TABLE 120-2 DIFFERENTIAL DIAGNOSIS OF DEMYELINATING DISEASES

DISEASE CATEGORY*	EXAMPLES OF DISORDERS†
Immune-mediated /autoimmune	Multiple sclerosis, neuromyelitis optica (NMO), acute demyelinating encephalomyelitis (ADEM), idiopathic optic neuritis, CRION, idiopathic transverse myelitis, Behçet's disease
Infectious	Progressive multifocal leukoencephalopathy (PML), HTLV-I, HIV, CNS abscess, Lyme disease, Whipple disease, neurosyphilis
Metabolic	Vitamin B12, vitamin E or copper deficiency, central pontine and extrapontine myelinolysis
Neurodegenerative	spinocerebellar ataxias, spine disease (e.g. compressive cervical spondylopathy)
Rheumatologic	Sarcoidosis, systemic lupus erythematosus, antiphospholipid antibody syndrome, Sjögren syndrome
Genetic Disorders	Adrenomyeloleukodystrophy/adrenomyeloneuropathy, hereditary spastic paraparesis, CADASIL, Leber's optic neuropathy, Perlizeus-Merzbacher, Wilson's disease
Neoplastic/Paraneoplastic	CNS Lymphoma, meningeal carcinomatosis, paraneoplastic CRMP-5 IgG, anti-Amphiphysin-1 Abs
Vascular	CNS vasculitis (e.g., giant cell arteritis, primary CNS vasculitis, etc.), spinal dural fistula, Susac syndrome
Iatrogenic	TNF inhibitors, CNS irradiation

*Several of the disorders listed could be placed in more than one category.
†This list is not comprehensive.

TABLE 120-3 SELECTED MS SYMPTOMS AND THEIR MANAGEMENT

SYMPTOM/SIGN	TREATMENT(S)
Stiffness/cramps/spasms/spasticity	baclofen, tizanidine (evidence level A)
Fatigue	Amantadine, modafanil, armodafinil, amphetamines
Depression	Selective serotonin reuptake inhibitors, cognitive behavior therapy
Pain/paresthesias/trigeminal neuralgia	gabapentin, carbamazepine, oxcarbazepine, pregabalin, amitriptyline
Gait impairment	Fampridine SR (Evidence level A)
Nystagmus, with visual impairment	Gabapentin
Dizziness/Vertigo	Meclizine, dimenhydrinate, benzodiazepines
Urinary urgency/incontinence/ neurogenic bladder	Oxybutynin, tolterodine, other anticholinergics, BOTOX injection
Impotence/erectile dysfunction	Sildenafil, tadalafil, testosterone supplementation if low
Tonic spasms	Phenytoin, carbamazepine

Relapses that alter function or cause pain are typically treated with corticosteroids. Severe relapses are usually managed with intravenous methylprednisolone at 500-1000 mg daily for 3 to 5 doses, followed by a short oral corticosteroid taper (usually prednisone). Oral corticosteroid tapering courses may be used for mild relapses. Blood pressure, serum electrolytes and glucose, and patient mood should be monitored during corticosteroid therapy. Based on the multi-center Optic Neuritis Treatment Trial (ONTT), this regimen will lead to more rapid recovery from the attack, but is unlikely to alter the degree of eventual recovery (evidence level A).

For severe relapses that do not respond to high-dose IV corticosteroids, a small randomized study showed that plasma exchange can be effective. Plasma exchange was followed by rapid functional improvement in over 40%, with early initiation of plasma exchange treatment the single factor most associated with significant improvement (level A). Subjects in this trial likely included patients with neuromyelitis optica (NMO) and acute disseminated encephalomyelitis (ADEM), in addition to MS.

Relapsing remitting MS (RRMS) is one of only a handful of chronic neurologic disorders with effective disease modifying therapies. The beta-interferons (BIFNs) and glatiramer acetate (GA) are FDA-approved for relapsing remitting MS (level A). The BIFNs and GA all reduced annualized relapse rate by about 30% in early pivotal studies. Most have also been shown to delay progression to definite MS in patients with clinically isolated syndrome who are at high risk for developing MS.

As of 2015, twelve different DMTs with seven different mechanisms of action are available for MS (Table 120-4). The approved agents have distinct and variable risk profiles. As there are currently no biomarkers that direct the choice of disease modifying therapies for an individual patient, selection of the disease modifying therapy for an individual is based on disease course and severity, patient comorbidities, and individual preferences.

Five BIFNs are approved for use in relapsing remitting MS and clinically isolated syndrome in the United States. They differ in dosage, side effects, and incidence of neutralizing antibody induction. Three BIFNs are identical to endogenous human BIFN-1a (poly ethyleneglycol has been covalently attached to one of the three for longer duration of effect); the other two are BIFN-1b, which differs by one amino acid. BIFNs are immunomodulators, though their exact mechanism of action in MS is not fully established. BIFN therapy is associated with increased circulating soluble VCAM-1, which could produce an effect similar to that of the monoclonal antibody natalizumab. Patients taking BIFNs require monitoring of hepatic transaminases and CBC; elevation of transaminases is uncommon, but may require dose adjustment or discontinuation. Common side effects include a "flu-like" feeling for several hours after a dose, which is usually improved by nonsteroidal anti-inflammatory medications or acetaminophen. BIFNs are given by injection and, as with any injectable drug, skin infection can occur. BIFNs are rated Pregnancy Category C; the BIFNs should be discontinued before conception.

Glatiramer acetate is given as a daily 20 mg subcutaneous injection, or 40 mg SQ three times per week. The drug is a random polymer of four amino acids that are abundant within myelin basic protein, a major protein in CNS myelin. It is considered immunomodulatory not immunosuppressive, although its mechanism of action is not fully understood. Glatiramer acetate has no known drug interactions, and laboratory monitoring is not needed. Side effects include injection site reactions and an uncommon transient tachycardia reaction that occurs soon after an injection. Lipoatrophy at injection sites may develop with prolonged use. Glatiramer acetate is pregnancy category B, and is