Three main clinical subtypes of MS are defined based on clinical course: relapsing remitting, secondary progressive, and primary progressive. Relapsing remitting MS is characterized by clinical stability between individual attacks from which the patient may or may not fully recover. Secondary progressive MS patients have gradual neurologic deterioration and may also have superimposed attacks. Secondary progressive MS develops following an initial relapsing-remitting course in a substantial proportion of relapsing remitting patients, although this proportion may be declining with the advent of disease-modifying therapies. About 10% of MS patients have primary progressive MS, which is characterized by gradual downhill progression from onset without any clinical attacks. It has been proposed to discontinue the uncommon fourth clinical designation, progressive relapsing MS, in favor of *primary progressive MS with activity*.

Diagnosis

The diagnosis of MS requires dissemination of CNS disease in time and in space. No other disease should provide a better explanation. MRI, spinal fluid analyses, evoked potentials (EPs) and ocular coherence tomography (OCT) are tools that may aid in the diagnosis. The McDonald criteria (Table 120-1) allow new MRI lesions to be used to define disease in time after an initial first attack (clinically isolated syndrome). These criteria have made diagnosis easier, without losing significant specificity.

MRI

Classic features seen on brain and spinal cord MRI greatly aid in the certainty of diagnosis. MS lesions are characterized by increased intensity on T2-weighted (T2w) and T2-FLAIR (fluid attenuated inversion recovery) images (Fig. 120-1A). Lesions are usually ovoid, and often localize to the periventricular or subcortical regions, the corpus callosum, the brainstem, and the cervical spinal cord. Periventricular lesions are typically at right angles to the lateral ventricles and bear the moniker "Dawson's fingers." On sagittal images, lesions in the corpus callosum are usually flame-shaped (Fig 120-1C). On T1w images, MS lesions may be isointense or hypointense. T1w hypointensity in a chronic inactive lesion denotes underlying tissue damage, including axonal loss (Fig.120-1D). Enhancement of lesions following administration of gadolinium containing contrast agents indicates blood-brain barrier breakdown, and that a lesion is active (Fig. 120-1B). Enhancing lesions are also often T1w hypointense, but the hypointensity resolves more than 50% of the time. A ring pattern of enhancement is common. Most enhancing MS lesions display no edema or mass effect, but occasional "tumefactive" MS lesions have significant edema on MRI and may require biopsy for diagnosis.

Spinal Fluid Analysis

Evidence of increased intrathecal immunoglobulin synthesis is present in more than 90% of MS patients. Elevated concentrations of CSF IgG and IgM, CSF-restricted oligoclonal bands of immunoglobulin (Fig. 120-2), and a high intrathecal IgG synthesis rate are seen. The IgG index, which is derived from the ratio of CSF to serum IgG and takes BBB integrity into account, is elevated. A mild lymphocytic pleocytosis is frequently seen in CSF during MS relapses.

TABLE 120-1 THE 2010 REVISED MCDONALD CRITERIA

CLINICAL PRESENTATION	LESIONS	ADDITIONAL DATA NEEDED FOR MS DIAGNOSIS*
≥2 attacks	Objective clinical evidence of ≥2 lesions or objective clinical evidence of 1 lesion and reasonable historical evidence of a prior attack	None
≥2 attacks	Objective clinical evidence of 1 lesion	DIS demonstrated by >1 T2w lesion in at least 2 of 4 MS-typical regions of CNS, or 2nd clinical attack at alternate site in CNS
1 attack	Objective clinical evidence of ≥2 lesions	DIT demonstrated by simultaneous presence of asymptomatic gad+ lesion and non-enhancing lesions or a new T2w and/or gad+ lesion on follow-up MRI after a baseline scan, or 2nd clinical attack
1 attack	Objective clinical evidence of 1 lesion (CIS)	For DIS, ≥1 T2w lesion in at least 2 of 4 MS-typical regions of CNS; For DIT, as above; or await a 2nd clinical attack implicating different CNS region
Gradual neurologic progression suggestive of MS (PPMS)	1 year or more of disease progression plus 2 of 3 of following criteria: evidence for DIS in the brain based on ≥1 T2w lesions characteristic of MS, evidence of DIS in the spinal cord ≥2 T2w cord lesions positive CSF (elevated IgG index or oligoclonal bands not present in serum)	

(Modified from Polman CH, Reingold SC, Banwell B, et al: Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria, Ann Neurol 69(2): 292–302, 2011, Table 4.)

DIS, Dissemination in space; DIT, dissemination in time.

*These criteria were developed using CIS presentations and are therefore most applicable in patients who present with a typical CIS suggestive of CNS inflammatory demyelinating disease. Alternative diagnoses that might better explain the disorder must be considered and reasonably excluded.

Evoked Potentials

Evoked potentials (EPs) detected by surface electrode recording have in the past been useful in detecting subclinical demyelination in the brainstem (auditory EPs), spinal cord (somatosensory EPs), and optic nerves (visual EPs). The advent of high resolution MRI has made these tests less useful.

Optical Coherence Tomography

Optical coherence tomography (OCT) is a safe and rapid means to image the retina and detect evidence of prior optic neuritis. OCT uses safe infrared light to provide images of the retinal layers, including the retinal nerve fiber layer (RNFL) which contains axons that form the optic nerve. The RNFL is thinner than normal in those with remote optic neuritis. Also, RNFL thickness correlates with neurodegenerative aspects of MS, such as brain atrophy.

Differential Diagnosis

The diagnosis of MS requires the exclusion of diseases that might better explain the clinical scenario. The differential diagnosis of MS is broad (Table 120-2). Some diseases that can mimic MS