REVIEW

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CME CREDIT

Multiple sclerosis: Treating symptoms, and other general medical issues

ABSTRACT

Multiple sclerosis (MS) has protean manifestations, and the care of people with MS presents many unique challenges. Clinicians can have an important impact on health, quality of life, and daily functioning by participating in open dialogue, tailoring focused treatment plans, and anticipating general medical needs.

KEY POINTS

Common symptoms of MS that should be addressed include spasticity, bladder dysfunction, bowel dysfunction, fatigue, pain syndromes, ataxia, tremors, vertigo, cognitive impairment, and mood disorders.

Spasticity is a central feature of MS. Treatments range from simple stretching exercises for mild spasticity to intrathecal baclofen for severe, refractory spasticity.

Bladder dysfunction—either overactivity or retention—affects quality of life and can lead to infections. Bladder infections in turn worsen MS symptoms. Identification, characterization, and treatment of bladder dysfunction is therefore quite important.

Although MS-related fatigue is common, clinicians should evaluate for coexisting medical conditions that could cause or contribute to it, such as thyroid disease, anemia, and sleep disturbance.

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[Multiple sclerosis] is, in fact, an eminently polymorphic affection.

Jean Martin Charcot, 1878

TREATMENT OF PATIENTS with multiple sclerosis (MS) demands a broad focus. We have to treat the whole patient, not just the disease or its manifestations. Therefore, we must integrate disease and symptom management into a personalized combination that accounts for and addresses general medical, personal, and socioeconomic issues.

MS is currently thought to be an immune-mediated disease of the central nervous system, and disease-directed therapies modulate or suppress the immune system. There are currently five therapies for MS approved by the US Food and Drug Administration (FDA), and all appear to reduce the relapse rate and the development of new lesions on magnetic resonance imaging. (A full discussion of the indications for and use of these therapies is beyond the scope of this article, but has been reviewed in this journal and elsewhere.[1,2])

To be sure, disease-modulating therapies have been a big advance in the field of MS. Unfortunately, however, these treatments do not appear to improve chronic neurologic deficits, and MS patients still experience a variety of neurologic symptoms (**TABLE 1**) that often interfere with daily activities and reduce quality of life.[3] The most common presenting symptoms of MS are visual abnormalities (49%), weakness (43%), and sensory deficits (41%).[4] Incoordination and bladder and bowel dysfunction are uncommon as presenting symptoms but occur in more than 50% of patients during the course of their disease.[4] Depression, fatigue, and cognitive problems are also extremely common.

TABLE 1

Common symptoms of multiple sclerosis

Bladder symptoms—urgency, frequency, hesitancy, retention, incontinence

Bowel symptoms—constipation, urgency, incontinence

Cerebellar symptoms—incoordination, imbalance, tremor

Cognition—concentration, memory, executive dysfunction

Fatigue—lassitude, reduced endurance

Mood disorders—depression, anxiety, emotional lability

Motor weakness and spasticity

Sensory symptoms—loss of sensation, positive sensations

Sexual dysfunction—decreased libido, erectile dysfunction

Visual loss and double vision

MS symptoms are challenging to address in a physician's busy practice, as patients can have multiple symptoms that are fluctuating and often subjective. Their treatment can require a simple intervention or a more complex multidisciplinary team approach.

Although the potential symptoms of MS are myriad, this article will focus on those that are common and for which treatments exist.

Ask about problems that may be uncomfortable for the patient to broach

GENERAL GUIDELINES FOR MANAGING MS SYMPTOMS

The following general guidelines may be helpful in managing MS symptoms.

Identify the symptoms

Although patients often share information about their symptoms spontaneously, we should remember to systematically ask about problems that may be uncomfortable for the patient to talk about, such as bladder or sexual dysfunction (TABLE 2). We may also need to ask other family members or a caregiver about issues into which the patient may lack insight, such as cognitive or mood changes.

Report of some symptoms should lead the health care provider to discuss other related possibilities. For example, complaints of fatigue or poor sleep should prompt questions about depression.

Evaluate the consequences of symptoms

Many MS symptoms affect other spheres of functioning. For example, spasticity may limit walking; nocturnal spasms may disrupt sleep, which in turn contributes to daytime fatigue.

It is important to ask patients how different symptoms affect their routine activities and quality of life. This will help you prioritize and streamline treatment.

Prioritize symptoms

It is often not possible or even desirable to address all of a patient's symptoms during a single encounter. Patients should be encouraged to prioritize their symptoms.

Clinicians also need to prioritize symptoms, focusing on those that may lead to medical or disease complications. For example, urinary retention may cause frequent urinary tract infections, which in turn can lead to worsening of MS symptoms.

Create and streamline a treatment plan

Prioritizing symptoms will help focus the treatment plan. The patient and clinician should agree on clear and realistic goals. These goals may change over time, necessitating ongoing discussion and patient education.

First, review the patient's medications to see if any of them may be contributing to his or her symptoms. For example, many medications cause sedation and aggravate fatigue. Next, evaluate for concurrent medical conditions that may be contributing to symptoms, such as thyroid dysfunction or anemia in the case of fatigue.

Consider nonpharmacologic treatments

For many symptoms, lifestyle changes and rehabilitative interventions can be first-line treatments. When considering drug therapy, keep in mind potential side effects, interactions, and additive toxicity with current treatments. In general, aim for monotherapy, start at low doses, and titrate slowly.

Know when to refer

When symptom management becomes complex, consider a dedicated visit. More-aggressive treatments are available for some symptoms, such as baclofen pumps for spasticity; clinicians should be aware of these treatments

TABLE 2

Sexual dysfunction in multiple sclerosis

Symptoms

In women: reduced libido, vaginal lubrication, and vaginal sensation; inability to reach orgasm
In men: reduced libido; erectile and ejaculatory dysfunction

Causes

Physiologic: spasticity, weakness, pain, fatigue
Psychological: depression, anxiety
Common medications: anticholinergics, baclofen, selective serotonin reuptake inhibitors, tricyclic antidepressants

Treatments

Sexual therapy to improve communication
Bupropion (Wellbutrin): less likely to cause sexual dysfunction compared with other depression therapies. May also have direct benefit on libido and orgasm[64]
Phosphodiesterase 5 inhibitors: sildenafil (Viagra), vardenafil (Levitra), tadalafil (Cialis); some evidence that these may also be helpful in women
Estrogen replacement: oral, topical, or vaginal ring; should be considered in conjunction with gynecologic evaluation
Devices: mechanical vibrators and vacuum devices can enhance arousal and orgasm

and know when to refer a patient to a specialty clinic. Complex symptomatic management of MS patients often requires a multidisciplinary approach involving physicians, nurses, and allied health professionals.

The Consortium of MS Centers and Paralyzed Veterans of America has published practice guidelines for managing selected symptoms in MS, which serve as practical references for clinicians.[5–7]

SPASTICITY

Motor pathway dysfunction with associated spasticity is a central feature of MS. In a California survey of 168 patients,[8] 70% reported difficulty with mild to severe spasticity.

Spasticity, typically a result of spinal cord involvement, preferentially affects the legs and trunk. Its manifestations are varied and include stiffness, involuntary muscle spasms, and loss of muscle function.

Treatment for spasticity involves an integrated approach. Rehabilitation should be tailored to the patient's degree of impairment and disability. Patients with mild spasticity often benefit from routine daily stretching, guided by an experienced physical therapist.[9] Patients who are more disabled may benefit from intensive physical therapy and also from occupational therapy. Potential focuses of occupational therapy include upper-extremity function, wheelchair evaluation, and workplace or home modifications.

Drug therapy for spasticity

Medications are often used as adjuncts to rehabilitation. When deciding on the dosage of medications for spasticity, remember that some patients with lower-extremity weakness may require a degree of spasticity to be able to walk.

Some MS patients may need some degree of spasticity to walk

Baclofen (Lioresal), an agonist of gamma-aminobutyric acid, is often the first-line drug for spasticity in MS. It has been shown to improve spasticity and muscle spasms in MS patients.[10,11]

Baclofen should be started at a low dose, eg, 10 mg three times per day. The dose can be slowly titrated upward as needed. In severe cases, doses higher than 120 mg/day may be used.

Baclofen can unmask underlying weakness. Common side effects include somnolence and confusion. Abruptly stopping baclofen can precipitate seizures as part of a withdrawal syndrome.

Intrathecal administration of baclofen (via a surgically implanted catheter and pump) is markedly more effective and better

tolerated than oral dosing in patients with severe spasticity who are wheelchair-dependent[12,13] and in a select group who can walk.[14,15] To maximize benefit and optimize outcome, patients should be referred to an experienced center to determine if this therapy is right for them and to have the pump placed and managed.

Tizanidine (Zanaflex) is the only alpha-2 agonist approved for treating spasticity. It appears to be as effective as baclofen but causes less weakness.[16] Additional benefit can be gained by combining baclofen and tizanidine.

A typical starting dose is 2 mg at bedtime, gradually increasing as tolerated up to 36 mg/day in three or four divided doses.

Sedation is the most common dose-limiting side effect of tizanidine. Other side effects include dry mouth, dose-dependent hypotension, and aminotransferase elevations.

Gabapentin (Neurontin) is an anticonvulsant that can be used to treat spasticity either as monotherapy[17] or in combination with baclofen or tizanidine.

Gabapentin is typically started at 100 mg three times a day, but the dose can be increased to 3,600 to 4,800 mg daily. A single bedtime dose of 100 to 300 mg can be adequate for nocturnal spasms.

Patients with mild spasticity often benefit from routine daily stretching

Gabapentin is generally well tolerated, Sedation is a common initial side effect, but it typically abates with continued use.

Levetiracetam (Keppra) is effective in reducing phasic spasticity (eg, spasms, cramps, and clonus), and can be a good adjunctive therapy for spasms when sedation limits upward titration of traditional therapies.[18]

Diazepam (Valium) and **clonazepam** (Klonopin) are of particular use in treating nocturnal spasms that are refractory to baclofen or tizanidine.

Dantrolene (Dantrium) is a third-line agent that acts locally at the motor unit by interfering with the release of activator calcium. It is typically reserved for patients who cannot walk and are therefore unaffected by the muscle weakness it causes.

Dose-dependent side effects include diarrhea, anorexia, nausea, and vomiting. Toxic hepatitis is a potentially fatal complication of dantrolene. Due to these issues and the availability of safer therapies, dantrolene is less commonly used.

Botulinum toxin type A or type B is increasingly used to treat spasticity in MS patients. Injected intramuscularly, it inhibits acetylcholine release at the neuromuscular junction. This therapy can be used in patients with focal spasticity as well as in those with diffuse spasticity with focal target areas (eg, difficulty with self-catheterization and hygiene due to spasticity of the hip adductors). Although botulinum toxin is not approved by the US Food and Drug Administration for this use, many insurance plans will pay for it.

Botulinum toxin is usually safe and well tolerated. Local muscle weakness and atrophy can occur, however, particularly with long-term use. The injection technique is simple, but localization with electromyelography or electrical stimulation may be needed for small or deep muscles.

The effects of botulinum toxin are seen from a few days to 2 weeks after injection, and typically last from 3 to 6 months. Periodic repeat injections are required to maintain the benefit.[19,20]

Other medications anecdotally used for spasticity include clonidine (Catapres) and skeletal muscle relaxants.

BLADDER DYSFUNCTION

Up to 90% of MS patients report having bladder dysfunction. This issue is particularly important to address because it has a large impact on quality of life and can exacerbate underlying MS disease via secondary infections.[21] The character and degree of bladder dysfunction correlate with disease severity and disability, but not duration.[22]

Detrusor hyperreflexia

Detrusor hyperreflexia typically results from spinal cord lesions and is the most common bladder disorder in MS patients. Patients commonly describe urinary urgency and frequency and voiding small amounts of urine. Over time, urgency can become more difficult to control, and patients may experience incontinence.

Detrusor hyperreflexia typically responds to anticholinergic agents such as oxybutynin (Ditropan) 2.5 to 5 mg three times a day or

tolterodine (Detrol) 2 mg twice daily. Extended-release formulations of both medications allow for once-daily dosing. A recent study[23] found these medications to have comparable efficacy, but tolterodine caused fewer systemic side effects. Oxybutynin is also available in a transdermal patch, which causes fewer anticholinergic side effects.[24]

Solifenacin succinate (VESIcare) was recently approved for treating overactive bladder and appears to be well tolerated.[25] However, it has not yet been studied in patients with neurogenic bladder dysfunction.

Detrusor sphincter dyssynergia

Detrusor sphincter dyssynergia—the inability to relax the urinary sphincter during micturition—often occurs in combination with an overactive detrusor muscle. Patients experience hesitancy, retention, and overflow incontinence.

Terazosin (Hytrin), an alpha-1 selective antagonist, can be used in this setting at a bedtime dose of 5 to 10 mg. Intermittent catheterization may also be needed. Botulinum toxin can be injected directly into the detrusor muscle or sphincter for treatment of detrusor hyperactivity or sphincter dyssynergia.

Detrusor areflexia

Detrusor areflexia causes symptoms that include urinary hesitancy and retention. Complications of detrusor areflexia include bladder infections, bladder stones, and, rarely, hydronephrosis and renal failure.

Bethanechol (Urecholine), a cholinomimetic agent, can be useful in doses of 10 to 50 mg up to four times a day. Many patients ultimately also require intermittent or continuous catheterization.

Urology consult is sometimes needed

General symptoms of bladder dysfunction (urgency or frequency) are often inaccurate indicators of underlying pathophysiology,[26] and a urology consult is sometimes needed to characterize the dysfunction. Measuring postvoiding residual volume by catheterization or ultrasonography is a useful screening test that can be performed routinely in the office. Urologic consultation should be considered in patients who have mixed symptoms of bladder dysfunction or for whom traditional medications fail.

A select group of patients may benefit from surgery for bladder dysfunction. Potential surgical interventions include suprapubic catheterization, electrical bladder stimulation, sacral root stimulation, and bladder augmentation.

BOWEL DYSFUNCTION

About 68% of MS patients report having bowel dysfunction,[27] although the underlying mechanism remains unclear. Constipation can be secondary to restricted oral fluids in patients with primary bladder incontinence or a medication side effect.

Treatment approaches combine adequate fluid intake with dietary fiber. Bulk-forming agents such as methylcellulose (Citrucel) or psyllium (Metamucil) may also be of use, and should be combined with scheduled voiding.

FATIGUE

Between 60% and 90% of MS patients report fatigue,[28] which often limits activities of daily living, job performance, and quality of life.

Urgency or frequency are often inaccurate indicators of underlying bladder dysfunction

Although MS-related fatigue is common, clinicians should evaluate for coexisting medical conditions that could cause or contribute to fatigue. Common culprits are thyroid disease, anemia, and sleep disturbance.

Sleep disturbance can be due to nocturia, nocturnal spasms, or painful sensory symptoms. MS patients can also have primary sleep dysfunction. Recent work has demonstrated abnormal sleep architecture and more apnea in MS patients compared with controls.[29] The clinical history should direct the need for a sleep study to evaluate fatigue. Medications should be reviewed for sedating agents that could be reduced or eliminated.

MS-related fatigue is best treated with a combination of aerobic exercise and medications. Occupational therapy can simplify tasks at work and home and teach energy conservation and heat management strategies.

When medication is needed, amantadine (Symmetrel)[30,31] or modafinil (Provigil)[32] are both appropriate first-line agents. Amantadine is started at 100 mg in the morning and

TABLE 3

Multiple sclerosis pain syndromes and their treatment

PAIN SYNDROME	ACUTE OR CHRONIC	CLINICAL EXAMPLE	TREATMENT APPROACHES
Neuralgia	Both	Trigeminal neuralgia	Gabapentin 100–900 mg three or four times daily Carbamazepine 200–400 mg three times daily; extended-release form also available Dilantin 300–600 daily Oxcarbazepine 150–900 mg daily Amitriptyline 10–100 mg daily at bedtime Other tricyclic antidepressants Baclofen (oral or intrathecal) as adjuvant therapy[65]
Meningeal irritation	Acute	Optic neuritis	Intravenous corticosteroids directed at underlying inflammation
Sensory pain	Both	Paresthesias	Same as for neuralgia
Skeletal muscle pain	Chronic	With spasticity or limited mobility	Rehabilitation (physical and occupational therapy) Assistive devices Nonsteroidal anti-inflammatory drugs

Look for coexisting conditions that could cause or contribute to fatigue

early afternoon. Modafinil is effective at 100 to 400 mg each morning. Modafinil can reduce the efficacy of hormonal contraception therapies[33]; therefore, before prescribing it to a woman of childbearing age, contraceptive choices should be reviewed.

Pemoline (Cylert) and methylphenidate (Ritalin), both previously used to treat MS fatigue, are now considered third-line agents.

Open-label studies have suggested that 4-aminopyridine[34,35] and fluoxetine (Prozac)[35] may be beneficial in MS-related fatigue.

PAIN SYNDROMES

MS patients experience both acute and chronic pain. Pain can be divided into four main categories: neuralgia, pain from meningeal irritation, dysesthesias (sensory pain), and skeletal muscle pain (TABLE 3).

Neuralgia is pain along the course of a nerve. There are several options for treating neuralgia, and if one of them fails the others should be tried sequentially. Gabapentin is a common first-line agent. Carbamazepine (Tegretol) has been both added to gabapentin and used as monotherapy. Other medications to consider are amitriptyline (Elavil) and other tricyclics, oxcarbazepine (Trileptal),[36] or baclofen.

Pain from meningeal irritation is due to inflammation. Pain of this type often improves with high doses of intravenous steroids aimed at treating the inflammation directly.

Dysesthesias are common and often difficult to treat. Treatment options are similar to those for neuralgia. Finding a balance between efficacy and side effect tolerability is often a process of trial and error.

Skeletal muscle pain can be the result of spasticity, abnormal gait, poor posture, or weakness. Commonly affected areas are the shoulders, hip, knees, and lower back.

Patients should be evaluated by physical and occupational therapists for weakness, joint mobility, and gait abnormalities. Some patients benefit from exercises to strengthen areas that in turn stabilize or support weaker areas, and others benefit from support devices. Nonsteroidal anti-inflammatory drugs can be used in conjunction with therapy to manage ongoing discomfort.

ATAXIA AND TREMOR

Cerebellar symptoms occur in an estimated 75% of MS patients. Incoordination and tremor can be extremely disabling, and response to therapy is generally poor.

Potential medications for tremor include clonazepam (Klonopin), gabapentin (Neurontin), primidone (Mysoline), and intravenous or oral odansetron (Zofran). Some patients benefit from adaptive equipment and gait training provided by occupational and physical therapists.

A small number of patients may benefit from surgery, either stereotaxic ablation of the ventrolateral thalamic nucleus or implantation of a deep-brain stimulator.[37,38] A risk of surgical treatment includes contralateral weakness, which may increase overall disability.

VERTIGO

Vertigo is defined as the false perception of movement in the self, the environment, or both. Traditionally, vertigo in MS patients was attributed to new inflammatory lesions involving the vestibular nuclei or root entry zone of cranial nerve VIII.

In a recent review of 1,153 MS patients, benign paroxysmal positional vertigo (BPPV) was the cause of new-onset vertigo in 52% of cases.[39] All cases of BPPV were successfully treated with either the Eply or Semont repositioning treatment.[39] Evaluation of new-onset vertigo in MS patients should begin with consideration of BPPV, which may respond to rehabilitative measures.[40]

Vertigo in MS patients can also be due to a concurrent migraine disorder. Migraine-related vertigo can be difficult to treat; anecdotally, some patients have benefitted from zonisamide (Zonegran), 100 to 200 mg at bedtime. This medication should not be given to patients with a sulfa allergy.

Centrally mediated vertigo resulting from an MS lesion may resolve following high-dose intravenous steroids for acute inflammation. Patients with residual vertigo or associated imbalance may benefit from rehabilitative gait training.

Nonvertiginous dizziness is also common in MS patients. Often there is more than one cause, including medication side effects, dehydration, and orthostatic intolerance. Treatment depends on the etiology, but meclizine (Antivert) and benzodiazepines may be of use.

COGNITIVE IMPAIRMENT

Cognitive impairment occurs in approximately 50% of MS patients, sometimes early in the disease course.[41] Patients have particular difficulty with speed of information processing, learning, and recall of new information.[42]

Cognitive impairment should be considered in patients who are struggling in their social or vocational activities. Formal neuropsychological testing is needed to accurately diagnose and characterize cognitive impairment. Formal testing also aids in identifying a patient's strengths and weaknesses, which helps to direct compensatory strategies that minimize the impact of deficits on daily function.

MOOD DISORDERS

The prevalence of depression in MS patients has been estimated to be 27% to 50%. In an alarming study of 140 MS patients, 36% had experienced major depression, 29% had expressed suicidal intent, and 6% had attempted suicide.[43] Other work has suggested that MS patients have a risk of suicide 7.5 times that of the general population.[44]

MS has no effect on fertility or pregnancy, but therapies may lead to infertility

The overall rate of depression in MS patients is higher than in most other chronic neurologic diseases, supporting the idea that some organic mechanism contributes to depression in MS. Studies have suggested that depression is secondary to the location and the degree of the demyelination itself.[45,46]

MS commonly affects young people in the prime of their lives, and its course is unpredictable, with no reliable prognostic factors to reassure patients about expected outcomes. These realities likely contribute to the higher prevalence of depression among MS patients, which is in some cases reactive. Depression can be present at the time of diagnosis, but may occur at any time in the disease course.

In view of the high prevalence and serious consequences of depression in MS, it is important for clinicians to ask patients about depressive symptoms. Treatment of MS-relat-

TABLE 4

Vaccinations and multiple sclerosis

VACCINATION	RECOMMENDATIONS	CONSIDERATIONS
Age-appropriate or clinically appropriate (eg, tetanus or pneumonia vaccine*)	Per general CDC criteria for particular vaccinations	Do not give during serious MS relapse; defer for 4–6 weeks after onset Do not give in patients who have received immune globulin (IvIg) in the previous 3 months
Live-attenuated vaccines	Per general CDC criteria for particular vaccinations	Do not give to patients receiving immunosuppressant therapies: corticosteroids, mitoxantrone, azathioprine, methotrexate, or cyclophosphamide Interferon and glatiramer acetate (Copaxone) are not immunosuppressants and are safe for these vaccinations
Influenza vaccination	Per general CDC criteria: Adults older than 50 years Residents of long-term care facilities People with chronic diseases (eg, diabetes) Pregnant women who will be in the 2nd or 3rd trimester during flu season People who can infect patients at high risk	No special considerations needed
Smallpox vaccination	Only MS patients who have been directly exposed to smallpox virus	Do not give to unexposed MS patients Do not give to unexposed family members of MS patients

CDC: US Centers for Disease Control and Prevention; MS: multiple sclerosis
*No specific studies have looked at the safety of pneumonia vaccine in MS patients. CDC guidelines are generallly recommended to guide use.

ed depression is similar to that of other forms of depression and includes both psychotherapy and pharmacotherapy.

Other affective disorders, such as bipolar disorder, anxiety, euphoria, or emotional incontinence are less common but can also occur in MS patients.[47] Lithium, valproic acid (Depakote), or carbamazepine may be useful in treating bipolar disorders. Serotonin reuptake inhibitors with indications for anxiety (eg, paroxetine [Paxil] or escitalopram [Lexapro]) are useful in treating isolated anxiety. Euphoria can be difficult to treat and is often disconcerting to others. Education about euphoria and emotional lability can help to alleviate discomfort. In some cases, low-dose amitriptyline is effective for "emotional incontinence."[48]

GENERAL MEDICAL ISSUES IN MS PATIENTS

Pregnancy and fertility

MS predominately affects women and commonly presents during the childbearing years.[49] Woman often have questions about fertility and pregnancy following the diagnosis of MS.

MS has no effect on fertility or the course of pregnancy; it causes no increased risk of toxemia, miscarriage, or fetal abnormalities.[50] However, although MS itself does not affect fertility, the immunosuppressive therapies used to treat it can lead to infertility.

In optimal circumstances, patients should discontinue MS therapies before attempting to conceive. In cases of unplanned pregnancy,

MS therapies should be stopped immediately.[51] Limited data suggest that interferon increases the rate of miscarriage in MS patients. There is, however, no apparent increased incidence of birth abnormalities in full-term infants.[51] Concurrent symptomatic medications should also be reviewed for safety during pregnancy and breastfeeding.

MS is typically quiescent during pregnancy, particularly during the third trimester.[52,53] Relapses during pregnancy are usually mild.[54] Treatment decisions for individual relapses should be made in conjunction with an obstetrician to minimize risk to the fetus.

Postpartum patients are at an increased risk for relapse, especially during the first 3 months.[52,53] An estimated 20% to 40% of patients experience relapse or worsening disability in the postpartum period.[55] Breastfeeding does not appear to be protective, and women with active disease may decide to forgo breastfeeding and restart MS therapies.[53]

Vaccinations

People with MS should receive all age-appropriate vaccinations.

Vaccinations do not appear to be associated with the development of MS.[56] Despite concern in the general public, a comprehensive study has refuted any association between hepatitis B vaccination and the development of MS.[57] Studies have also documented the safety of vaccinations in MS patients.[58]

Other things to consider about vaccination are outlined in **TABLE 4**. Clinical practice guidelines for vaccinations in MS patients were published in 2001 and are a useful reference for clinicians.[59]

Osteoporosis

People with MS have a higher risk of fractures and lower bone mineral density than their age-matched and sex-matched peers.[60]

Limited mobility and weight-bearing—not exposure to corticosteroids—may be the cause.[61] Further, there is evidence that the use of a single course of steroids in MS patients increases mobility, which in turn increases bone mineral density in some patients.[61] Chronic exposure to corticosteroids in intravenous pulse regimens does not appear to cause more loss of bone mass compared with oral prednisone in patients with rheumatoid arthritis.[62] Similarly, MS patients receiving high-dose pulse steroids are not at increased risk of osteoporosis.[63]

MS patients with steroid exposure should have bone density monitoring with dual energy x-ray absorptiometry every 12 months; those without steroid exposure should have monitoring every 24 months. All MS patients should take daily vitamin D and calcium supplements.

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