

# Jean-Martin Charcot on 'Sclérose en plaques' (Multiple Sclerosis)

Although not the first to describe multiple sclerosis, Charcot formulated ideas on the clinical features and pathology so effectively that Julius Althaus (1877) suggested naming the condition after him. Charcot first encountered three patients whose symptoms had begun in 1855. In that year Alexandrine C. became aware during pregnancy of difficulty in using her legs although she may have had symptoms for the previous two years. The diagnosis was established clinically at the Salpêtrière in 1863. Later, Charcot realised that a maid employed in his house had sclérose en plaques and not, as he first thought, Parkinson's disease. He presented three cases to the Société Médicale des Hôpitaux on March 8th 1865 (Vulpian 1866) and published four original papers at around that time (Charcot 1865; 1868a; 1868b; 1868c). But Charcot's observations on sclérose en plaques are best known through his published lectures (Charcot 1872; 1875) and clinical demonstrations (Charcot 1887), the early volumes of his collected works (Charcot 1886) and the English translations of these lectures published by the New Sydenham Society (Charcot 1877). Charcot left a brilliant account of the clinical features, delineating the cerebral, spinal and mixed cerebrospinal forms. He formulated views on the pathogenesis and pathophysiology, provided the first attempts at clinical measurement, and threw down a therapeutic gauntlet to his successors. His clinical descriptions were vivid and, with access to pathological material (Figure 1), he was clearly thinking about disease mechanisms. On visual involvement, he wrote:

"Amblyopia is a persistent and frequent symptom of cerebro-spinal disseminated sclerosis but it rarely issues in complete blindness ... patches of sclerosis have been found after death occupying the whole thickness ... of the optic nerve, in cases where during life an enfeeblement of sight simply had been noted. This discrepancy between symptom and lesion constitutes one of the most powerful arguments to show that the functional continuity of the nerve tubes is not absolutely interrupted although these, in their course through the sclerosed patches, have been despoiled of their medullary sheaths and reduced to axis cylinders."



Figure 1. The pathological anatomy of sclérose en plaques (Charcot 1886).

On cognitive manifestations of multiple sclerosis, and pathological laughter and crying:

"Most of the patients affected by multilocular sclerosis, whom I have had occasion to observe, have presented at a certain stage of the disease a truly peculiar facies. ... there is marked enfeeblement of the memory; conceptions are formed slowly; the intellectual and emotional faculties are blunted in their totality. ... it is not rare to see them give way to foolish laughter for no cause, and sometimes, on the contrary, melt into tears without reason."

Charcot described the triad of nystagmus, dysarthria and ataxia resulting from involvement of brainstem-

cerebellar connections:

"When the patient wishes to lift a glass full of water to her lips, the rhythmical agitation of the hand and forearm is scarcely noticeable when taking hold of the object; ... but ... at the moment when the goal is being attained, the glass is ... dashed with violence against the teeth, and the water is flung out to a distance."

On spinal disease, Charcot described the characteristic weakness, spasticity, ankle clonus (spinal epilepsy) and loss of function resulting from de-afferentation:

"Some of the symptoms of ataxia are found ... when the sclerosed islets in certain regions of the cord spread over a certain height of the posterior columns ... In order to grasp and use a pin [the patient] is required to have her eyes open, otherwise the pin drops from her fingers."

We can admire Charcot for the attempt to measure deficits, and to explain their origins in terms of disordered physiological mechanisms (Figure 2). On pathophysiology he wrote:

"transmission of voluntary impulses would still proceed by means of the denuded axis cylinder ... deprived of medullary sheathing in the midst of the foci of sclerosis .. but it would be carried on irregularly in a broken or jerky manner and would thus produce the oscillations which disturb the due execution of voluntary movement."

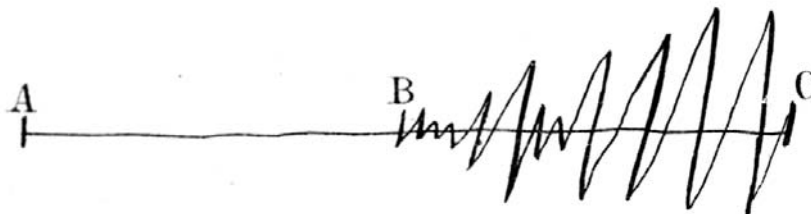
Many of Charcot's students were also put to work on the disorder. In his thesis, Leopold Ordenstein first depicts the lesions of sclérose en plaques using material from Charcot's laboratory (Ordenstein 1868). Désiré-Magloire Bourneville and Louis Guerard (1869) completed the clinical description and provided additional illustrations. Joseph Babinski emphasised hemiplegia as a manifestation of multiple sclerosis (Babinski 1885). The work also contains an elaborate depiction of early multiple sclerosis lesions, showing the interaction of macrophages with demyelinated and remyelinated nerve fibres. Babinski is the young physician catching the swooning Blanche Wittmann in the much reproduced painting by Pierre Brouillet of Charcot demonstrating hysteria at La Salpêtrière during one of his Tuesday lectures. Gilles de la Tourette (1886) described the gait in neurological disease and depicted the footprints of ataxic patients with sclérose en plaques. The last of Charcot's pupils to write at length on multiple sclerosis was Pierre Marie who sought to classify and record the typical gait disturbance - distinguishing spastic from cerebellar components. He was no less thorough in his descriptions of upper limb tremor and sensation, dealing at length with the special senses, hearing and vision, and distinguishing disorders of acuity and colour vision from those of eye movements. He was awarded the Civrieux prize of the Academy of Medicine in 1885 for his account of disordered bladder, bowel and sexual function in multiple sclerosis. Marie recognised the variable symptoms at onset, delineating a number of stereotyped presenting syndromes and documenting the subsequent clinical course, including the category of benign multiple sclerosis. He made the distinction between progression from



Alastair Compston (MBBS PhD FRCP FRSA FMedSci FIBiol) is professor of neurology and head of the Department of Clinical Neurosciences in the University of Cambridge. His research focuses on the clinical science of human demyelinating disease. With others, he writes McAlpine's Multiple Sclerosis (4th edition to be published in November 2005). Outside Cambridge, he contributes to the administration of academic neurology. He is a past chairman of the Neurosciences and Mental Health panel of the Wellcome Trust and former president of the European Neurological Society. He is currently Editor of Brain.

**Correspondence to:**  
Professor Alastair Compston,  
Department of Clinical  
Neurosciences,  
University of Cambridge Clinical  
School,  
Addenbrooke's Hospital,  
Hills Road,  
Cambridge CB2 2QQ.  
Email: alastair.compston@  
medschl.cam.ac.uk

Figure 2. Measurement of tremor at rest and on attempted movement (Charcot 1887).



onset and its development later in the course of the illness - in fact, his account of primary progressive multiple sclerosis is faultless, noting the later age of onset, the worse prognosis, the relative absence of histological (or clinical) involvement of the cerebrum, and the more frequent axon degeneration.

Charcot described axon loss in some lesions of sclérose en plaques (Charcot 1868b) and linked these to clinical disability:

"The paresis advances with extreme slowness ... but at last the day comes when ... they may be confined to bed ... this resistance of the axis cylinders ... may account for the slowness with which the paretic symptoms advance in disseminated sclerosis and for the long space of time which elapses before they give place to complete paralysis and permanent contracture."

He suggested that the naked axis cylinders might again clothe themselves with myelin and thus effect a "restituto ad integrum". Neither he nor Babinski realised that this is what they had already depicted (Babinski 1885). For Charcot, sclérose en plaques was a toxin- or microorganism-induced condition in which overgrowth of glia strangles the myelin sheath, sometimes leading to degeneration of the axis cylinders and with secondary changes in blood vessels (Figure 3).

"undoubtedly, the multiplication of nuclei and the concomitant hyperplasia of the reticulated fibres of the neuroglia constitutes the initial, fundamental fact, and necessary antecedent; the degenerative atrophy of the nerve elements, is consecutive and secondary."

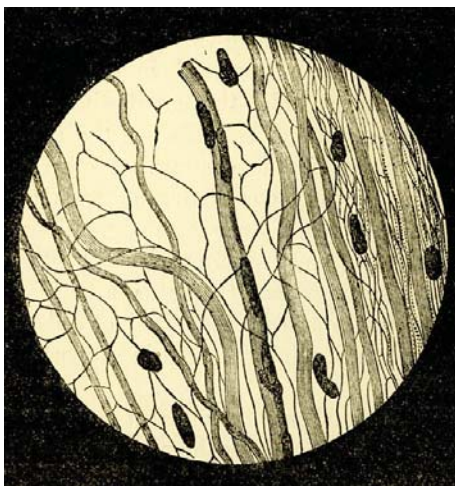


Figure 3. The 'primary' glial overgrowth that is the basis for sclérose en plaques (Charcot 186 8b).

On treatment, Charcot came straight to the point:

"After what precedes, need I detain you long over the question of treatment? The time has not yet come when such a subject can be seriously considered."

Charcot only saw 30 cases of sclérose en plaques during his working lifetime but he observed most of the cardinal clinical and pathological features and showed great intuition in thinking about the clinical science of what is now recognised to be the commonest potentially disabling neurological disease of young adults in the western world.

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