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History of MS

MS was first recognised as a condition in the middle of the 19th century. Prior to this time, there are reports of a few instances of what may have been MS, although the variety of symptoms, the range of other possible causes and the incompleteness of records make these impossible to confirm.

Early reports of MS



Specialist MS centres

St Lidwina of Schiedam

The oldest and best recorded of these early reports concerns St Lidwina of Schiedam, in Holland. Knowledge of her symptoms comes from a biography written shortly after her death in 1433.

In 1396, following a fall whilst skating, Lidwina developed walking difficulties, headaches and violent pains in her teeth. Within a few years, she was walking with difficulty and a weakness in her face caused her lip to droop on one side. Throughout the remainder of her life, Lidwina's condition slowly deteriorated, although with apparent periods of remission.

During her life and subsequently, Lidwina's forbearance with her symptoms led to the development of a cult. She was canonised in 1890 and is now the patron saint of skaters.

The bones of St Lidwina were discovered in 1947 and do show evidence of restricted mobility in the legs and right arm. Though it had previously been suggested that St Lidwina had MS, doubts have been cast on this and the evidence is not considered persuasive.

Augustus d'Este

The first identifiable instance of MS does not occur until the early 19th century. Augustus d'Este (1794-1848) was a grandson of George III. The course of his MS, which wasn't diagnosed during his lifetime, is known from the diaries and records he kept from 1822 until shortly before his death.

D'Este's initial symptom was the onset of blurred vision, which cleared up without treatment and then recurred a few years later. He later had episodes of double vision, weakness in his legs, numbness, bladder and bowel problems and impotence. By 1843 he was experiencing persistent symptoms including tremor and nocturnal spasms and in his last years became confined to his bed.

The medical history of MS

Although MS was not recognised until 20 years after d'Este's death, the early part of the 19th century had seen major advances in the understanding of the nervous system and the development of the science of neurology. From this period, there are several reports of individual cases that show many of the signs of what would later be recognised as MS.

Damage to the brain caused by MS was first recorded by Robert Carswell in 1838 in a book of detailed diagrams of patches of discoloured scarring or lesions found on the brain and spinal cord during autopsies.

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Working independently, Jean Cruveilhier also recorded scarring on the brain and spine in a book published in 1841. Although not identifying the cause, Cruveilhier was the first person to link these scars to symptoms such as tremor and walking difficulties experienced during the person's lifetime.

The following decades saw a number of discoveries that advanced knowledge of the as yet unnamed condition until the findings of the previous 30 years were finally drawn together by the Parisian neurologist Jean-Martin Charcot.

Jean-Martin Charcot

In a lecture in 1868, Charcot expanded on the work of his predecessors to describe the distinct characteristics of MS. He described MS lesions in detail and reported on inflammation and the loss of the covering of the nerves (myelin) at these sites. He attributed symptoms to impaired conduction in the central nervous system, though with periods of remission, and identified the 'triad' of symptoms - nystagmus, slurring of speech and loss of coordination - as indicators of MS.

Although Charcot considered MS to be quite rare - he published reports of fewer than 40 cases - his description of the structure of a lesion holds true and his work is considered the beginnings of the study of MS.

With Charcot's clarification of the condition, an increasing number of cases were reported in the late 19th century. The first description of MS in patients in Britain was published by William Moxon in 1873 and in the United States by Dr Edward Seguin in 1878, although in both countries earlier cases had been reported but not identified.

MS in the 20th century

The 1921 meeting of the Association for Research in Nervous and Mental Diseases (ARNMD) focussed research into possible causes, distribution and clinical features of MS that had been gathering pace in the preceding 50 years. This meeting was influential in stimulating surveys that began to create a better picture of the extent and nature of MS around the world.

From 1930 until his death in 1966, Russell Brain described MS across several editions of his textbook Diseases of the Nervous System. This work helped to clarify what was becoming an increasingly diverse field. As well as describing symptoms and signs, Brain recognised uneven geographical distribution of MS and published early work on the differences between prevalence rates in different locations.

Another influential textbook was Multiple Sclerosis by Douglas McAlpine, Nigel Compston and Charles Lumsden, published in 1955. Now in a third edition, edited amongst others by Compston's son, this has become one of the key reference works on MS. Although several names described the condition in the first half of the 20th century – disseminated sclerosis, insular sclerosis, polysclerosis – the title of this book helped establish multiple sclerosis as the accepted name in the English speaking world.

Advances in technology

The second half of the 20th century saw advances in technology that gave a better understanding of MS.

Lumbar puncture

<u>Lumbar puncture</u> – the extraction of a sample of the fluid surrounding the spine – had been used in medicine since the 19th century. Although distinctive abnormalities associated with MS were recognised by the mid 1920s, these weren't properly explained until the 1940s when Elvin Kabat of Colombia University identified proteins in the fluid as resulting from damage to the coverings of nerves.

Imaging

Imaging techniques that can show damage caused by MS began to appear in the 1970s. CT or CAT (computed or computerised tomography) scans used x-rays to show cross sections of the brain that previously were impossible in live patients. Whilst groundbreaking at the time, the process was imprecise and could easily miss areas of scarring.

Work on developing <u>magnetic resonance imaging (MRI)</u> developed during the 1970s and in 1978 the first MRI cross section of a human head was created. MRI produced much clearer and more accurate images than CT scans and the role of the technique in observing MS was quickly recognised. The process was improved further in 1986 when gadolinium was developed as a marker that, when injected before a scan, made it possible to distinguish between active lesions and previous areas of scarring.

Disease modifying drugs

The first drugs that were shown to have some effect on altering the disease course of MS were based on interferons. Interferons, which occur naturally in the immune system, were first identified in 1957. The different types of interferon are released by white blood cells to alter the response to infections. In the 1970s and 1980s, researchers started looking at harnessing this process as potential treatments for MS. Studies showed that beta interferon, which helps to quieten activity in the immune system, slowed the relapse rate of someone with MS by a third on average. In 1995 a beta interferon drug became the first licensed disease modifying therapy for use in MS in the UK, two years after the treatment had become available in America.

At the same time as beta interferon was being developed, research was also looking at another drug that, although different in make up and action, has a similar effect. It was found that injecting some protein fragments (amino acids) from the structure of myelin (the covering of nerves) reduced disease activity. This led to the development of a mixture of protein fragments that was originally called copolymer-1 but which is now known as glatiramer acetate. This was licensed in the UK in 2000.

Whilst these drugs can slow disease activity for some people with relapsing forms of MS, they are not a cure and treatment is predominantly based on medication and management techniques for the various symptoms that people experience. Research continues for new disease modifying drugs.

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