

THE DIAGNOSIS OF MULTIPLE SCLEROSIS

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Demyelinating diseases in adults, in which the pathology is predominantly in the white matter of the central nervous system, are caused by a variety of viral infections and anoxic-toxic conditions⁽¹⁾. However, the most common primary demyelinating disease is multiple sclerosis (MS) which is characterised by multifocal inflammatory demyelination in the central nervous system and recognised by its relapsing and remitting character. As there are no pathognomonic laboratory tests, the diagnosis has always been a clinical one. Diagnostic criteria have continued to evolve since its delineation as a disease entity by Charcot more than a century ago. The disease typically occurs in young women of northern European Caucasian descent in temperate countries⁽²⁾. The prevalence of the disease is low in Asian countries and the optic-spinal form, often with severe visual impairment, is by far the most common pattern of presentation among Orientals⁽³⁾.

The diagnosis of MS has always depended upon the clinical recognition of white matter lesions disseminated in both time and space for which another cause cannot be established. The Schumacher Panel criteria, published in 1965, for the diagnosis of clinically definite multiple sclerosis (CDMS) had served as the standard diagnostic guide for many years and has an accuracy of 90-95%⁽⁴⁾. Several other proposed classifications followed, building upon the Schumacher criteria to include the categories of probable and possible MS when the diagnostic criteria fall short of those for definite MS⁽⁵⁾.

Over the past decade, newer diagnostic tools to detect immunological evidence of central nervous system inflammation or evidence of clinically asymptomatic lesions have been developed. The oligonal IgG band in the cerebrospinal fluid (CSF) of patients with MS correlates with the presence of plasma cells in MS plaques and is present in 90% of patients with CDMS⁽⁶⁾. Multimodality evoked potentials and central motor conduction using a magnetic stimulator are now widely used in evaluating patients with suspected demyelinating diseases. Pattern-shift visual evoked potential (VEP) is abnormal in up to 85% of clinically classified definite MS. For brainstem auditory evoked response (BAER) and somatosensory evoked potentials (SSEP) the yield is about 67% and 77% respectively in CDMS⁽⁷⁾. In Oriental patients, the abnormality rate for BAER is much lower while abnormal VEPs tend to involve loss of amplitude rather than prolonged latency reflecting the differing disease pattern alluded to earlier^(8,9). Magnetic resonance imaging (MRI) is extremely sensitive in detecting white matter lesions in the cerebral hemisphere, brainstem and the spinal cord. It is superior to CT scan in demonstrating MS lesions and has been reported to be abnormal in 87-93% of patients with CDMS⁽¹⁰⁾. These paraclinical findings which show asymp-

tomatic dissemination in space or detect evidence of inflammation in the central nervous system are useful aids in the diagnosis of MS. The risk of developing MS following an isolated acute syndrome of brainstem or spinal cord is much higher in patients with disseminated lesions on MRI and in those with positive oligoclonal band^(11,12). Similarly, the risk of developing MS in isolated optic neuritis may be higher in patients who have abnormal white matter lesions on MRI⁽¹³⁾. The existing diagnostic criteria for MS were revised at a Workshop on the Diagnosis of Multiple Sclerosis in 1982 whereby paraclinical findings were incorporated for the purpose of extending the limits of the diagnostic criteria thus making a larger reservoir of patients for investigative purposes⁽¹⁴⁾. A new category of laboratory-supported definite multiple sclerosis (LSDMS) was proposed for use in research protocols although it is now widely used in clinical practice.

The diagnosis of LSDMS is dependent on the presence of oligoclonal bands or an increased IgG synthesis rate in the CSF. When such immunological abnormalities are present, LSDMS can be diagnosed with a history of 2 episodes of neurological disturbance and clinical evidence of one lesion and paraclinical evidence for a second lesion. When the CSF changes are present, LSDMS may also be diagnosed in patients with steadily progressive deficit from onset, provided the illness has been present for at least 6 months and sequential discrete involvement of the CNS white matter can be demonstrated clinically or paraclinically. The category of probable MS for patients in whom all criteria are not fulfilled was also expanded to include CSF and other investigative results. The diagnosis of LSDMS could certainly be made earlier and more readily than the diagnosis of CDMS. In a short follow-up study, 10% of patients who qualified for LSDMS went on to develop clinically definite MS in less than one year⁽⁹⁾. However, only long-term follow-up studies will show how well the category of LSDMS predicts the development of CDMS.

The use of these laboratory aids however must be put into the proper perspective. None of the laboratory abnormalities are specific for MS. Oligoclonal bands can be found in other inflammatory conditions like subacute sclerosing panencephalitis, chronic meningitis, neurosyphilis, vasculitis, sarcoidosis and T-lymphotropic virus type 1 related myelopathy⁽¹⁵⁾. An abnormal visual evoked response may be due to a compressive lesion on the optic nerve. Similarly, abnormal BAER and SSEP may be due to compressive lesions or degenerative and vascular diseases. In serial MRI studies in MS patients, it has been shown that asymptomatic new lesions may appear and disappear. Among the paraclinical tests, MRI has the most frequent overall abnormality rate and in one study it could identify all the patients that could be diagnosed as having LSDMS⁽¹⁰⁾. However, MRI is also extremely sensitive in demonstrating white matter lesions from a variety of diseases including migraine, encephalitis, vasculitis, head trauma and often even in the normal aged. The specificity of these MRI lesions dubbed "UBO" (unidentified bright object) is still not established, partly because of lack of adequate clinicopathological correlative studies⁽⁹⁾. Hence, a conservative ap-

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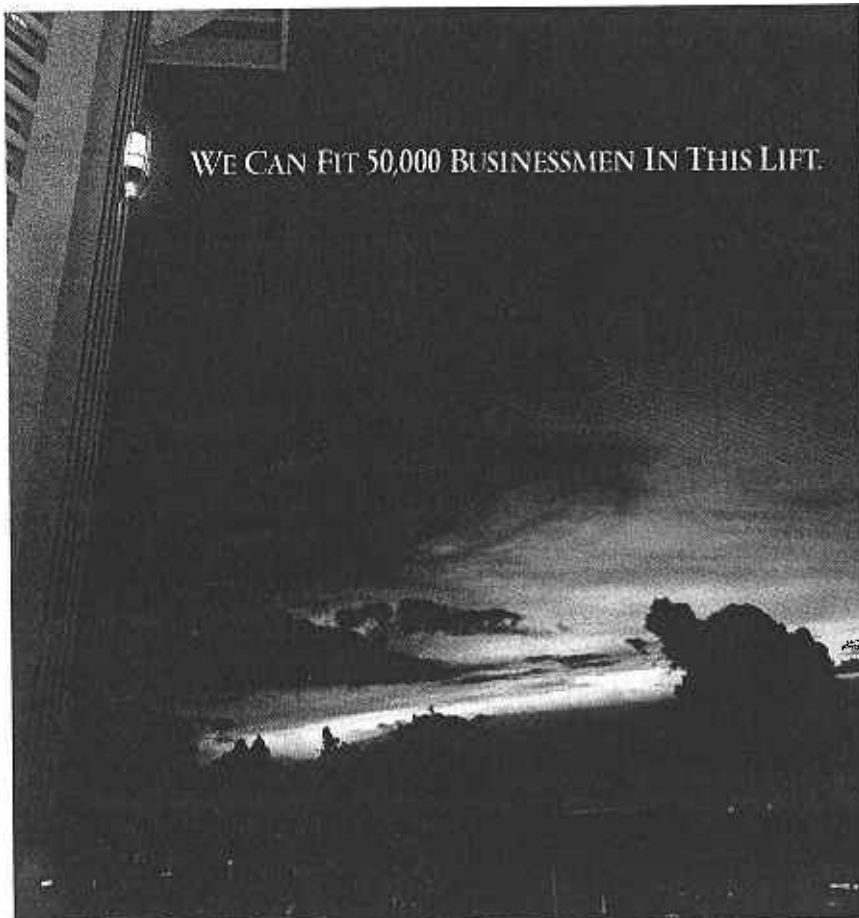
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proach must be taken in interpreting MRI to avoid making false positive diagnoses of multiple sclerosis.

There is as yet no effective treatment for the disease and in the words of Foster Kennedy, the diagnosis of MS is also a prognosis of utter disaster to any human to whom it is given⁽¹⁶⁾. It is therefore essential that the physician should sort out the clinical and paraclinical findings to exclude other potentially treatable conditions before ascribing them to multiple sclerosis. Most clinicians would also agree that the diagnosis of MS must be based on clinical evidence of dissemination and not solely on the basis of laboratory tests.

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