Multiple Sclerosis for the internist

You will not start the DMT · you will see the first attack, the pseudorelapse, and the immunosuppression complication

Fever first
pseudorelapse before relapse

⚠ THE WARD ERROR: PSEUDORELAPSE *commoner than a true relapse on a general medical service*

⚠ TREAT THE INFECTION, NOT THE MS

Infection (especially UTI), fever, heat and metabolic derangement transiently impair conduction in already-demyelinated axons (the Uhthoff phenomenon), unmasking or worsening OLD deficits **with no new inflammatory activity**. The deficits resolve as the temperature and infection settle. **Steroids here treat nothing and add hyperglycemia, worsened infection and delirium.** If deficits persist after the infection clears, then reassess for a true relapse.

ACUTE RELAPSE, WHEN IT IS REAL

High-dose methylprednisolone 1 g IV daily for 3-5 days (or equivalent high-dose oral, comparable efficacy). **Steroids speed recovery but do NOT change long-term disability** -so reserve them for functionally significant attacks and say the limitation plainly. **Plasma exchange** for severe steroid-refractory relapses. Mild sensory relapses may need no acute treatment at all.

RECOGNIZE THE ATTACKS

Optic neuritis: subacute monocular loss, **pain on eye movement**, red desaturation, RAPD, and a **normal-looking disc** because the lesion is retrobulbar. **Partial transverse myelitis** (asymmetric, under 3 segments). **Internuclear ophthalmoplegia in a young patient** is highly suggestive. **Lhermitte sign and Uhthoff phenomenon are conduction effects, not new attacks.**

DIAGNOSIS: SPACE AND TIME *and how one scan can prove both*

Requirement	Detail
Dissemination in SPACE	Lesions in **at least two of four characteristic regions: periventricular, cortical/juxtacortical, infratentorial, spinal cord**. Periventricular ovoid lesions perpendicular to the ventricles (Dawson fingers) are characteristic
Dissemination in TIME	A new lesion on follow-up, **OR simultaneous enhancing and non-enhancing lesions on a SINGLE scan** -since gadolinium enhancement lasts only weeks, that combination proves two different ages at one sitting. **CSF-specific oligoclonal bands can substitute** for dissemination in time
Imaging and LP	**MRI brain and spinal cord with and without gadolinium.** CSF typically shows normal or mildly raised protein with a mild lymphocytic pleocytosis. ⚠ **A MARKED pleocytosis argues AGAINST MS** -redirect toward infection, neurosarcoidosis or antibody-mediated disease rather than over-reading the LP as confirmatory
Exclude the mimics	**B12 and copper deficiency** (subacute combined degeneration), neurosarcoidosis, Behçet, SLE and Sjogren with CNS involvement, CNS lymphoma, small vessel ischemia in older patients, and **HIV, syphilis and Lyme**. Baseline: CBC, CMP, ESR/CRP, B12, TSH, ANA plus relevant serologies
The invisible symptoms	**Fatigue, cognitive slowing, depression, bladder dysfunction, spasticity and pain determine quality of life more than the relapse count** -and are the parts most often left unaddressed in a visit that focuses on imaging and drug choice. Ask about them explicitly

⚠ THE DISTINCTION THAT CAUSES HARM IF MISSED *this is not a labeling error, it is a treatment harm*

WHEN TO SEND AQP4 AND MOG ANTIBODIES

Longitudinally extensive transverse myelitis spanning three or more vertebral segments (MS causes partial, asymmetric lesions under 3 segments), **severe or bilateral optic neuritis, area postrema syndrome** (intractable hiccups, nausea and vomiting), or any severe first attack.

WHY IT MATTERS ENORMOUSLY

Neuromyelitis optica spectrum disorder (AQP4) and MOG antibody disease are treated differently, and several MS disease-modifying therapies -including interferon beta- make NMOSD substantially WORSE and can precipitate severe relapses. **Send the antibodies before any DMT** when the presentation is atypical.

DMT COMPLICATIONS THE INTERNIST WILL MEET *you inherit these patients years after someone else started the drug*

Agent class	What to watch for
⚠ **Anti-CD20** *ocrelizumab, rituximab*	**Hypogammaglobulinemia and infection risk, and hepatitis B reactivation -screen HBsAg AND anti-HBc before starting**, exactly as before rituximab for any other indication. Ocrelizumab is also the agent with evidence in **primary progressive** disease
⚠ **Natalizumab**	**Progressive multifocal leukoencephalopathy (PML)**, risk-stratified by **JC virus antibody status, prior immunosuppression, and duration beyond ~2 years**. Unlike a relapse, PML progresses **subacutely over weeks with cognitive and behavioral change**. **Any new neurologic change in a natalizumab patient is PML until disproven**: stop the drug, urgent MRI and CSF JC virus PCR, involve neurology
S1P modulators *fingolimod and relatives*	**First-dose bradycardia requiring monitoring, macular edema, lymphopenia, and rebound disease activity on abrupt discontinuation** -so never stop these casually
All DMTs	**Live vaccines are contraindicated on most**, so update vaccination status BEFORE starting. DMTs **reduce relapses and new lesions but do not repair existing damage**, which is why early treatment matters and delay is costly

DISEASE COURSES

Relapsing-remitting is the great majority at onset: discrete attacks with partial or complete recovery. **Secondary progressive** follows, with gradual disability accumulation. **Primary progressive** is a minority -progression from onset without distinct relapses, presenting later, often as a progressive myelopathy, and affecting men and women more equally. **Clinically isolated syndrome** is a first attack not yet meeting full criteria, where **MRI findings determine whether it is treated as MS** and early treatment delays conversion.

WHO GETS IT

Typically presents between **20 and 40**, more common in women, and rises in incidence with distance from the equator. Risk associations include **low vitamin D, smoking, adolescent obesity, and Epstein-Barr virus exposure**. Progressive forms respond poorly to immunomodulation, so management there shifts toward **symptom control and rehabilitation** rather than escalating immunosuppression.

SYMPTOM CARE: WHERE MOST QUALITY OF LIFE IS WON

- **Fatigue is the commonest and most disabling symptom.** Treat the reversible contributors first: depression, poor sleep, sleep apnea, anemia, thyroid disease, deconditioning. Exercise helps.
- ⚠ **Check a post-void residual BEFORE any anticholinergic for urgency.** Incomplete emptying mimics an overactive bladder, and an antimuscarinic then causes frank retention and recurrent UTIs -which cause the pseudorelapses.
- **Spasticity: look for the trigger** -infection, constipation, pressure ulcer or an ingrown toenail all worsen it- then baclofen or tizanidine with physiotherapy.
- **Smoking accelerates disability accumulation, so cessation is itself disease-modifying.** Add vitamin D, exercise, heat avoidance, screening for depression, and **bone health** given reduced mobility plus repeated steroid courses.

References: McDonald criteria for the diagnosis of multiple sclerosis · AAN practice guideline on disease-modifying therapies for adults with multiple sclerosis · international consensus diagnostic criteria for neuromyelitis optica spectrum disorders · ECTRIMS/EAN guidance on MS treatment.

Educational aid; verify against current guidance, local formulary and patient factors.

roundsrx.com
roundsrx Infographic Series · #206