Q&As

The Evolving Management of MS

What GPs Need to Know

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Multiple sclerosis (MS) is one of the most common disabling neurologic conditions in young adults. Prevalence rates are in the range of 100/100,000.[1-3] In 70% of patients, symptoms develop between ages 20 and 40.[4]

Q *What is the clinical course of MS?*

A *Relapsing-remitting (RR) MS*

RR MS is defined by relapses with complete or partial recovery. There is no disease progression during the periods between disease relapses. It is the most common presentation pattern.

Primary-progressive (PP) MS

PP MS is characterized by disease progression from onset with no improvement.

Secondary-progressive (SP) MS

SP MS is characterized by an initial RR disease course, followed by progression.

Benign MS

Benign MS is used in the literature to describe MS patients who have accumulated minimal deficits 10 to 20 years after the disease onset.

Malignant MS

Malignant MS refers to a rapid progressive course, leading to significant disability in multiple neurologic systems, or death in a relatively short time after disease onset.

The Kurtzke Expanded Disability Status Scale is a method of quantifying disability in MS. It is a score based on the composite measure of different functional systems deficits (Table 1).

Dana's case

Dana, 32 and right-handed, presents with a numb and weak left leg. The symptoms had come on gradually and resolved after two weeks, but then returned. There were no precipitating factors, however, overwhelming fatigue and bladder frequency accompanied the numbness.

She is otherwise well, but remembers blurriness in her left eye a year ago, associated with pain on ocular movement.

Dana's exam reveals normal cranial nerves, although the left optic disc appears more pale than the right. She has normal tone and normal strength in all limbs. Her plantar response is extensor on the left. Her vibration sense is impaired in the lower limbs. She has normal co-ordination and gait.

- **Where are the lesions?**
- **What investigations would you perform?**
- **What treatment options are available for her symptoms?**

For a followup on Dana, go to page 87.

Table 1

Kurtzke Expanded Disability Status Scale

Level	Significance
0.0	Normal neurologic exam
1.0	No disability, minimal signs in 1 FS
1.5	No disability, minimal signs in > 1 FS
2.0	Minimal disability in 1 FS
2.5	Mild disability in 1 FS or minimal disability in 2 FS
3.0	Moderate disability in 1 FS, or mild disability in 3 or 4 FS; fully ambulatory
3.5	Fully ambulatory, but with moderate disability in 1 FS and more than minimal disability in several others
4.0	Fully ambulatory without aid, self-sufficient, up and about some 12 hours/day despite relatively severe disability; able to walk 500 m without aid or rest
4.5	Fully ambulatory without aid, up and about much of the day, able to work a full day, may otherwise have some limitation of full activity or require minimal assistance; characterized by relatively severe disability; able to walk 300 m without aid or rest
5.0	Ambulatory without aid or rest for about 200 m; disability severe enough to impair full daily activities
5.5	Ambulatory without aid or rest for about 100 m; disability severe enough to preclude full daily activities
6.0	Intermittent or unilateral constant assistance (cane, crutch, brace) required to walk about 100 m, with or without resting
6.5	Constant bilateral assistance (canes, crutches, braces) required to walk about 20 m without resting
7.0	Unable to walk beyond approximately 5 m even with aid, essentially restricted to wheelchair; wheels self in standard wheelchair and transfers alone; up and about in wheelchair some 12 hours/day
7.5	Unable to take more than a few steps; restricted to wheelchair; may need aid in transfer; wheels self, but cannot carry on in standard wheelchair a full day; may require motorized wheelchair
8.0	Essentially restricted to bed or chair or perambulated in wheelchair, but may be out of bed much of the day; retains many self-care functions; generally has effective use of arms
8.5	Essentially restricted to bed much of day; has some effective use of arms; retains some self-care functions
9.0	Confined to bed; can still communicate and eat
9.5	Totally helpless patient; unable to communicate effectively or eat/swallow
10.0	Death due to MS

FS: Functional system

Q *What are the signs and symptoms?*

A Common presenting symptoms and signs in MS patients include:

- sensory disturbances,
- unilateral optic neuritis,
- diplopia secondary to internuclear ophthalmoplegia,
- limb weakness,
- clumsiness, gait ataxia,
- neurogenic bladder and bowel symptoms,
- Lhermitte's sign, and
- Uhthoff's phenomenon.

More unusual clinical presentations can include transient recurring abnormal postures, and paroxysmal transient symptoms (*e.g.*, dystonias or trigeminal neuralgia). Rarely do cortical features (*e.g.*, aphasia, apraxia, recurrent seizures, and early dementia) dominate the clinical picture. Typically, many of these symp-

toms or signs present subacutely, but resolve after a few weeks to months in clinical relapse.

Q How is MS diagnosed?

A The diagnosis of MS is based on clinical history and exam. Supporting paraclinical evidence can include neuroimaging studies, cerebrospinal fluid (CSF) exam, and electrophysiologic testing. PP MS may be suggested clinically by a progressive course that lasts longer than six months, but paraclinical studies to obtain supportive evidence are strongly advised.

Magnetic resonance imaging (MRI) has revolutionized the diagnosis of MS; however, the appropriate clinical history and exam findings remain the hallmark features of diagnosis.

Typical brain MRI findings in MS patients include lesions in characteristic locations, such as:

- the periventricular region,
- the corpus callosum,
- within the brainstem, and
- at the juxtacortical zones.

CSF studies and evoked potential testing can be useful when the clinical history and MRI findings reveal equivocal results. There are conditions that mimic MS, some of which are listed in Table 2.

Table 2

Differential diagnosis of MS

Inflammatory diseases
- Acute disseminated encephalomyelitis
- Systemic lupus erythematosus
- Polyarteritis nodosa
- Behçet's disease
- Granulomatosis angiitis
- Paraneoplastic encephalomyelopathies

Infectious diseases
- Lyme neuroborreliosis
- Human T-cell leukemia virus-1
- Progressive multifocal leukoencephalopathy
- Neurosyphilis

Granulomatous diseases
- Sarcoidosis
- Wegener's granulomatosis
- Lymphomatous granulomatosis

Myelin diseases
- Adult metachromatic leukodystrophy
- Adrenomyeloleukodystrophy

Other
- Vitamin B_{12} deficiency
- Arnold-Chiari malformation
- Spinocerebellar disorders
- Lymphoma

Q What are the treatment options?

A *General considerations*

In addition to the primary care physician and the neurologist, MS management typically involves a designated MS nurse, occupational and physical therapists, a speech therapist, and a social worker.

Management of MS includes:

- symptomatic treatment,
- acute relapse treatment, and
- disease-modifying therapy.

Symptomatic treatment

Symptomatic treatment remains vital in improving the quality of life in MS patients. Table 3 sum-

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Table 3

Symptomatic therapy in MS patients

Symptom	Drugs used			
Fatigue	Amantadine, 100 mg bid	Modafinil, 100-200 mg Qam, Qpm	Methylphenidate, 5-10 mg Qam, Qnoon	Fluoxetine, 10-20 mg Qam
Spasticity	Diazepam, 5-20 mg	Baclofen, 5 mg bid	Dantrolene, 25 mg OD to 200 mg	Tizanidine, 6-24 mg OD
Urinary frequency	Oxybutynin, 5 mg bid-tid	Tolterodine, 1-2 mg OD	Flavoxate, 100-200 mg tid-qid	Bladder exercises
Paroxysmal dystonia/sensory symptoms	Carbamazepine, 200-400 mg OD	Gabapentin, 300 mg tid	Phenytoin, 100 mg bid	Amitriptyline, 25-150 mg OD
Depression	Mirtazapine, 15-45 mg OD	Fluoxetine, 20-60 mg OD	Seratraline, 25-250 mg OD	Bupropion 200-400 mg OD
Pain	Amitriptyline, 25-100 mg OD	Gabapentin, 300 mg OD	Baclofen, 20-120 mg OD	Opioid analgesics
Tremor	Propranolol, 400 mg bid	Carbamazepine, 100-200 mg OD	Gabapentin, 300 mg tid	Weights

OD: Once daily
bid: Twice daily
tid: Three times daily
qid: Four times daily
Qam: Every morning
Qnoon: Every afternoon
Qpm: Every evening

marizes the usual pharmacologic armamentarium in the management of various symptoms.

It is important to note that infections may trigger MS relapses, therefore, patients are advised to limit exposure to viral illnesses. In those who are at risk for influenza, vaccinations may be safely administered.

Relapse treatment

Clinically significant relapses can be treated with corticosteroids. Intravenous methylprednisolone, 1.0 g/day for three to five days, followed by a tapering course of oral prednisone, can be used. It is important to recognize steroids have been demonstrated to expediate recovery of relapse signs and symptoms, but do not alter ultimate outcome.

Rarely, plasma exchanges may be considered in those patients who develop catastrophic and fulminant neurologic deficits unresponsive to corticosteroids.

Disease-modifying therapy

Recent clinical trials, conducted in double-blind, placebo-controlled, randomized fashion, suggest two classes of medications are effective in the treatment of RR MS. These include interferons and glatiramer acetate.

These two medications have an effect in reducing relapse frequency by one-third, reducing the MRI burden of disease, and possibly even delaying the progression of disability.

Typical dosages include:

- interferon beta-1a, 30 µg intramuscularly once weekly, or 22/44 µg every other day
- interferon beta-1b, 8 million IU subcutaneously every other day,
- glatiramer acetate, 20 µg subcutaneously daily.

A followup on Dana

The history is suggestive of lesions disseminated in space (optic nerve, spinal cord) and time.

Magnetic resonance imaging of the brain reveals multiple periventricular white matter lesions, consistent with demyelinating disease. Evoked potentials reveal optic nerve conduction abnormalities.

She is diagnosed with relapsing-remitting multiple sclerosis and started on disease-modifying therapy. Her fatigue and urinary frequency respond well to amantadine and oxybutinin.

It is recommended interferon beta and glatiramer acetate be considered in RR MS patients who have active disease with ongoing relapses.

SP MS

Results have been less encouraging with this form of MS. Use of interferons have resulted in some inconsistent findings; however, mitoxantrone hydrochloride, 5 mg/m^2 or 12 mg/m^2 of body surface area intravenously every three months for two years, has been used for patients in whom interferons failed.

PP MS

Currently, there are no proven therapies for PP MS. Chemotherapy (*i.e.*, methotrexate) has been used in patients with progressive MS, but there is little evidence of effective treatment. Management is mainly supportive.

Q *What is the GP's role?*

A It is important the family physician be aware of the presenting symptoms of MS. Initiation of investigations can be undertaken and the further management of these patients can be done in conjunction with the neurologist. Dx

Take-home message

How is MS diagnosed?

- While MRI has revolutionized the diagnosis of MS, clinical history and exam findings with dissemination in time and space remain the hallmark features of the disease.

How is MS treated?

- Symptoms are treated with various pharmacologic agents (Table 3).
- Relapses can be treated with corticosteroids.
- Disease-modifying therapies include interferons and glatiramer acetate.

References
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