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Clinical Features and Diagnosis of Multiple Sclerosis

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The signs and symptoms of MS are the consequence of underlying neuropathologic changes that occur in the central nervous system (CNS). The primary mechanism of injury is inflammatory demyelination and, to a variable degree, axonal damage, which can occur early in disease course and concomitant with acute inflammation [1,2]. Either mechanism may produce clinical features. The role of axonal damage is clear-cut, disrupting conduction completely. Demyelination may result either in slowing of conduction or complete failure of transmission. The former produces symptoms when the slowing becomes critical. Because the pathologic damage may involve any area of the CNS, the location of the lesions also play a role in symptom production.

MS can produce any symptom or sign that might occur with damage to the CNS and, despite growing evidence for gray matter involvement [3], the clinical features best reflect damage mostly to white matter tracks. The most common findings include optic neuritis, weakness, sensory loss, ataxia, nystagmus, bladder dysfunction, and cognitive impairment; the full list is quite long.

Diagnosing multiple sclerosis

The diagnosis of MS is based on finding clinical evidence of lesions of the CNS that are disseminated in time and space. Dissemination in time suggests that there is more than one episode of CNS dysfunction. Dissemination in space suggests involvement of more than one area of the CNS. Diagnosis is accomplished through careful medical history and a detailed neurologic examination. Although all MS begins with a first attack, the essence of the

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clinical disease is the multiplicity of attacks. There have been several diagnostic criteria proposed in the past several decades, all affirming the need for dissemination, primarily white matter involvement, at a young age (20–50 years old) and including an important caveat: that there is no better diagnosis.

The diagnostic criteria for MS have been refined by Rose et al [4] and, penultimately, by the Poser criteria in 1982, which were developed by a committee established by the National Multiple Sclerosis Society (NMSS) [5]. The latter were established for use in clinical trials of MS. The categories proposed were clinically definite MS, laboratory-supported (dependent on positive cerebrospinal fluid [CSF] analysis) definite MS, probable MS (either clinically or laboratory supported), and possible MS. Because MRI scanning was relatively new at the time these criteria were developed, it was included as a paraclinical element (along with urodynamic testing and evoked potentials) but not defined further or quantified. The Poser criteria were used for almost 20 years but in the intervening years, there have been hundreds of studies better integrating MRI results into the diagnostic schema for MS and providing considerable knowledge of the importance of MRI in providing an in vivo view of the neuropathology of MS and the likelihood of developing MS [6].

In 2000, the NMSS convened a committee to update and revise the diagnostic criteria for MS, with the intention of increasing the role of MRI in the diagnostic schema. Other objectives for this revision were to simplify the categories and produce guidelines useful to practicing clinicians. The deliberations of that group then were reviewed by outside experts and published [7]. The need for this most current revision is underscored by the development of MS disease-modifying agents (DMAs) during the past decade. Since the advent of DMAs, the need for early, accurate diagnosis has become increasingly important, because the accumulated data suggest that the earlier treatment is started, the lower the risk for accumulating impairment or disability.

The general conclusions from the new criteria are that the diagnosis of MS requires objective evidence of lesions disseminated in time and space. MRI findings may contribute to determination of dissemination in time or space, and other supportive investigations include CSF analysis and visual evoked potential (VEP). The diagnostic categories are possible MS, MS, and not MS (the category of probable MS, used by Poser, had little practical value for clinicians, other than suggesting more certainty than possibility, and was of no value in clinical trials). The new guidelines reaffirmed the classical approach to diagnosing MS by clinical means only: the finding of evidence of lesions of the CNS; dissemination in time and space, based on a detailed history; and a complete neurologic examination. This schema allows for diagnosing MS in regions of the world where there is limited access to newer and more expensive technologies.

Most MS starts with an attack, relapse, or exacerbation (ie, an acute episode of CNS dysfunction lasting at least 24 hours [by convention],