Multiple Sclerosis: What Triggers Exacerbations?

July 25, 2012

Common MS exacerbation triggers: infection, vaccination, stress, smoking, vitamin deficiency, or environmental changes.

An exacerbation (relapse, attack, or flare-up) of multiple sclerosis (MS) is indicated by a new sign or symptom that lasts more than 24 hours, worsening of an old symptom that lasts more than 24 hours, or a repeated paroxysmal phenomenon (eg, bouts of vertigo or trigeminal neuralgia). Surgery, general and epidural anesthesia, and trauma have not been found to be associated with exacerbations.

Potential triggers of an exacerbation include:

**Infection.** Viral, bacterial, and—to a lesser degree—fungal infections (eg, those involving the upper respiratory tract or urinary tract) are common precipitants. There is some evidence that organisms causing an infection or the immune response to different antigens may increase the risk of an exacerbation. The common assumption is that MS is an immune-mediated disease and infections trigger an immune response and by doing that the immune system becomes increasingly activated, which might elicit a relapse. Therefore, it is important to minimize the risk of infection; for example, it is recommended that patients with MS receive an influenza vaccination every year and that they maintain vigilant bladder hygiene. In addition, patients with MS may have a pseudo-relapse in the presence of an infection and treating the infection may reverse the symptoms.

**Vaccinations.** There is no clear relationship between vaccines and relapse, but there is a potential association. For example, vaccines against influenza, tetanus, and DTP have not been linked with exacerbation, but others do trigger MS relapse.

Vaccines for yellow fever and for shingles are usually not recommended for patients with MS but warrant a thorough discussion between patients and care teams. These vaccines are “live,” or attenuated, vaccines that require higher immune response as compared with “dead” (ready made) vaccines such as flu vaccine (the shot and not the flu mist) or pneumovax. If a live vaccine is required, however, such as one against rabies, it should be given and the patient monitored closely for potential neurologic changes. The decision to use a specific vaccine will of necessity be based on a risk-benefit calculation made by the patient and the partners in his or her care.

**Stress.** The belief that stress causes exacerbations of MS is widespread among patients; some clinicians also believe that stress is a trigger. However, a specific association between stress and MS exacerbations is unclear. Stress may have different effects on different patients, and most MS specialists recognize the impact of stressful events on MS symptoms intermittently throughout a patient’s life. A meta-analysis of 14 studies found a modest but clinically meaningful association between stressful life events and MS relapses.

**Postpartum period.** Evidence from a few studies shows that there is an increased risk of MS exacerbation in the postpartum period, although the reason for this is not clear. Hormonal effects on the immune system postdelivery or immune system changes may be the cause. There is some evidence that exclusive breast-feeding may decrease the risk of an exacerbation in the first trimester postpartum.

Women who are at high risk for exacerbations should begin MS treatment immediately after delivery. The medications for MS are not recommended during breast-feeding; however, for women at high risk for relapse, some clinicians approve the use of glatiramer acetate (Copaxone) because it is designated as pregnancy category B, whereas all other MS disease-modifying agents are classified as pregnancy category C. In general, the postpartum treatment plan should be discussed with patients and their partners, the patient’s obstetrician/pediatrician, and the MS team.
**Fertility drugs/treatments.** Some fertility treatments may increase the risk of MS exacerbations, although there are no data or evidence on the types and durations of these treatments. For women with MS who are considering fertility treatments, a discussion on the associated and potential risks for MS exacerbations is important and should be an integral part of their overall care.

**Vitamin D deficiency.** There is an association between vitamin D deficiency and an increased risk of MS exacerbations. Therefore, the serum level of 25-hydroxyvitamin D3 should be monitored in patients with MS, and supplements should be administered if needed. Levels should be checked more frequently during the winter months because sun exposure affects the body’s ability to synthesize vitamin D.

**Dietary supplements.** There are some data to suggest that omega-3 supplementation may reduce the risk of relapses, but there is no controlled evidence. Patients with MS are advised to eat a balanced diet and discuss the use of dietary supplements with their primary care physician or their MS team.

**Smoking.** Cigarettes have been linked with progression of MS, but there are no data that indicate a direct relationship between smoking and risk of exacerbations. However, patients with MS are advised to quit smoking because of the multiple ill effects of nicotine on the body.

**Seasonal changes.** The seasons may have an effect on the risk of MS exacerbations. The frequency of exacerbations increases in early spring and summer. Also, the frequency differs from year to year. It is thought that the increased frequency of MS relapses in different seasons may be linked to infections or toxins and may not be related to sun exposure or vitamin D deficiency.

**References**

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