

Cross Currents | in multiple sclerosis

MS relapse: to treat or not to treat

by Dr. Sarah A. Morrow

Managing multiple sclerosis (MS) takes a three-pronged approach: treatment strategies to modify the long-term course of the disease, symptom control and relapse management.

MS is a leading cause of nontraumatic disability for young adults worldwide¹ and it is especially common in Canada — 240 Canadians out of 100,000 live with this chronic neurological disease². Yet, a survey in Southwestern Ontario found that although 92.2% of general practitioners (GPs) treated MS patients, only 43.1% of respondents correctly identified the appropriate treatment, and a mere 16% identified the appropriate dose³. The situation is bleaker still when it comes to managing MS relapses. Specialized care for relapses may be rendered inaccessible to some patients since MS Clinics in Canada are often located at tertiary care centres. Consequently, the task of treating relapses often falls to GPs at community clinics or in emergency departments. However, GPs are often unfamiliar with the approach to a potential relapse in MS patients. To close the gap in MS patient care, the following guidelines and treatment algorithm were developed to help GPs navigate through the diagnosis and treatment of relapses.



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The Rundown on Relapses

Of the different forms of MS, 85% of cases present with the relapsing-remitting (RRMS) type⁴, characterized by periods of relapse with possible residual deficit separated in time by quiescent periods. Fifteen percent of cases are slowly progressive from the onset (primary progressive, PPMS), and 50% of RRMS will evolve into a progressive form (secondary progressive, SPMS). Relapses are most prevalent in RRMS although many with a progressive course can also have super-imposed relapses^{4,5}.

A relapse is defined as a new neurological symptom lasting for more than 24 hours *or* worsening of neurological symptoms that have been stable for at least 30 days^{6,7}. Onset of these symptoms may either be acute or subacute. The most common presentations are optic neuritis, brainstem syndromes such as ocular motor syndromes, and acute partial transverse myelitis.

Pseudo-relapse: Eliminate the Possibility

Although the clinical definition is helpful, distinguishing between what is a relapse and what is not can be tricky. In order to diagnose a relapse, it is first necessary to rule out a “pseudo-relapse.” A pseudo-relapse is a neurological worsening caused by an increase in body temperature that is sparked by an underlying infection — which may not yet be symptomatic, an increase in ambient temperature due to a hot shower or a hot/humid environment, or physical or psychological stress. Typically, once the underlying cause of the pseudo-relapse is eliminated, symptoms will resolve.

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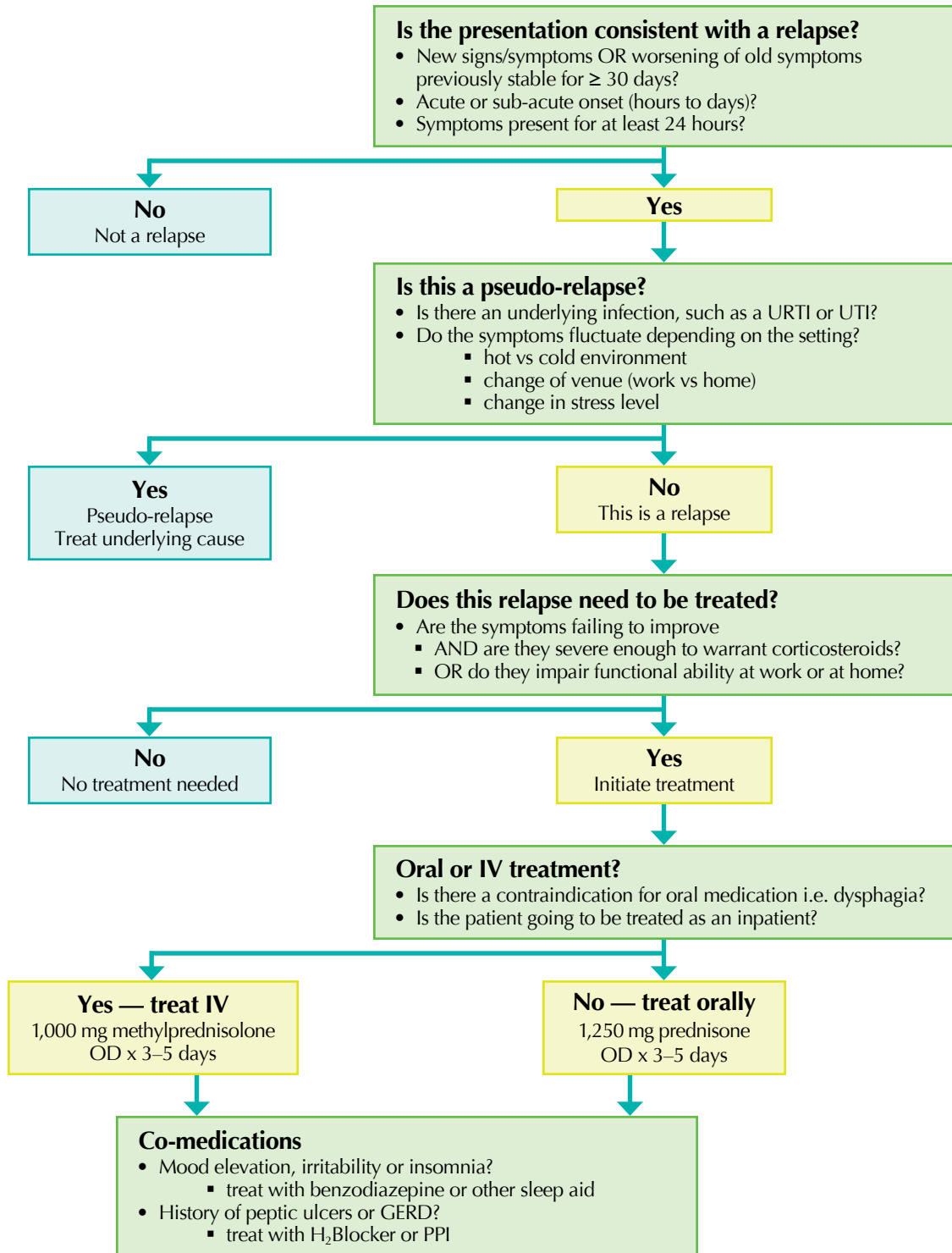
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When to treat MS relapse



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Know When to Treat

The current standard of care for MS relapses is high-dose multi-day corticosteroid administration: 3 to 5 days of 1,000 mg of IV prednisolone or 1,250 mg of oral prednisone. Both routes of administration are comparable in terms of efficacy^{8,9} and are used equally in Canada¹⁰. Debate is ongoing regarding the need for a corticosteroid taper — most studies support its use in patients who have had a rebound of relapse symptoms following the termination of treatment^{11,12}. That said, not all relapses need to be treated — neurologists report treating approximately one quarter of relapses¹³. Ultimately, the side effects of corticosteroid use must be weighed against the benefits. A short course of treatment commonly causes insomnia and elevated mood, gastrointestinal effects in those with a history of GI disease, and transient hyperglycemia and hypertension in MS patients with a history of glucose intolerance or hypertension, respectively^{2,14,15}. Long-term side effects, such as bone demineralization, are only seen in MS patients given multiple corticosteroid pulses (3 or more) per year^{5,14}.

Essentially, corticosteroids decrease the duration of the relapse with no effect on long-term outcomes and only treatment of more severe relapses demonstrated any benefit^{16,17}. There are no specific guidelines but, generally, relapses that are multi-focal, severe and/or causing disability are treated. Adverse event treat-

Recommendations on MS Relapse

The decision to treat an MS relapse rests with both the patient and the treating physician and should take the following key factors into consideration:

- The risks and benefits of high-dose corticosteroids as well as relapse severity
- Pseudo-relapses should be ruled out prior to treatment, particularly urinary tract infection — a common occurrence in MS that is often asymptomatic in its early stages
- Treatment with 1,000 mg of IV prednisolone or 1,250 mg of oral prednisone for 3 to 5 days is recommended, with the management of adverse events decided on an individual basis
- Patients should be referred to an MS specialist if there is any doubt as to the nature of the new symptoms, or if there is a higher than expected frequency of relapses.

ment using benzodiazepines, sleep-aids or gastric protectors can be used in those with a significant medical history or a previous reaction to corticosteroids. In the case of an unusual relapse or 2 or more relapses a year, re-referral to a neurologist is recommended. ■

References

1. Rotstein Z, Hazan R, Barak Y, et al. Perspectives in multiple sclerosis health care: special focus on the costs of multiple sclerosis. *Autoimmun Rev* 2006;5:511-516.
2. Beck CA, Metz LM, Svenson LW, Patten SB. Regional variation of multiple sclerosis prevalence in Canada. *Mult Scler* 2005;11:516-519.
3. Morrow SA, Kremenchutzky M. Familiarity of family physicians with relapse evaluation and treatment in multiple sclerosis patients. In press, *International Journal of MS Care*.
4. Lublin FD, Reingold SC. Defining the clinical course of multiple sclerosis: results of an international survey. National Multiple Sclerosis Society (USA) Advisory Committee on Clinical Trials of New Agents in Multiple Sclerosis. *Neurology* 1996;46:907-911.
5. Sellebjerg F, Barnes D, Filippini G, et al. EFNS guideline on treatment of multiple sclerosis relapses: report of an EFNS task force on treatment of multiple sclerosis relapses. *Eur J Neurol* 2005;12:939-946.
6. Polman CH, Reingold SC, Edan G, et al. Diagnostic criteria for multiple sclerosis: 2005 revisions to the "McDonald Criteria." *Annals of Neurology* 2005;58:840-846.
7. Thrower BW. Relapse management in multiple sclerosis. *Neurologist* 2009;15(1):1-5.
8. Morrow SA, Stoian CA, Dmitrovic J, Chan SC, Metz LM. The bioavailability of IV methylprednisolone and oral prednisone in multiple sclerosis. *Neurology* 2004;63:1079-1080.
9. Burton JM, O'Connor PW, Hohol M, Beyene J. Oral versus intravenous steroids for treatment of relapses in multiple sclerosis. *Cochrane Database Syst Rev* 2009;CD006921.
10. Morrow SA, Kremenchutzky M, Metz LM. High dose oral corticosteroids are commonly used to treat relapses in Canadian MS clinics. *Canadian Journal of Neurological Sciences* 2009;36(2):213-5.
11. Perumal JS, Caon C, Hreha S, et al. Oral prednisone taper following intravenous steroids fails to improve disability or recovery from relapses in multiple sclerosis. *Eur J Neurol* 2008;15:677-680.
12. Levic Z, Micic D, Nikolic J, et al. Short-term high dose steroid therapy does not affect the hypothalamic-pituitary-adrenal axis in relapsing multiple sclerosis patients. Clinical assessment by the insulin tolerance test. *J Endocrinol Invest* 1996;19:30-34.
13. Tremlett HL, Luscombe DK, Wiles CM. Use of corticosteroids in multiple sclerosis by consultant neurologists in the United Kingdom. *J Neurol Neurosurg Psychiatry* 1998;65:362-365.
14. Leary SM, Porter B, Thompson AJ. Multiple sclerosis: diagnosis and the management of acute relapses. *Postgrad Med J* 2005;81:302-308.
15. Metz LM, Sabuda D, Hilsden RJ, Enns R, Meddings JB. Gastric tolerance of high-dose pulse oral prednisone in multiple sclerosis. *Neurology* 1999;53:2093-2096.
16. Nos C, Sastre-Garriga J, Borrás C, Rio J, Tintore M, Montalban X. Clinical impact of intravenous methylprednisolone in attacks of multiple sclerosis. *Mult Scler* 2004;10:413-416.
17. Beck RW, Smith CH, Gal RL, et al. Neurologic impairment 10 years after optic neuritis. *Archives of Neurology* 2004;61:1386-1389.

