

Identifying and Managing MS Relapse

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Multiple sclerosis (MS) is a chronic, autoimmune-mediated disorder of the central nervous system that affects more than 40,000 people in the United States. About 85% of cases are categorized as *relapsing remitting multiple sclerosis* (RRMS), based on the clinical and radiographic pattern of focal demyelination in different regions of the brain and spinal cord over time. Though not fully understood, the pathophysiology of RRMS involves axonal degeneration and inflammatory demyelination; the latter is considered a relapse in patients with an established MS diagnosis.

OVERVIEW

MS relapse can have a significant impact on patients' short- and long-term function, quality of life, and finances. Relapse may be identified via

- New neurologic symptoms reported by the patient
- New neurologic findings on physical examination
- New radiographic findings on contrast-enhanced MRI of the central nervous system, or
- Abnormal results of cerebrospinal fluid analysis.

Patient-reported symptoms and abnormal signs identified on physical exam should correspond with the area of the central nervous system affected. In some cases, patients may have radiographic evidence of relapse without symptoms or signs.

It is essential for health care providers to identify relapse, as it is an important marker of disease activity that may warrant treatment—particularly if symptoms are impact-

ing function or if there is optic neuritis. MS relapse is also an indicator of suboptimal response to disease-modifying therapies.

Treatment of relapse is one component of RRMS management, which also includes symptom management and use of disease-modifying therapy to reduce risk for disease activity and decline in function.

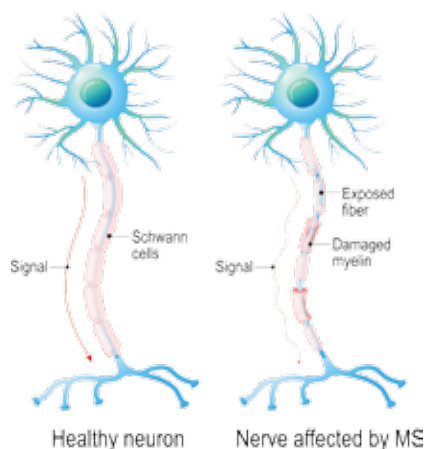
DIAGNOSING RELAPSE

Because risk for MS relapse cannot be predicted, both patients and providers need to have a high index of suspicion in the setting of new neurologic symptoms or decline in function. Relapse should be considered when these symptoms last longer than 24 hours in the absence of fever or infection. The clinical features of relapse should have corresponding radiographic evidence of active demyelination on contrast-enhanced MRI.

A *pseudo-relapse* is characterized by new or worsening neurologic symptoms lasting longer than 24 hours with concurrent fever, infection, or other metabolic derangement. Pseudo-relapse does *not* show radiographic evidence of active demyelination on contrast-enhanced MRI.

Aggravation of longstanding neurologic symptoms is not considered a relapse, as no new radiographic evidence of disease progression will be seen on MRI. Factors that may contribute to aggravation of established symptoms include an increase in core body temperature, sleep deprivation, and psychosocial stress.

When a patient with suspected or diagnosed RRMS presents with new neurologic



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symptoms of more than 24 hours' duration, the first step is to conduct a physical exam to assess for objective evidence of neurologic deficits and signs of infection, including fever. The provider should also order select laboratory testing—including a complete blood cell count and urinalysis with culture—to exclude infection. In certain cases, contrast-enhanced MRI of the brain and/or spine may be ordered; however, this may delay treatment initiation if the study cannot be promptly scheduled.

Evaluation and management should involve communication, if not face-to-face consultation, with the patient's neurology provider who is responsible for MS management.

IMMEDIATE MANAGEMENT

Acute relapses are managed with anti-inflammatory agents. For some patients, treatment may provide symptomatic relief, shorten the recovery phase, and improve motor function. Long-term benefits have not been demonstrated, except in patients with optic neuritis.

Firstline therapy for MS relapse is high-dose corticosteroids, which can be administered at home, at an ambulatory infusion center, or (in some cases) in a hospital setting. The preferred regimen is methylprednisolone (1 g IV for 3-5 d), with or without prednisone taper. Another option is dexamethasone (80 mg bid for 3-5 d), with or without prednisone taper.¹⁻³

Common adverse effects of corticosteroids include headache, emotional lability, insomnia, glucose intolerance, hypertension, dyspepsia, and exacerbation of psychiatric conditions; drug interactions should also be considered. Patients with diabetes may need to be admitted to the hospital for

glycemic monitoring and control.

High-dose corticosteroids are associated with a rare, non-dose-dependent risk for aseptic femoral necrosis. For patients who are refractory to or not candidates for corticosteroids, adrenocorticotropic hormone (ACTH) gel (80 U/d IM or subQ daily for 10 d) is an option. This medication may be better tolerated, although it is much more expensive than corticosteroids. Plasmapheresis and IV immunoglobulin are also options for patients with refractory symptoms or contraindications to recommended therapies.¹⁻³

ONGOING MANAGEMENT

Once a treatment plan is initiated, providers should carefully follow the patient's response in terms of adverse effects, symptom improvement, and functional recovery. Those with refractory symptoms may need additional doses of the initial therapy or an alternative therapy.

The relapse recovery period may last several months and be complete or incomplete, so providers may also need to manage neurologic symptoms and functional deficits (with pharmacologic and/or non-pharmacologic options). Patients who have had a relapse should also meet with their neurology provider to discuss their disease-modifying therapy plan, since relapse indicates a suboptimal response to current therapy. **CR**

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