Symptomatic Management of Multiple Sclerosis

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Abstract  A majority of patients with multiple sclerosis (MS) experience a variety of symptoms related directly or indirectly to the disease. For many patients, carefully chosen medications can control these symptoms successfully, especially when used with physical and/or occupational therapy and, when indicated, surgery. At a course given during the 66th Annual Meeting of the American Academy of Neurology, experts discussed the current management of spasticity; locomotion difficulties; sleep disorders; fatigue; cognitive dysfunction; pain; mental depression; and gastrointestinal, genitourinary, and sexual dysfunction in patients with MS. The strategies they use and recommend form the basis of this review.

Since the introduction of disease-modifying therapies (DMTs) for multiple sclerosis (MS), researchers have focused on developing stronger, more tolerable treatments for the disease. However, relatively less attention has been paid to improving the symptoms experienced by most patients with MS, including fatigue, muscle spasms, pain, gait and sleep disturbances, and others. Inattention to these symptoms can lead to a vicious cycle of worsening and perpetuation. Their correction improves the quality of life (QOL) of MS patients, their social interrelationships, and their work performance and functionality.

During the 66th Annual Meeting of the American Academy of Neurology (AAN), an innovative course on managing the most common MS symptoms highlighted common manifestations of the disease and current strategies for managing them.

Gait Disturbances

Based on a presentation by Andrew Goodman, MD, FAAN, Professor of Neurology, Chief of the Neuroimmunology Unit, and Director of the Multiple Sclerosis Center, University of Rochester, Rochester, New York.

One of the most frequent problems reported by MS patients is gait disturbances. Leg weakness, spasticity, cerebellar or sensory ataxia, foot drop, knee instability with buckling, spastic paresis, or stepwise gait are manifestations of walking disturbances. These abnormalities can be detected by asking patients to walk several feet quickly or repeating the 25-foot walking test (T25FW) two or three times.

About 50% of MS patients require some assistance with walking within 15 years of disease onset. In an online interview of 1,011 MS patients and caregivers, 41% reported walking difficulty; 70% confirmed that walking was the most challenging aspect of their disease. Gait impairment affects QOL by causing loss of independence, physical disability, unemployment, and depression.

Physical and Occupational Therapy

A multidisciplinary approach involving physical and occupational therapists and physiatrists plays a crucial role in the treatment of gait disturbances. Regular, tailored physical therapy that addresses specific patient needs is essential in managing gait problems. To prevent injuries, healthcare professionals must evaluate patients for any need of assistive devices; these devices may include ankle or foot orthotics for individuals with food drop and devices to assist with walking, such as a single-point or quad cane, forearm crutches, or a rollator (wheeled walker).

Ideally, occupational therapists should assess the patient’s home for safety and recommend any alterations in the home environment. These changes may include installation of grab bars in showers and bathrooms, limitation of obstacles, and clearance of pathways within the home.

Pharmacologic Management

The only pharmacologic therapy currently approved by the US Food and Drug Administration (FDA) to treat gait abnormalities is 10 mg of dalfampridine given twice daily. This drug represents the extended-released form of fampridine (4-aminopyridine), a potassium channel blocker that may improve electrical transmission across the demyelinating axons and facilitate synaptic transmission.

Dalfampridine has class I level of evidence based on two phase 3 studies. In one by Goodman et al, 10 mg of dalfampridine or placebo was given twice daily to 301 MS patients with gait disturbances for 14 weeks; 35% of the active treatment group and 8% of the placebo group were considered to be “timed-walk responders.” This improvement was maintained during the 14-week treatment period. The most common side effects reported have been...
seizures (7%), insomnia (8%), nausea, and paresthesias.⁷

Because not all MS patients respond to dalfampridine, a 2- to 4-week treatment trial may be a practical approach. Patient response may be evaluated using the T25FW and the patient’s self-report. Treatment should be discontinued if no objective improvement is noted. This drug should not be used in patients with a history of seizures or renal failure.

### SPASTICITY

Based on a presentation by Andrew Goodman, MD, FAAN.

Spasticity may be described as a state of increased muscle tone with velocity-dependent increased resistance to passive movement. It is present in 70%–80% of MS patients and is caused by interruption of inhibitory effect by descending pathways to control group II spinal interneurons, which results in overactivity of a motor neurons. Spasticity contributes to worsening of pain, gait abnormalities, and falls, and it may contribute to urinary symptoms.⁸

#### Physical Therapy

A nonpharmacologic approach is essential. Physical therapists must instruct patients to perform stretching and exercise routines necessary to treat MS-related spasticity.

#### Pharmacologic Therapy

**Baclofen** therapy increases presynaptic inhibition in the spinal cord by acting as a γ-aminobutyric acid (GABA) agonist. Patients may be prescribed 20–80 mg of baclofen given in three to four divided daily doses. Unfortunately, the drug’s short half-life requires frequent dosing during the night and limits its use. Physicians should use caution when ordering patients to walk more often, since weakness may worsen. Sedation is the most common side effect of baclofen reported. When discontinuing baclofen therapy, physicians should prescribe a slowly tapering regimen to prevent withdrawal symptoms.⁹

The baclofen pump releases liquid baclofen into the subarachnoid space. It has been effective in refractory and severe cases of spasticity in ambulatory and non-ambulatory patients. It has class I level of evidence; the FDA has approved its use for spasticity related to MS. Neurologists should be aware of technical difficulties and should be familiar with dosing, refilling and programming the pump, and managing baclofen withdrawal in case of pump failure.⁺

**Tizanidine.** This α₂-adrenergic agonist reduces the release of excitatory neurotransmitters in the central nervous system (CNS). Its use was approved by the FDA for spasticity; it is as efficacious as baclofen, and it causes less muscular flaccidity. Use of the drug is limited by sedation, dizziness, and hypotension. Combining tizanidine with baclofen or other muscle relaxants may be considered.⁹

**Unapproved drugs.** Benzodiazepines are GABAₐ agonists, which increase presynaptic inhibition of a motor neurons in the spinal cord. Because benzodiazepines can cause habituation, tolerance, and sedation, they are not commonly used to treat spasticity in MS patients.

Botulinum toxin can improve the functioning of small muscles of the upper and lower extremities; it also can prevent ulcers (eg, with tonic clenching of fingers toward the palm). Bigger muscles require larger doses, which limits use of this toxin and increases the risk of side effects.

Cannabinoids act as a CNS cannabinoid 1 (CB1) receptor agonist. Cannabidiol (CBD) and tetrahydrocannabinol (THC) are the major components of cannabis; a synthetic form of THC is available to treat nausea, pain, and anorexia in cancer patients. Cannabis extracts can be administered using oral, oromucosal, or smoked forms.

Nabiximols are cannabis extracts or synthetic forms of THC (eg, dronabinol) to treat spasticity and pain. A level B recommendation was given for nabiximols. Reduction of spasticity by the modified Ashworth scale was not met during studies that served as the backbone of treatment guidelines.¹⁰,¹¹ However, a significant number of patients reported a reduction in spasticity. Side effects of cannabinoids include drowsiness, dizziness, dry mouth, and disinhibited encephalopathy.

### FATIGUE

Based on a presentation by Timothy West, MD, Director, Multiple Sclerosis Clinic, Cleveland Clinic Lou Ruvo Center for Brain Health, Cleveland Clinic, Cleveland, Ohio.

Fatigue in MS patients is defined by the Multiple Sclerosis Council for Clinical Practice Guidelines as a “subjective lack of physical and/or mental energy that is perceived by the individual or caregiver to interfere with usual and desired activities.”¹² It is described by patients as a lack of motivation, physical and mental exhaustion, or an increase in mental effort.

Fatigue is one of the most common complaints of MS patients.¹³ In a US population-based cohort of people with MS, fatigue was reported by more than 80%. Two thirds of these individuals identified fatigue as a major factor that limited social and occupational responsibilities. Fatigue frequently causes unemployment and incapacity and is recognized by the US Social Security Administration as a qualifying condition for disability status.

This poorly understood symptom likely is multifactorial. It can be divided into primary fatigue and secondary fatigue.

#### Primary Fatigue

Primary fatigue is a direct consequence of CNS inflammation, circulating cytokines, and/or use of DMTs (Table 1), which may reduce CNS reserve and cause demyelination and axonal loss.

Filippi and Rocca¹⁴ performed functional magnetic resonance imaging in 15 MS patients with fatigue, 14 MS patients without fatigue, and normal controls performing a simple motor task. MS patients with fatigue activated more motor areas than did the other two groups, suggesting...
that fatigue in MS is related to impaired interactions between functionally related cortical and subcortical areas.

Circulating pro-inflammatory cytokines—interleukin (IL)-1, IL-6, IL-10, and tumor necrosis factor-alpha (TNF-α)—are related to MS-associated fatigue. Interferon therapy can lessen fatigue by reducing the levels of these cytokines but also can cause fatigue and other flu-like symptoms after injection. Finally, lesions that alter the hypothalamic-pituitary-adrenal axis may cause changes in sleep patterns or may result directly in fatigue.

**Occupational therapy.** Energy conservation management (ECM) and optimization of use of available energy are the primary goals of occupational therapists treating fatigue. A meta-analysis showed that ECM decreased fatigue over the short term. To optimize energy, patients are taught to balance between work and rest, delegate activities, use their bodies efficiently, organize work spaces, and use assistive devices.

**Physical therapy.** Overall, exercise can improve fatigue. Physical therapists help patients to increase energy by presenting a planned, structured, and repetitive exercise regimen that includes aerobic exercises, yoga, and resistance exercise.

**Pharmacologic management.** To reduce the fatigue of MS, 100 mg of amantadine has been given twice daily. This antiviral agent exerts dopaminergic effects; however, a 2007 Cochrane review showed insufficient evidence to recommend the use of this drug for fatigue in MS patients. Its main side effects are orthostatic hypotension, leg edema, and headache. Amantadine should be used with caution in patients with congestive heart failure, seizures, or cardiac arrhythmia.

Modafinil is a nonamphetamine CNS stimulant currently indicated for treatment of excessive daytime sleepiness in patients with narcolepsy, obstructive sleep apnea, or work-shift disturbances. When given at a dosage of 100–200 mg/d, modafinil may increase cortical activity in the frontal lobes. However, this drug has not been approved by the FDA to treat MS-related fatigue, and controversial data exist regarding its effectiveness in patients with MS. Rammohan et al demonstrated that 200 mg/d of modafinil was well tolerated and that its use significantly improved fatigue associated with MS. However, a randomized, double-blind, placebo-controlled trial by the French Modafinil Study Group showed no difference in Modified Fatigue Impact Scale scores between groups given modafinil or placebo. Common side effects related to modafinil therapy include anxiety, headache, hypertension, and palpitations.

Little or no data exist to support the use of pemoline, L-carnitine, or dalfampridine for treating MS-associated fatigue.

Interestingly, 650 mg of aspirin given twice daily improved fatigue in a small, randomized, placebo-controlled trial in patients with MS. Shaygannejad et al reproduced these results with 500 mg of aspirin given once daily. Most likely, these benefits resulted from the anti-inflammatory effects of aspirin. However, use of this drug is limited by an increased risk of gastrointestinal bleeding and gastritis.

**Secondary Fatigue**

Secondary fatigue results from indirect events that cause or exacerbate fatigue, such as sleep disorders (eg, obstructive sleep apnea, central sleep apnea, or restless sleep), restless leg syndrome, insomnia due to anxiety or mood disorders, and fragmented sleep due to pain, spasticity, or nocturia. Because depression is closely related to fatigue, identification and treatment of mental depression likely will increase energy.

The use of medications such as opioids or corticosteroids and drugs used to treat comorbidities (eg, anemia, hypothyroidism, chronic obstructive pulmonary disease, infections) should be considered when MS patients present with fatigue. Heat, humidity, or working night shifts may exacerbate or cause fatigue. Before considering administration of stimulants, physicians should identify contributors and the etiology of fatigue (Figure 1).

**Sleep disorders** were identified in 24%–50% of patients with fatigue in some series. Poor sleep hygiene, nocturia, spasticity, and pain are well-known contributors to poor sleep in MS patients.

Using polysomnography in a cross-sectional study of 66 MS patients, Veauthier and colleagues reported that nearly three fourths of these patients exhibited sleep disorders; 12% had either obstructive or central sleep apnea, 36% had restless leg syndrome and/or painful limb muscle spasms, and 26% reported poor sleep hygiene.

**Obstructive and central sleep apnea.** Patients who gasp or choke while sleeping, experience daytime sleepiness, or have a large body habitus should be evaluated for obstructive sleep apnea and should be considered for sleep studies. Continuous positive airway pressure is the standard treatment for sleep apnea, and it may improve several MS symptoms.

**Restless leg syndrome** is seen in 13%–37% of MS patients and usually in individuals who have advanced stages of the disease. Administration of gabapentin or a dopamine agonist (eg, pramipexole, ropinirole) can improve the duration and quality of sleep. Allen and colleagues recently reported that use of pregabalin to treat restless leg syndrome improved treatment outcomes with lower augmentation rates when compared with placebo.
Patients with MS may experience pain from a variety of sources, including:
- Neuropathic pain directly related to MS, such as painful paroxysmal symptoms (e.g., trigeminal or glossopharyngeal neuralgia), painful tonic spasms, and painful paresthesias and dysesthesias;
- Pain indirectly related to MS as a consequence of other symptoms (e.g., spasticity, dysynergic sphincter);
- Treatment-related pain (e.g., skin irritation after injection of DMTs); or
- Pain unrelated to MS (e.g., headache, back pain, arthritis).

Foley et al.27 demonstrated that MS patients commonly experienced headache (23%), dysesthetic limb pain (26%), painful spasms (15%), Lhermitte’s symptom (16%), and trigeminal neuralgia (4%).

Management of pain syndromes in MS requires a multidisciplinary approach that includes physical and occupational therapy, psychology, and medical management (Figure 2). The effectiveness of drug therapy depends upon the other components of treatment.

**Treatment Strategies**

**Trigeminal neuralgia** tends to occur in younger MS patients. Abnormal compression of the ganglion in the third division of the trigeminal nerve (V3) is suspected to be the cause of sensory deficits and pain between attacks.

Carbamazepine, the only FDA-approved therapy for trigeminal neuralgia, is the treatment of choice. The initial dose is 100 mg given twice daily (maximum dose, 1,200 mg/d); to reduce side effects, rapid titration should be avoided. Therapy may be related to Stevens-Johnson syndrome and toxic epidermal necrolysis among patients of Asian descent; these individuals may be screened for HLA-B*1502, which increases the risk. Side effects of carbamazepine include sedation, dizziness, hyponatremia, and, less commonly, pancytopenia and aplastic anemia.

Oxcarbazepine, given at a dosage of 300 mg twice daily, is similar to carbamazepine in its efficacy and safety profile, but it is more commonly associated with hyponatremia.

Pregabalin and lamotrigine are alternatives when the aforementioned drugs

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**FIGURE 1** Algorithm for treating fatigue in patients with multiple sclerosis. Adapted, with permission, from Krupp.22
are ineffective or not tolerated. In severe refractory cases, two or three of these drugs may be used in combination.

Surgical approaches for refractory cases include percutaneous thermoregulation (50% recurrence risk), percutaneous retrogasserian glycerol rhizotomy (30% recurrence risk), and Gamma Knife or CyberKnife (Accuray, Inc; Sunnydale, CA; 22% recurrence risk) surgery.

**Paroxysmal painful tonic spasms** or **paroxysmal painful dyskinesias**, which can be secondary to spinal and cerebral demyelinating lesions, occur in 15%–19% of MS patients. These manifestations usually occur during later MS and in patients with neumyelitis optica.

Carbamazepine and gabapentin appear to be the most effective drugs for treating these movement disorders; topiramate, lamotrigine, or valproate may be considered as alternatives.

**Chronic painful dysesthesias.** Described as unpleasant “burning” sensations, dysesthesias of the arms, legs, and trunk occur in 14%–29% of MS patients and can be exacerbated by heat and physical or emotional stress. These symptoms are difficult to treat, although physical therapy with ice, carbonated baths, or electrotherapy may alleviate discomfort.

First-line pharmacologic therapies for painful dysesthesias include tricyclic antidepressants (eg, amitriptyline, nortriptyline), gabapentin, and lamotrigine.

**Pain indirectly related to MS** may result from improper positioning, spasticity, or nerve compression. Visceral pain indirectly associated with MS (eg, pelvic floor muscle spasticity, spastic external sphincter) may manifest itself as burning pain during micturition. Tamsulosin, an α-adrenergic antagonist, may be useful in relieving pain. Pain associated with detrusor spasms may be treated with an antimuscarinic agent, such as oxybutynin or solifenacin, or with injection of botulinum toxin into the detrusor muscle.

**DEPRESSION**

Based on a presentation by Bruce A.C. Cree, MD, PhD.

About 20%–50% of MS patients experience depression. Risk factors include female gender, age < 35 years, and a family history of depression. Diagnosis can be difficult, since several physical symptoms of MS, such as fatigue, can cause depression. To identify depression in an MS patient, the physician may ask whether, over the previous 2 weeks, the patient has been disturbed by feeling down, depressed, or hopeless or by having a lack of interest or pleasure in activities. These simple questions have a high positive predictive value of 71% (false-positive rate, 27%).

Interferon therapy may cause depression, which contributes to the underlying mood disorder.

**Treatment Strategies**

Treatment of depression is similar for all patients—a comprehensive approach and screening for suicidal ideation are important.

Physicians should consider the physiologic effects of common antidepressants. Citalopram, a selective serotonin reuptake inhibitor, may prolong the QT interval on an electrocardiogram; use caution if the patient is on fingolimod therapy.

Tricyclic antidepressants can increase the risk of suicide at the beginning of treatment. Side effects of some of these medications may confer benefit in MS patients. For example, their anticholinergic effects may mitigate urinary symptoms.

Duloxetine, a serotonin and noradrenaline reuptake inhibitor, can be helpful in treating depression and pain. Bupropion, a norepinephrine and dopamine reuptake inhibitor, may be helpful in treating depression and smoking cessation.

Patients should be referred to a psychiatrist promptly if they fail to respond to conventional antidepressant therapy after 6 weeks, show signs of suicidal tendencies, or have other psychiatric diseases.

**COGNITIVE IMPAIRMENT**

Based on a presentation by Bruce A.C. Cree, MD, PhD.

Often reported by patients and caregivers, cognitive impairment has an overall prevalence of 30%–50% in MS patients. Most commonly, speed of processing, memory, complex attention, and executive function are affected. Referral for neuropsychologic evaluation and cognitive rehabilitation needs to be considered when activities of daily living are affected.

**Treatment Strategies**

Due to methodologic limitations, there is no clear evidence that cognitive rehabilitation provides a significant impact on a patient’s life. An occupational therapist may provide targeted interventions for specific cognitive deficits.

Pharmacologic interventions (eg, methylphenidate, modafinil, or dalfam-
Bladder dysfunction is seen in up to 75% of MS patients. It can fall into one of the following categories:

- **Failure to store urine due to detrusor overactivity** is clinically manifested by urgency, frequency, nocturia, and/or urine incontinence. Overactive bladder is the most common type of bladder dysfunction noted among MS patients. Urodynamic studies may show detrusor overactivity.

- **Detrusor sphincter dyssynergia** results from asynchrony between detrusor contracture and sphincter relaxation. It is manifested by hesitancy, straining, and urinary retention (> 150 mL of post-void residual volume). Urodynamic studies show disrupted coordination of sphincter relaxation and detrusor contraction.

- **Hypoactive bladder** is manifested by urinary retention or overflow incontinence. It is the least common bladder dysfunction noted among MS patients. It is associated more often with upper urinary tract infections and renal injury; therefore, early urologic referral is recommended.

Urinalysis, urine culture, post-void residual urine testing, and, ideally, the keeping of a 3-day “bladder diary” can help a physician assess bladder dysfunction.

**Behavioral Modifications**

Behavioral modifications are the first step in treatment. Symptomatic improvement has been demonstrated in up to 50% of MS patients with bladder dysfunction using this approach, including adequate control of comorbidities (hyperglycemia, congestive heart failure, urinary tract infections), avoiding common bladder irritants (caffeine, alcohol, citrus juices, tobacco), avoiding consumption of water and other fluids by mouth 2–3 hours before bedtime, scheduled voiding, bladder retraining, and strengthening of the pelvic muscles with Kegel exercises.

**Pharmacologic Treatment**

Drug treatment of bladder dysfunction is guided initially by the patients’ symptoms, post-void residual urine testing, and, ultimately, urodynamic studies.

Antimuscarinic agents (Table 2) relieve urinary symptoms in an overactive bladder by dampening the amplitude of detrusor muscle contraction and decreasing involuntary detrusor activity, thereby improving bladder capacity. Common side effects of these drugs are constipation, dry mouth, and sedation. Neurologists should be cautious in giving antimuscarinics to patients with narrow-angle glaucoma, gastric stasis, or a history of urinary retention.

Alternatively, nonantimuscarinic drugs for overactive bladder can be used to treat bladder dysfunction (Table 3). Mirabegron is a β3 adrenergic receptor agonist that recently was approved to treat overactive bladder; it has fewer side effects and is better tolerated than antimuscarinics.

Tricyclic antidepressants used for pain and depression provide symptomatic relief of bladder dysfunction due to their anticholinergic effects.

Desmopressin (DDAVP), 0.1–0.6 µg orally or 10 µg intranasally, increases water absorption in the renal collecting duct and reduces urine production. This drug may be helpful when nocturia is the prevalent symptom; its use is recommended only for short periods. Water intoxication and hyponatremia are possible side effects.

**Other Treatment Strategies**

When behavioral modifications and pharmacologic management are not ef-
effective, urodynamic studies may guide the course of treatment. In refractory cases of overactive bladder, intradetrusor botulinum toxin injections may be effective, although they may produce temporary urinary retention, which requires regular self-catheterization.\textsuperscript{35} More severe bladder dysfunction can be treated with sacral nerve stimulation or intermittent tibial nerve stimulation.

In cases of urinary retention, early urologic referral is recommended. Treatment for these cases includes intermittent self-catheterization, suprapubic catheterization, and urinary diversion.

\section{Bowel Dysfunction}

Based on a presentation by Elizabeth Crabtree-Hartman, MD.

Bowel dysfunction occurs in >50\% of MS patients. Neurogenic bowel, usually spastic bowel, produces constipation and/or bowel incontinence.

\subsection{Constipation}

Constipation may be caused by any of a variety of factors, including autonomic dysfunction resulting in slow gastric emptying; weakened abdominal muscles; inadequate water intake; and decreased colonic transit, rectal sensory feedback, or patient activity.

**Behavioral modifications.** Advise MS patients who are constipated to avoid bowel irritants such as caffeine and alcohol; candy and gum artificially sweetened with sorbitol or xylitol; and, if feasible, drugs that can cause or worsen constipation, such as opioids, tricyclic antidepressants, and sedatives. Maintaining good fluid and fiber intake, regular morning bowel habits, and frequent light exercise also may be helpful.

**Nonpharmacologic treatment.** Other nonpharmacologic approaches to combating constipation include digital rectal stimulation to activate the anorectal reflex, abdominal massage, and biofeedback.

**Pharmacologic treatment.** Generally, bulk-forming agents and stool softeners are recommended. Laxative or colonic rectal stimulants should be used with caution. Enemas can cause loss of rectal reflexes and are not indicated routinely except for cases of fecal impaction. In more severe and intractable cases, a determination of colonic transit time and anorectal manometry by a gastroenterologist will help to determine the correct treatment.

\section{Fecal Incontinence}

Fecal incontinence may result from increased colonic transit or lack of sphincter control. It is less common than constipation in MS patients. Patients should avoid bowel irritants such as caffeine or alcohol and should attempt to schedule bowel movements. Bulk-forming agents produce more consistent stools, and anticholinergic agents can reduce bowel transit. Referral to a gastroenterologist should be sought in refractory cases.

\section{Sexual Dysfunction}

Based on a presentation by Elizabeth Crabtree-Hartman, MD.

Up to 60\% of MS patients report sexual dysfunction,\textsuperscript{36} a disturbing consequence of the disease for both patients and their spouses or partners. Sexual dysfunction can be divided into three main categories:\textsuperscript{37}

**Primary sexual dysfunction.** Symptoms caused directly by MS include erectile dysfunction (50\%–75\%), ejaculatory dysfunction and/or orgasmic dysfunction (50\%), reduced libido (39\%), and anorgasmia (37\%) in men and sensory genital dysfunction (61\%), difficulty achieving orgasm (24\%–60\%), decreased vaginal lubrication (36\%), and reduced libido (40\%) in women.\textsuperscript{37}

**Secondary sexual dysfunction** is a consequence of other MS-related symptoms (eg, fatigue, pain, bowel dysfunction) and drug therapy.

**Tertiary sexual dysfunction** results from psychologic factors, such as mood dysregulation, negative self-image, fear of rejection, and communication problems.

\subsection{Management}

Management of sexual dysfunction is complex and should include an open dialog with patients and spouses, optimization of DMTs, identification of possible contributors, and assignment of appropriate urology and gynecology referrals. In men, reduced testosterone levels can be corrected with hormonal supplementation. For erectile dysfunction, sildenafil (a phosphodiesterase 5 [PDE5] inhibitor) has improved erections in 90\% of 217 MS patients.\textsuperscript{38} Vardenafil and tadalafil are newer PDE5 inhibitors with extended half-lives that permit more spontaneous erections over a longer period.

In a population of individuals with spinal cord injuries, 93\% of patients receiving intracavernosal injections of alprostadil (prostaglandin E1) and using vacuum erection devices achieved satisfactory erections, which improved sexual and reproductive function.\textsuperscript{37,38}

\section{Conclusion}

Treatment of MS patients can be complex and challenging. Effective management of MS symptoms has a remarkable impact on the QOL of patients and their families. Several symptoms are interrelated, and treatment of one may alleviate others. Healthcare providers must be patient and diligent when addressing the multiple clinical manifestations of MS. It may be impossible to address each symptom in detail at every visit, so continuity of care is essential. Clinicians need to identify and focus on one or two relevant symptoms that most impact their patients’ lives during each encounter and then do what they can to address those problems.

\textbf{References}


