

ASSI.SM onlus



SCLEROSI MULTIPLA (e non solo)

Cronologia delle osservazioni scientifiche dal 1380 al 2001 d.C.

1380	Lidwina born in Scheiden, Holland, patient
1677	Antoni van Leeywenhoek observed the myelin sheath on nerves
1701	Death of Margaret Davis (in Antiquities and Memoirs of the Parish of Myddle), patient
1790	Birth of William Brown, Hudson Bay Trader, patient
1794	Birth of Augustus d'Esté, grandson of King George III of England, patient
1797	Birth of Heinrich Heine, poet, patient
1807	Birth of Alan Stevenson, lighthouse designer, patient
1809	Birth of Margaret Gatty, Victorian writer and naturalist, patient
1824	First description of a case resembling MS by Charles Prosper Ollivier d'Angers
1831	Richard Bright described a case resembling MS
1836	Christian Gottfried Ehrenberg noted myelin and unmyelinated nerve fibers
1838	Richard Carswell illustrated a case of MS in his atlas
1841	Jean Cruveilhier illustrated cases of MS in his atlas
1849	Friedrich Theodor von Frerichs diagnosed "Hirnsklerose" in a patient during life
1855	Ludwig Türck described the pathology in MS
1857	Carl Rokitansky described the pathology of MS and the "fatty corpuscles" in the lesions
1863	Edward Rindfleisch noted the blood vessel in the center of the lesions
	E. Leyden described 34 cases and summarized the knowledge of the disease
1864	Carl Frommann published a well-illustrated book of sections of the spinal cord with the earliest illustration of demyelination
1866	Edmé Vulpian and Jean-Martin Charcot presented three cases to Société Médicale, Paris
1866	Vulpian published the three cases he and Charcot presented to Société Médicale
1868	Jean-Martin Charcot gave three lectures, later published, on sclérose en plaque disséminée
	J. C. Morris presented and published a case of MS in Philadelphia (with S. Weir Mitchell)
	Aggregation thesis on sclérose en plaque by L. Ordenstein, Charcot's student
	Charcot cases with illustrations published in Gazette Hôpitaux de Paris
1869	D.M. Bourneville and I. Guérard published monograph on MS with Charcot drawings
1870	Heinrich Schüle in Germany published 40-page report on a case of multiple Sklerose
	Meridith Clymer of Philadelphia reviewed 16 cases of MS and summarized Charcot's ideas
	Clifford Allbutt described optic neuritis and myelitis, later (1894) called Devic's disease
1871	A case of MS published in Allbutt's monograph on the ophthalmoscope
	William Hammond described nine cases in A Treatise on the Diseases of the Nervous System, the first American textbook of neurology
1872	Publication of Charcot's collected lectures
1872/73	Single case reports by Baldwin, Cook, Noyes, Boardman, and Kennedy
1873	MacLauren of Australia reported a case of retrobulbar neuritis
	C.H. Boardman of Minnesota, and Stiles Kennedy of Michigan published single cases
	MacLauren published a case of optic neuritis in Australia
1873-75	William Moxon published four anonymous reports in The Lancet
1875	William Moxon published a report of eight cases, two with autopsy
	Alfred K. Newman published a treatise on insular sclerosis in Australia
1875/76	Thomas Oliver published a translation of Charcot's lectures in Edinburgh Medical Journal
1877	London and Philadelphia publication of Charcot's lecture in English (Sigerson translation)
	Julius Althus coined the term "Charcot's Disease" for MS, though it was later discarded
1878	Description of the regular internodes in the myelin sheath by Louis Anthonie Ranvier
1878	Two cases published by Edward Constant Seguin of New York with autopsy findings
1879	William Osler presented three cases in Montreal
1880	Osler publication of three cases with pathology
	Seguin published three cases of optic neuritis and transverse myelitis
1882	Byrom Bramwell reviewed MS in his textbook on spinal disease
	Ribbert postulated vascular thrombosis due to infection as cause of MS plaques
	Carl Weigert of Frankfurt developed a stain for myelin
1884	Pierre Marie postulated infection as the cause of MS, which he felt would soon be

- prevented by a vaccine
- 1885 Joseph Babinski wrote a thesis on MS
Julius Althus of London wrote on the sclerosis of the spinal cord, with the last chapter on MS
Pelizaeus described a family with 12 cases of MS
Ehrlich showed injected aniline dyes did not stain the CNS, a fact that suggested a barrier
- 1887 **Hermann Oppenheim suggested toxins as a cause of MS**
- 1888 William Gowers summarized the knowledge of MS in his Manual of Diseases of the Nervous System
- 1890 Wilhelm Uhthoff described blurring of vision with exercise in MS (Uhthoff's phenomenon)
- 1891 Quinke developed therapeutic lumbar puncture
- 1893 Gowers reviewed MS in his textbook on diseases of the nervous system
- 1894 Devic and Gault described findings in optic neuritis with myelitis (Devic's disease) and Devic showed autopsy findings (1895)
- 1895 Pierre Marie published 25 cases of MS and argues infection as the cause in Insular Sclerosis and the Infectious Diseases
- 1897 **Joseph Babinski presented paper on plantar reflex at International Congress of Neurology, Brussels**
- 1899 Risien Russell reviewed MS
Robertson described the oligodendrocyte
- 1906 **Marburg postulated a myelinotoxic substance that caused breakdown of myelin in plaques**
Marburg described fulminant forms of MS (Marburg's disease)
- 1909 Curschmann described benign MS
- 1913 Kuhn and Steiner reported a spirochete (spirochete myelophthora) in MS CSF, which caused MS-like disease in guinea pigs and rabbits
- 1913 Bullock (Gye) reported transmission of MS from man to rabbits
Schilder described myelinoclastic diffuse sclerosis (Schilder's disease)
- 1915 James Dawson published his major work on the pathology of MS
- 1919 W.N.P. Barbellion (B.F. Cummings) published "Diary of a Disappointed Man"
- 1920 Curshman reported familial MS
- 1921 Meeting on MS at Association for Research on Nervous and Mental Disease (ARNMD), New York
Teague discounted transfusion experiments
Davenport demonstrated geographic pattern of MS in study of US Army draftees
Ayer and Foster described characteristics of CSF in MS
- 1922 Percival Baillie described incidence of MS in United States troops in World War I
- 1924 Follow-up ARNMD meeting on MS
Penfield described the morphology of oligodendrocytes and transformation of microglia to scavenger cells
Jacques Lhermitte described the shock-like sensation on neck flexion with posterior column irritation (Lhermitte phenomenon)
- 1926 Wilson and Cottrell systematically studied emotional and mental changes in MS
- 1927 Balo described (1913, 1924) concentric bands of demyelination (Balo's disease)
- 1928 Wechsler's Textbook of Neurology
- 1929 Ombredane's MD thesis on psychometric evaluation of 50 MS patients
- 1930 Russell Brain's landmark review of MS (Quarterly Journal of Medicine)
Kathleen Chevassut and James Purves-Stewart reported spherula insularis as the virus that causes MS, and a vaccine against it
- 1931 **Tracy Putnam injected oil into dog carotids and claimed to produce MS-like patches of demyelination**
Brickner announced his discovery of a lipolytic enzyme in MS plasma
A. Carmichael reported Chevassut–Purves-Stewart work valueless
- 1932 **Glanzmann publications on immune mechanisms in postinfectious leukoencephalopathy**

- 1933 Rivers, Sprunt, Berry developed model of EAE
Curtius outlined hereditary evidence in MS
Rivers and Schwentker developed EAE in monkeys
- 1936 Greenfield and King further described nature of MS plaque
Brickner advocated the "toxemia theory" of MS
- 1940-43 G. Schaltenbrand experiments on transmission of MS on institutionalized patients
- 1941 S.A. Kinnier Wilson review of MS in his posthumously published textbook
- 1942 Kabat showed pattern of immunoglobulins in MS CSF
- 1943-60 "Outbreak" of MS on Faeroe Islands
- 1944 Rucker noted retinal periphlebitis in some MS cases
Ferraro summarized nature of demyelinating diseases
- 1945 Atrophy in MS seen on pneumocephalography (Freeman, Cohen)
Sylvia Lawry placed an ad in the New York Times for information on MS for her brother
- 1946 Sylvia Lawry founded the Association for the Advancement of Research in MS (AARMS)
Reese reviewed MS
- 1947 Evelyn Opal began MS group named for Dr. Colin Russel in Montreal
Harry Bell in Montreal began Canadian MS Research Organization
Lawry brought them together in 1948 to form Multiple Sclerosis Society of Canada
- 1948 MS Society of Canada founded
AARMS renamed the National MS Society (NMSS)
Kabat reported IgG in the spinal fluid of MS patients
Bender clarified the internuclear ophthalmoplegia sign as a reflection of damage to the medical longitudinal fasciculus in the brain stem
ARNMD conference on MS
New York Academy of Sciences conference on "the status of MS"
Limberg geographic study of MS
Bing and Rees epidemiology study in Switzerland
Medawar postulated concept of the brain as an immunologically privileged site
MacKay reviewed all familial reports 1896-1948 (published 1950)
Kurland and Westlund showed no relationship of trauma and MS
Roy Swank and Bert Cosgrove began the MS Clinic at the Montreal Neurologic Institute (MNI)
- 1950 Swank published relationship of dietary fat intake and MS
Swank developed his low fat diet for MS, assisted by dietician Aagot Grimsgard
Schumacher reviewed MS and outlined early MS diagnostic criteria
NMSS funded first major study of MS in the United States and Canada
NMSS lobbied for formation of NINBD
Schumacher classified MS as remittent and progressive forms
Leo Alexander began MS Clinic in Boston
- 1951 **Jonsson reported use of cortisone in MS**
Alexander defined criteria for MS trials and assessment
Houston Merritt asked resident William Sibley to compile information on MS therapies for report to NMSS
- 1952 Lord Howard invited Sylvia Lawry to meet with Richard Cave in London
- 1953 Kurtzke designed trial of isoniazid using evaluation that would become the DSS
Multiple Sclerosis Society of Great Britain and Northern Ireland formed
- 1954 Waxman showed proteolipids of myelin were encephalitogenic
MS lesion seen on isotope brain scan (Seaman et al.)
Bert Cosgrove and Roy Swank began MS Clinic at the Montreal Neurological Institute
Leo Alexander of Boston began his MS clinic
- 1955 First edition of Multiple Sclerosis by McAlpine, Compston, and Lumsden
Kurtzke outlined Disability Status Scale (DSS)
International Neuropathological Conference, London, satellite meeting on MS
- 1956 Kies, Roby, and Alford showed myelin basic protein to be encephalitogenic

- 1957 Melvin Thomas opened MS Clinic at the University of Pennsylvania
 NMSS co-sponsored conference on new research techniques of neuroanatomy
Interferons discovered by two groups (Issacs and Lindenmann, Negano and Kojima)
 1958 George Guillain wrote biography of Charcot
 HLA system described by Dausset
- 1959 Scandinavian conference on blood and CSF studies in MS
 First conference on the geography of MS, Copenhagen
- 1960 Royal Society of Medicine Symposium on MS
 R.H.S. Thompson postulated lysolecithin as a lytic substance in brain
 NMSS sponsored epidemiology study of MS in Australia, Norway, Israel, and Iceland
- 1961 Henry Miller carried out first placebo-controlled doubleblind trial in MS showing prednisone ineffective
Bunge, Bunge, and Ris showed oligodendrocyte responsible for myelination and remyelination
 Milton Alter established the Israeli National Register of Neurological Disease
 Second conference on the geography of MS, Copenhagen
- 1962 NMSS co-sponsored conference on mechanisms of demyelination
 New York Academy of Medicine republished an 1881 version of Charcot's lectures
 LeGac said MS due to rickettsia; created LeGac treatment
 Adams and Imagowa reported higher measles antibodies in MS
 McDonald showed conduction block in dorsal root ganglia of cats with diphtheria toxin
- 1963 **Second Scandinavian Conference on MS, focused on vesselplaque relationships and on CSF changes**
- 1964 Lature demonstrated oligoclonal bands in MS CSF
 Wheelock and Sibley noted appearance of interferon in serum after viral infections
 Multiple Sclerosis Treatments Investigation Group (MSTIG) set up as a breakaway U.K. group to foster research on therapy
- 1965 Criteria for the diagnosis of MS described
 Schumacher criteria outlined
 First electron microscopic pictures of MS plaque by Perier and Gregoire
 International Federation of MS Societies formed (now the MS International Federation)
- 1969 E.J. Field found no evidence of antibodies to rickettsia organisms in MS
- 1970 Controlled study by Augustus Rose showed that ACTH is beneficial in acute attacks
 McDonald showed effects of experimental demyelination on conduction
 MacDougall diet explained in book "No Bed of Roses"
- 1971 MS Conference at Newcastle-Upon-Tyne
- 1972 NIH and NMSS fund virology program at Pennsylvania (Silberberg and Wistar Institute) (Koprowski)
 McDonald and Halliday showed conduction slowing and block in demyelinated nerves
 McDonald and Halliday applied evoked potential methods to MS
 Relationship of MS to HLA-A3 (Naito et al.)
 Tolbutamide widely used for MS therapy
- 1973 Preliminary Belfast-London trial of diet low in animal fat plus evening primrose oil suggested some benefit for MS patients
- 1974 National Advisory Commission on MS (DHEW)
 CAT-scan demonstration of an MS lesion confirmed by biopsy (Davis, Pressman)
 PET scans developed
 Multiple Sclerosis Action Group (U.K.) formed as a breakaway group to speed up research
 American Academy of Neurology formed Ad Hoc
 Committee on Neuroimaging, with first meeting in 1977 at Hilton Head, SC
- 1975 Compston demonstrated relationship of MS to HLA-DR2
- 1976 Carp reported inhibition of tissue culture cells by MS tissue, later called "Carp Agent"
 Rose criteria of MS
 Atrophy seen in 45 percent of MS CAT scans (Gyldensted)

- 1976-89 Transfer factor trials, mostly negative
- 1977 General considerations for clinical evaluation of drugs (DHEW)
Michelle Revel developed interferon beta-1a in CHO cells at Weitzman Institute
American Society of Neuroimaging founded by William Oldendorf
McDonald and Halliday diagnostic criteria of MS
Jacobs administered interferon intrathecally to MS patients
- 1978 Prineas demonstrated the fine structure of the MS plaque
Prineas showed macrophages, plasma cells, and microglia in areas of myelin destruction and reaction to antigen in new lesions
Prineas demonstrated patterns of myelin repair in MS plaques
Waksman suggested trial of interferons in MS
- 1979 Design of clinical studies in MS (Brown et al.)
Prineas and Connell showed process of remyelination in MS
Cord atrophy (contracting cord sign in MS) on myelography (Haughton)
Nobel Prize to Hounsfield and Cormack for CAT scan technology
- 1980 Wessman takes out patent for coliform produced interferon World Health Organization
International classification of impairments, disabilities, and handicaps
- 1981 First MRI scans of brain (Doyle et al.)
MS Costar initiated by Studney and Paty
Grand Island conference on clinical trials in MS
First MRI images of MS lesions (Young et al.)
Jacobs reported reduced attacks of MS with intrathecal interferon
- 1982 Therapeutic claims in MS published by IFMSS
More MS lesions demonstrated by high-volume delayed (HVD) CAT scanning (Vinuela et al.)
- 1983 Poser criteria for MS
Proceedings of 1981 International Conference on
Therapeutic Trials in MS (Herndon and Murray)
Bray suggested Epstein-Barr virus may be involved in MS
Lassman showed thin remyelinated fibers formed by oligodendrocytes
Kurtzke outlined Expanded Disability Status Scale (EDSS)
Hauser ambulatory scale
- 1984 Sipe reported Scripps Neurologic Rating Scale (NRS)
First systematic study of MRI in MS by Paty and Li 53 percent of HVD-CAT scans positive in acute relapses (Ebers)
- 1985 Incapacity Status Scale (Haber, LaRocca)
Minimal Record of Disability (MRD) (Haber, LaRocca)
Jack Conomy organized Consortium of MS Centers (CMSC)
- 1986 Canadian collaborative study on twins (Ebers and Sadovnick)
Troiano scale (proposed by Cook et al.)
Functional independence scale outlined (Granger et al.)
MRI lesion correlated with pathology (Stewart et al.)
Gadolinium-enhanced developed (Gd-DPTA) MRI (Crossman)
- 1987 Pilot trial of Cop 1 (Bornstein)
Duquette and Murray review childhood MS
Jacqueline du Pré died
- 1988 **Trial of azathioprine**
MRI criteria for MS lesions and diagnosis (Paty et al.)
MRI studies related to pathological and MS dynamics (Paty)
MRI criteria for MS lesions and diagnosis (Fazekas et al.)
- 1990 Canadian trial of cyclophosphamide and plasma exchange in progressive MS
Trial of cyclosporin
- 1991 McDonald suggested axonal damage might be the determinant of progression in MS
Sibley et al. showed no relationship of stress and trauma to MS attacks
Rehabilitation in MS (RIMS) formed in Milan, Italy

- 1992-95 McDonald et al. demonstrated series of events in development of MS lesions
- 1993 **Betaseron® trial positive. Early approval by FDA in United States**
Prineas showed inflammatory process and debris removal was crucial to remyelination
 Pathology on a case 10 days after Gd-DTPA-enhanced MRI (Katz)
- 1994 Arnold showed axonal loss on MR spectroscopy
Avonex® trial positive
 Film on life with MS of actress Annette Funicello
- 1995 **Betaseron® approved for use in MS patients in Canada**
Copaxone® approved by FDA (United States)
Rebif® –PRISMS study reported
- 1996 Advisory Committee on Clinical Trials (NMSS) classification of MS types
 Compston focused on the need for remyelination therapy in MS (Charcot lecture)
Avonex® approved by FDA (United States)
 International Symposium on retrovirus in MS, Copenhagen
 NARCOMS database (Vollmer)
- 1997 **Copaxone® approved in Canada**
 WHO International Classification of Impairments, Disabilities and Handicaps Update (ICIDA-2)
- 1998 Trapp illustrated and quantified axonal loss in new and old plaques and in “normal” white matter
 Linomide trial discontinued due to cardiac effects
 RISMS trial shows benefit for Rebif®
Rebif® excluded from United States markets by FDA due to orphan drug legislation protecting Avonex®
- 1999 **Research Council established funding for research on medical benefits of marijuana**
 Oral myelin trial failed to show benefit (Weiner)
 ETOMS trial positive for early therapy in MS
 Sonya Slifka longitudinal study initiated (NMSS)
- 2000 CHAMPS trial showed interferon beta-1a (Avonex®) beneficial after the first symptoms indicative of MS
Mitoxanthrone (Novantrone®) approved for treatment of MS (United States)
SPECTRIMS trial shows no effect of Rebif® in secondary progressive MS
 MS drugs again rejected for coverage by National Health Service (U.K.)
Risk of MS in children of conjugal MS parents 30.5 percent, similar to risk of identical twins (Canadian Collaborative Project on Genetic Susceptibility to MS)
 Position paper on diagnostic criteria for primary progressive MS (Thompson et al.)
 MNSS gave its largest grant (\$1.8 million) to the MS Lesion Project under Claudia F. Lucchinetti
- 2001 Confavreaux et al. showed no relationship of vaccines and MS
 Institute of Medicine (IOM) report on a strategic review of MS research (Sponsored by NMSS)
New criteria for diagnosis of clinically definite multiple sclerosis (McDonald et al.)
 EVIDENCE trial first head-to-head trial of immune modulating drugs (Rebif® and Avonex®)
 Position paper of international committee to define the classification of MS types (McDonald)

INCOMIN Trial