

Onset symptoms of multiple sclerosis

Definite:

These symptoms must last for at least 24 hours.

Unilateral optic/retrobulbar neuritis
 Acquired monocular colour blindness
 Oscillopsia
 True binocular diplopia
 Tic douloureux (under age 40)
 Hemifacial spasm (under age 40)
 Acute unilateral diminution of hearing (under age 40)
 Transient acute non-positional vertigo (under age 40)
 Transient scanning speech
 Transverse myelitis
 Lhermitte symptom
 Gait ataxia
 Unilateral dysmetria/intention tremor/incoordination
 Sensory useless hand syndrome
 Transient weakness/paraesthesiae of one entire limb
 Transient painless urinary retention (under age 40)
 Transient painless urinary urgency/incontinence in men (under age 40)

Possible:

For these symptoms to be used as onset markers, they must be followed by a definite symptom within two years.

Unilateral facial palsy
 Transient painless urinary frequency in men (under age 40)
 Transient hemiparesis (under age 40)
 Organic erectile dysfunction
 Painful tonic seizures

To accept a Lhermitte symptom, it is desirable, although not required, that the symptom be transient. More important, however, is the fact that other causes for this symptom, in particular herniated nucleus pulposus or spondylosis in the cervical region, must have been ruled out. Gait ataxia and unilateral dysmetria/intention tremor/incoordination may be manifestations of involvement of the cerebellum or of the posterior columns with loss of position sense. Unusual clumsiness, dropping things, changes in handwriting, and inability to perform fine hand movements or activities such as sewing, embroidery, or fine instrument manipulation, may be the expression of these problems affecting the hands. The reason that they must be unilateral to indicate multiple sclerosis is to rule out familial essential tremor or the fine tremor of hyperthyroidism, which are invariably bilateral.

The useless hand syndrome² has an acute or subacute onset and consists of paraesthesiae and numbness in one arm and a decreased ability to use the hand properly. Men often report that they cannot use that hand to identify coins in their pocket, and the same applies to women trying to search for objects in their purse. Handwriting is usually impaired as well.

Transient paraesthesiae are understood to involve only one entire limb to differentiate them from the much more common carpal tunnel syndrome, as well as from the frequent complaint of bilateral numbness of the arms and hands on awakening or involving both legs with lumbosacral spine disease. Painless urinary urgency or incontinence in women is very often a symptom of bladder infection and therefore is relevant only when it occurs in men. Acute urinary retention occurring under the age of 40 distinguishes it from the problems caused by prostatic enlargement and some gynaecological difficulties in women.

Symptoms considered as "possibly relevant" should be counted only if a definite symptom as listed here occurs within two years. Facial palsy is a very common problem but rare as a presenting symptom of multiple sclerosis. In men urinary frequency

and transient hemiparesis, both occurring under the age of 40, are fairly specific, but other conditions causing these same symptoms occur often enough to dictate caution in using them in this set of criteria. Impotence to be classified as organic erectile dysfunction must include the lack of morning erection. It does not, however, include the inability to achieve orgasm. Finally, painful tonic seizures again are non-specific although probably more frequent in patients with multiple sclerosis than in any other conditions.

The original lists were reviewed by the following multiple sclerosis specialists: Johan Aarli, Bergen, Norway; Peter Behan, Glasgow, UK; John Benedikt, Reykjavik, Iceland; Alastair Compston, Cambridge, UK; Floyd Davis, Chicago, USA; Geoffrey Dean, Dublin, Eire; John Kurtzke, Washington, DC, USA; Brian Matthews, Oxford, UK; Ian MacDonald, London, UK; Donald Paty, Vancouver, Canada; Sigrid Poser, Göttingen, Germany; Giulio Rosati, Sassari, Italy; Randall Schapiro, Minneapolis, USA; Labe Scheinberg, New York, USA; and Donald Silberberg, Philadelphia, USA. Many useful comments and suggestions were made, most of which were incorporated into the final list. Endorsement of the lists of symptoms by these specialists is not implied.

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- Poser C, Paty D, Scheinberg L, *et al.* New diagnostic criteria for multiple sclerosis. *Ann Neurol* 1983;13:227-31.
- Paty D, Poser C. Clinical symptoms and signs. In: Poser C, ed. *The diagnosis of multiple sclerosis*. New York: Thieme-Stratton, 1984:p33.

Multiple sclerosis in the Parsis

During the course of a search for patients with multiple sclerosis among Asian immigrants resident in England, five Parsis have been found with definite multiple sclerosis, one male and four female. The Parsis are Zoroastrians who left Persia (Iran) and set-

led in India, mostly in Bombay. They are a closely knit community. According to the Religious and Cultural Centre of the Parsi and Irani Zoroastrian community there are around 5000 Parsi resident in England and Wales and most of the adult members of the community came to England from the Indian subcontinent or East Africa.

By contrast with the Parsis multiple sclerosis is very uncommon among ethnic Indian immigrants to England and Wales,¹⁻³ and also among Indians in India.^{4,5} During a 25 year search for patients with multiple sclerosis among Asian immigrants to England only 23 patients have been found among ethnic Indian immigrants, although in 1981 there were 383 000 immigrants from India and a further 193 000 immigrants from East Africa resident in England and Wales and most of these immigrants were of Indian ethnic origin.

The prevalence of multiple sclerosis in the Parsis of Bombay is also much higher than among ethnic Indians.^{4,6} The high prevalence of multiple sclerosis among Parsi immigrants to England, by contrast with the very low prevalence among ethnic Indian immigrants, may be an important clue to the genetic and environmental factors responsible for the disease.

We would be most grateful if any doctor who knows of a Parsi with multiple sclerosis would, with the permission of the patient, notify Dr Geoffrey Dean at the address below.

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- Dean G, McLoughlin H, Brady R, Adelstein AM, Tallett-Williams J. Multiple sclerosis among immigrants in Greater London. *BMJ* 1976;1:861-4.
- Dean G, Brady R, McLoughlin H, Elian M, Adelstein AM. Motor neurone disease and multiple sclerosis among immigrants to Britain. *British Journal of Preventive and Social Medicine* 1977;31:141-7.
- Elian M, Dean G. Motor neuron disease and multiple sclerosis among immigrants to England from the Indian subcontinent, the Caribbean, and East and West Africa. *J Neurol Neurosurg Psychiatry* 1993;56:454-7.
- Bharucha NE, Bharucha EP, Wadia NH, *et al.* Prevalence of multiple sclerosis in the Parsis of Bombay. *Neurology* 1988;38:727-9.
- Wadia NH, Bhatia K. Multiple sclerosis is prevalent in the Zoroastrians (Parsis) of India. *Ann Neurol* 1990;28:177-9.
- Trikanad VS, Wadia NH, Krishnaswamy PR. Multiple sclerosis and HLA-B12 in Parsi and non-Parsi Indians: a clarification. *Tissue Antigens* 1982;19:155-7.

A new treatment of spasticity with repetitive magnetic stimulation in multiple sclerosis

Electromagnetic fields easily penetrate tissues, independent of tissue density and resistance. This property is applied in transcranial magnetic stimulation of neocortical neurons used to evaluate motor pathway function. Similarly, deep seated neurons in the spinal cord can be evoked by non-invasive trans-spinal magnetic stimulation. We designed a magnetic stimulator with repetitive stimulation capability to study the effect of magnetic stimulation on spasticity in multiple sclerosis.

The study was performed as a comparison of pretreatment and post-treatment

Electrophysiological and biomechanical data before and after repetitive magnetic stimulation in 12 patients with multiple sclerosis (median range)

	Maximum voluntary contraction (Nm)		Stretch reflex amplitude (% M_{max})	Threshold of stretch reflex (%)
	Dorsi	Plantar		
Before treatment	15.5 (0-23.0)	19.0 (1.7-32.0)	1.23 (0-10.4)	22 (6.0-88.0)
After treatment	20.0 (1.4-48.0)**	26.0 (3.2-44.0)**	0.88 (0.002-10.5)*	33 (12.0-88.0)*

* $p < 0.05$; ** $p < 0.01$.

values in 12 patients with clinical definite multiple sclerosis.¹ All had spasticity of the lower extremities, a preserved capability of continuous walking for at least 30 meters, and a clinical stable condition during the six months before study. Eight patients had not been treated recently for spasticity and four patients stopped drug treatment one week before the study. The magnetic stimulus has a biphasic waveform with a pulse width of 400 μ s, a rise time of 200 μ s, and a maximum magnetic field of 2.1 Tesla. The oil cooled coil was placed in the midline at the midthoracic level with the caudal part of the coil positioned at the eighth thoracic vertebra. The patients were stimulated in a relaxed supine position for 30 minutes with stimulation for eight seconds at 12 Hz followed by 22 seconds of rest. The range of stimulation intensity was 40-65% of maximal stimulator intensity. At the start of the study and 24 hours after the last magnetic stimulation clinical, electrophysiological, and biomechanical performances were registered. The same physician evaluated the spasticity at both knee and ankle joints by an Ashworth's score (0-4)² with a total maximum score of 32 arbitrary units (AU) as well as the patellar and Achilles tendon reflexes according to conventional clinical grading (0-4) with a maximum score of 16 AU.

For the electrophysiological and biomechanical measurements the patients were seated in a chair with the foot strapped to a pedal rotated by a strong motor.³ Spasticity was electrophysiologically evaluated by the threshold and amplitude of the stretch reflex by EMG of the soleus muscle and expressed as a percentage of the supramaximal direct muscle response (M_{max}). The short latency stretch reflex was elicited by rotating the platform at different stretch velocities in the range from 7.5 to 120°/s.⁴ Stretches and releases of 4° were delivered with a duration of 500 ms and were applied randomly with an interval of 4.0 (SD 0.2)s. The amplitude of the stretch reflex was measured at a stretch velocity of 90°/s. Maximum voluntary contraction of dorsi and plantar flexion of the foot was measured as the highest value the patient could maintain for one second out of three attempts. The patients self scored the ease of daily activities (0-10) with a score of 5 as the preset level. Group values and delta difference values between the pretreatment and post-treatment condition are given as median values and ranges. Differences were tested by Wilcoxon signed rank test with a 5% limit of statistical significance.

Self score of ease of daily activities improved significantly ($p = 0.01$) by 2 (4-0) AU pretreatment and post-treatment group values were 5 (5-5) AU and 7 (9-5) AU. The clinical score of spasticity decreased significantly by 1.5 (8-(-1)) AU ($p = 0.03$); pretreatment and post-treatment group values were 9.5 (17-1) AU and 5.5 (10-2) AU. The score of hyper-reflexia decreased signif-

icantly by 1.0 (3-(-1)) AU ($p = 0.03$); pretreatment and post-treatment group values were 6.5 (11-4) AU and 6.5 (11-2) AU. Electrophysiological measures of spasticity improved. The table shows a significant decrease of EMG amplitude of the stretch reflex of 28% ($p = 0.04$) and an increase in the threshold of the stretch reflex of 50% ($p = 0.03$). Maximum voluntary contraction of plantar and dorsiflexion of the foot strengthened significantly, by 27% and 29% respectively ($p = 0.008$ and $p = 0.009$).

No major side effects of magnetic stimulation were found. All patients reported a tight feeling as if wearing a narrow ring around the midthoracic level during stimulation. One patient had a single episode of brief dizziness but otherwise magnetic stimulation was well tolerated. By contrast, con-

ventional pharmacotherapy often induces side effects including loss of muscle strength, drowsiness, dizziness, and nausea. A double blind and sham stimulation controlled study of the effect of repetitive magnetic stimulation on spasticity is under way.

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- Poser CM, Paty DW, Scheinberg L, McDonald IW, Davis FA, Ebers GC, et al. New diagnosis criteria for multiple sclerosis: guidelines for research protocols. *Ann Neurol* 1983;13:227-31.
- Ashworth B. Preliminary trial of carisoprodol in multiple sclerosis. *Practitioner* 1964;192:540-2.
- Sinkjaer T, Toft E, Andreassen S, Hornemann BC. Muscle stiffness in human ankle dorsiflexors: intrinsic and reflex components. *J Neurophysiol* 1988;60:1110-21.
- Sinkjaer T, Toft E, Larsen K, Andreassen S, Hansen HJ. Nonreflex and reflex mediated ankle joint stiffness in multiple sclerosis patients with spasticity. *Muscle Nerve* 1993;16:69-76.

Patients with clinically definite multiple sclerosis, white matter abnormalities on MRI, and normal CSF: if not multiple sclerosis, what is it?

Clinical overdiagnosis of multiple sclerosis may occur in as many as 10% of patients according to Hendon and Brooks.¹ Whereas diagnosis has been facilitated by the use of MRI,^{2,3} the detection of focal disease scattered throughout the CNS in young adults is not specific for multiple sclerosis (table).

We therefore estimated the proportion of diagnostic mistakes still found in our large cohort of clinically diagnosed patients with multiple sclerosis.

Four hundred and five new patients were studied between 1988 and 1992. Three hundred and fifty two patients of our cohort met the Poser criteria for "clinically definite multiple sclerosis" and 184 had a complete CSF examination. Of these 184 patients, 166 had positive immunological findings for multiple sclerosis. The remaining 18 had no CSF abnormalities. These eighteen patients

had a duration of disease of at least one year, an upper age limit below 45 at onset, and the presence of multiple white matter lesions on MRI and they were given repeat CSF and MRI examinations between January and April 1993, together with a variety of tests screening for mitochondrial encephalomyopathy, adrenoleukodystrophy, Lyme disease, AIDS, coagulopathy, vasculitis, sarcoidosis, and cardiac embolic sources.

The MRI characteristics of multiple sclerosis are "multiple small lesions mainly involving white matter with asymmetric distribution that have optimal specificity if the following three features are present: size > 6 mm, abutting ventricular bodies, infratentorial location".⁴

We defined the MRI as: (a) "typical" and (b) "compatible" when not all the three features for optimal specificity were present.

In 16 of these 18 cases, the MRI was typical for multiple sclerosis, but four had a final diagnosis that was not multiple

Differential diagnosis of brain MRI mimicking multiple sclerosis

Multiple sclerosis-variants: Charcot type, Devic type, Schilder type, Marburg type, isolated syndromes

Normal aging*

Alzheimer's disease*

Migraine

Subcortical arteriosclerotic encephalopathy or Binswanger's disease*

Multiple metastases

Vasculitis: Sjögren's syndrome, polyarteritis nodosa, systemic lupus erythematosus, Beçhet's disease, giant cell arteritis

Sarcoidosis

Leucodystrophies

Encephalitis:

Viral: HTLV-I myelopathy, progressive multifocal leucoencephalopathy (Papova), subacute sclerosing panencephalitis (measles), acute disseminated encephalomyelitis

Bacterial: tuberculosis

Spirochaetal: syphilis, neuroborreliosis, or Lyme disease

Chronic demyelinating inflammatory polyneuropathy

Subacute combined degeneration of the spinal cord

*Excluded by age.