

MS Consult

Fighting Fatigue in MS

Q Why do my patients with multiple sclerosis experience so much fatigue, and what can I do to help them?

Fatigue is an extremely common symptom of multiple sclerosis (MS) and one of the most disabling complications of the disease.¹ More than 75% of patients with MS experience fatigue, which can worsen motor function, sleep quality, mood, and overall quality of life.^{1,2} Fatigue can also adversely affect employment; among patients with MS who reduce their work hours from full- to part-time, 90% do so because of fatigue.³

The Multiple Sclerosis Clinical Council Guidelines define MS-related fatigue as a “significant lack of physical and/or mental energy that is perceived by the individual or caretaker to interfere with usual or desired activity.”⁴ Described as “overwhelming,” this type of fatigue is generally unrelated to activity level.⁵ It differs from fatigue experienced by patients without MS in that it generally comes on suddenly, impairs functioning, and prevents patients from attending to responsibilities.^{1,5,6}

Patients with MS may have primary or secondary causes of fatigue. *Primary fatigue* is believed to result from the disease itself. Although it is not well understood, one hypothesis suggests that it is caused by an immune-related process involving inflammation and immune-mediated neurodegeneration.⁷ Another theory relates it to impaired nerve conduction.⁸

Secondary fatigue is unrelated to MS itself, and it is often treatable. Common causes include anemia, infection, or insomnia (see Table 1, page 24).^{9,10} These possibilities should be considered and ruled out in all patients with MS who complain of fatigue. A com-

prehensive history, exam, and evaluation performed by the clinician may help identify alternative reasons for fatigue.

Once any secondary causes have been addressed, primary fatigue should be evaluated and managed. One method for assessing the severity of fatigue and its impact on functional disability is to discuss it with the patient. The Fatigue Severity Scale can also be used as a measure; this self-assessment is quick, easy, and can be downloaded for free at www.saintalphonsus.org/documents/boise/sleep-Fatigue-Severity-Scale.pdf.¹¹

Identifying potential triggers of fatigue can help clinicians develop appropriate interventions. Heat intolerance is common and can precipitate or contribute to fatigue; cooling equipment can be a helpful solution (see Figure). Urinary tract infections frequently cause fatigue and can exacerbate many symptoms of MS. Bladder dysfunction and subsequent nocturnal waking may contribute to the problem. Psychological

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FIGURE
Cooling Equipment



Courtesy: POLAR Products

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TABLE 1
Secondary Causes of Fatigue

Anemia	Malignancies
Cardiac/pulmonary causes	Medications
Endocrinopathies	Mood disturbance
Infections	Poor diet/malnutrition
Lack of exercise	Sleep disturbances

Sources: Ponka. *Can Fam Physician*. 2007⁹; Rosenthal. *Am Fam Physician*. 2008.¹⁰

stress is another common trigger; managing it can reduce fatigue.^{1,12} Screening for depression in patients with MS who complain of fatigue is imperative; if diagnosed, it must be addressed as the first line of treatment.¹

Other clinician-initiated intervention strategies include exercise, therapy, and medication. Modafinil is frequently prescribed for MS fatigue; small trials have demonstrated dramatic improvements with its use.¹³ Interestingly, aspirin has been shown to reduce fatigue in randomized controlled trials.¹⁴ This may be due to its indirect effects on neuroendocrine and autonomic responses, both of which are involved in the perception of fatigue.¹⁴ Additional interventions are listed in Table 2. As always, before prescribing any new medication, ensure that it is appropriate and that the patient's other medical providers agree to the plan.

Counsel patients by emphasizing the importance of good sleep hygiene, a healthy diet, and avoidance of unhealthy habits. Taking an interdisciplinary approach can help patients with MS receive the best possible health care. While you may not be treating your patient's disease, you will be managing much of his or her health care; treating the underlying causes of fatigue can significantly improve quality of life. —SA

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TABLE 2
Fatigue Management Strategies

Cognitive behavioral therapy	Strategies to decrease symptoms
Energy conservation	Rest, delegate
Exercise	Aerobic exercise, yoga
Medications	Modafinil, amantadine, methylphenidate, aspirin
Occupational therapy	Streamline tasks
Physical therapy	Exercise regimens
Stress management	Relaxation techniques

Sources: Krupp. *Expert Rev Neurother*. 2010¹; Saint Alphonse¹¹; Motl. *Mult Scler*. 2005¹²; Lange. *J Neurol*. 2009.¹³

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To Vaccinate, or Not, in Patients With MS

Q Are vaccines safe for patients with multiple sclerosis?

Vaccines are an important component of general disease prevention and are especially useful for patients with chronic illnesses, such as MS, who may be at elevated risk due to disability or medications that alter the immune system. Currently, there are many disease-modifying therapies that attempt to reduce relapses and impact the immune system, MRI activity, and disability. But is it safe for patients with MS to receive vaccines, given the multitude of studies suggesting that infections may increase relapse rate?

In 2002, the American Academy of Neurology published a summary of evidence and recommendations to provide guidance for practitioners.¹ The data showed an increased risk for MS relapse during the weeks following infection.^{2,3} Therefore, preventing infections is beneficial for patients with MS. An analysis of studies in patients with MS who were vaccinated with inactivated vaccines (influenza, hepatitis B, tetanus) found sufficient evidence to support this practice. Studies of patients with MS who were given attenuated vaccines did not find enough evidence to support or reject these vaccines, except in the case of varicella. A study with sufficient follow-up concluded that varicella vaccination was safe for patients with MS who were not immunosuppressed. As a result of this effort, the MS Council for Clinical Practice Guidelines recommends that patients and health care providers follow the CDC's indications for immunizations (www.cdc.gov/vaccines/schedules/hcp/adult.html).¹

On the other hand, administration of the live-virus yellow fever vaccine in patients with clinically relapsing MS was correlated with an increased risk for disease progression in one study.⁴ The researchers followed disease progression, measured by relapses and MRI activity, in patients taking glatiramer acetate and interferon β . Relapse rates reached 8.57 within three months af-

ter vaccination, compared to a rate of 0.67 the year prior to vaccine administration. Additionally, significant changes were seen on MRI; new or enlarging T2-weighted lesions and gadolinium-enhancing lesions were observed at three months, compared to 12 months prior and nine months after.⁴ Therefore, the researchers concluded that patients with MS traveling to endemic yellow fever areas should be cautioned regarding the risk for disease progression with vaccination, versus the risk for exposure to yellow fever.

Over the past decade, as newer therapies with different mechanisms of action have become available, concern has risen that patients may not respond to immunizations or may have a higher risk for infection after vaccination. For that reason, several studies have evaluated the ability of patients with MS to mount a normal antibody and cellular immune response after vaccine administration. In 2016, a study by Lin et al determined that patients who received daclizumab were able to mount a normal response after influenza vaccination.⁵

By contrast, Kappos et al, in a 2015 study, found that patients receiving fingolimod had lower response rates to influenza and tetanus booster vaccines than patients who took a placebo.⁶ Similarly, in a 2014 study, Olberg et al examined patients receiving interferon β , glatiramer acetate, natalizumab, and mitoxantrone after receiving influenza and H1N1 vaccinations. The researchers found that those treated with any therapy other than interferon β had a reduced rate of response and should therefore be considered for vaccine response analysis.⁷ Bar-Or et al also published data on response rates of patients treated with teriflunomide (7 mg or 14 mg) or interferon β ; rates were reduced with 14-mg teriflunomide compared to the other treatments—but most patients exhibited seroprotection regardless.⁸ Studying vaccine efficacy in 2013, McCarthy et al



International Organization of Multiple Sclerosis Nurses (IOMSN) is the first and

only international organization focusing solely on the needs and goals of nurses involved with the care, education, research, and advocacy for multiple sclerosis and related autoimmune disorders of the central nervous system. For more information on IOMSN, visit www.iomsn.org.

evaluated serum antibodies against common viruses before and after treatment with alemtuzumab and found that antibodies remained detectable six months post-alemtuzumab.⁹

In summary, most specialists agree that vaccines are helpful for patients with MS. However, due to the varied response rates among disease-modifying therapies and the correlation between infection and increased relapse rates, special care should be taken when treating this population. Generally, inactivated vaccines are safe, but seroprotection should be established to determine if a booster is necessary. Attenuated vaccines are generally safe for patients who are not immunosuppressed and can reduce the risk for infection if given prior to immunosuppression. After immunosuppression, attenuated vaccines should not be given until immune recovery has been established. —PP

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