deterioration in bulbar function. Rehabilitation may aim to improve level of function or be directed towards coping with the recent deterioration. In patients with very severe disability, this may be directed towards setting up the environment to accommodate the patient, maximise what little independence they have, and educate the carer(s). Occasionally, the changes relate to an acute relapse in which recovery may be expected—though may be slow or incomplete. Deterioration resulting from insidious disease progression may be more difficult to address but benefits can be seen following expert assessment and targeted input. Inevitably there will be patients who are unlikely to benefit from rehabilitation or who are functioning at their maximum capacity. Assessment in these situations can be helpful if only to clarify the situation and to guide other health care professionals involved in the management of the patient.

Service delivery

A recent study has provided some evidence that coordinated, multidisciplinary care is of greater benefit than medical care alone in MS. The importance of continuity of care, and in particular the link between hospital and community, has been emphasised in earlier sections. Recent studies have emphasised how poor this continuity of care is and how sparse and variable is the support received by people with MS living in the community. Much of the support, in many instances up to 90%, is currently provided by family and friends. More recently, an important link is being provided by MS nurse specialists and the contribution of their role is currently being evaluated.

The development of standards of care (more appropriately called guidelines) for the management of MS is an important first step and serves to emphasise both patient needs and the paucity of evidence available to guide the way in which we minimise the impact of the disease (fig 3). The National Institute for Clinical Excellence has recently commissioned the Royal College of Physicians and the Chartered Society of Physiotherapists to develop guidelines for the management of MS, which hopefully will make a useful contribution to improving services throughout the country.

Figure 3 A potential framework for standards of care identifying the key issues of the four stages of multiple sclerosis.

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SYMPTOMATIC MANAGEMENT AND REHABILITATION IN MULTIPLE SCLEROSIS

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