

Geschichte der MS

Erste Beschreibungen von MS-Kranken aus dem 14. Jahrhundert

- **Lidwina von Schiedam (1380 - 1433)**
- Schubförmige Erkrankung
- Erblindung links
- Parese linker Arm
- Leiden als Prüfung Gottes angesehen



Geschichte der MS

- **Augustus Frederick d'Este (1794 - 1848)**
- Enkel des britischen Königs Georg III.
- Schubförmige Erkrankung
- Sehstörung mit 28 Jahren
- Paresen
- Schmerzen
- Sensibilitätsstörungen



Geschichte der MS

- **Heinrich Heine (1797 – 1856)**
- Chronisches Nervenleiden
- Parese der linken Hand
- Zwei Jahre später Sehstörung
- Neun Jahre später bulbäre Störung
- Schließlich Paraplegie



Geschichte der MS

Erstbeschreibung

- Robert Carswell (1793 – 1857)
und Jean Cruveilhier (1793 - 1873)

gelten als Erstbeschreiber der MS



Geschichte der MS

Erste klinische Beschreibung

- Friedrich von Frerichs (1819 - 1885)
- Erste klinische Beschreibung
- „Hirnsklerose“ 1849
- Diagnosesicherung post mortem durch Valentiner



Geschichte der MS

Charcot-Trias

Jean-Martin Charcot (1825 - 1893)

- Erarbeitete Histologie
- Mit Markscheidenzerfall
- Beschrieb typische Symptome:
 - Unkontrollierbare Augenbewegungen (Nystagmus)
 - Gliedmaßenzittern bei zielgerichteter Bewegung (Intentionstremor)
 - Besondere Sprachstörungen (skandierende Sprache)



Geschichte der MS

1935 – EAE - als Tiermodell

- Durch Rivers und Schwentker
- Injektion von Hirngewebe mit abgetöteten Tuberkelbazillen
- Markscheiden werden nach der Geburt gebildet – keine Immuntoleranz
- Keine Lymphbahnen im ZNS
- Blut-Hirn-Schranke
- Immunologische Sonderstellung des ZNS



Geschichte der MS

1946 – US National MS Society

- Sylvia Lawry (1915 – 2001)
- Ihr Bruder erkrankte an MS
- Gründet mit 20 Neurologen die erste MS-Gesellschaft
- Infolge entstehen weltweit 43 MS-Gesellschaften
- Sie setzen sich für die Belange der Erkrankten ein



Geschichte der MS

1957 – Interferone werden entdeckt

Virus interference. I. The interferon

BY A. ISAACS AND J. LINDENMANN*

National Institute for Medical Research, London

(Communicated by C. H. Andrewes, F.R.S.—Received 7 March 1957)

During a study of the interference produced by heat-inactivated influenza virus with the growth of live virus in fragments of chick chorio-allantoic membrane it was found that following incubation of heated virus with membrane a new factor was released. This factor, recognized by its ability to induce interference in fresh pieces of chorio-allantoic membrane, was called interferon. Following a lag phase interferon was first detected in the membranes after 3 h incubation and thereafter it was released into the surrounding fluid.



Geschichte der MS

1993 – Interferon beta-1b wird eingeführt

Interferon beta-1b is effective in relapsing-remitting multiple sclerosis.

I. Clinical results of a multicenter, randomized, double-blind, placebo-controlled trial

The IFNB Multiple Sclerosis Study Group*

Article abstract—We report a multicenter, randomized, double-blind, placebo-controlled trial of interferon beta-1b (IFNB) in 372 ambulatory patients with relapsing-remitting multiple sclerosis (MS). Entry criteria included an Expanded Disability Status Scale (EDSS) score of 0 to 5.5 and at least two exacerbations in the previous 2 years. One-third of the patients received placebo, one-third 1.6 million international units (MIU) of IFNB, and one-third 8 MIU of IFNB, self-administered by subcutaneous injections every other day. The primary end points were differences in exacerbation rates and proportion of patients remaining exacerbation-free. The annual exacerbation rate for patients receiving placebo was 1.27; for 1.6 MIU IFNB, 1.17; and for 8 MIU IFNB, 0.84 after 2 years. Exacerbation rates were significantly lower in both treatment groups compared with the placebo group (8 MIU versus placebo, $p = 0.0001$; 1.6 MIU versus placebo, $p = 0.0101$; and 8 MIU versus 1.6 MIU, $p = 0.0086$), suggesting a dosage effect. The reduction in exacerbation severity in the 8 MIU group was attributable to a twofold reduction in the frequency of moderate and severe attacks. More patients in the 8 MIU group ($n = 36$) were exacerbation-free at 2 years compared with the placebo group ($n = 18$; $p = 0.007$). EDSS scores changed little from baseline in both the placebo and treatment arms. Accordingly, a significant change in disability could not be discerned in this trial. Finally, in serial MRIs, MS activity was significantly less in the high-dose IFNB group. IFNB treatment was well tolerated: the significant reductions in exacerbation rates, severity of exacerbations, and accumulation of MRI abnormalities occurred in the absence of serious side effects. IFNB is the only treatment that has substantially altered the natural history of MS in a properly controlled clinical trial.

NEUROLOGY 1993;43:655-661



Geschichte der MS

1996 – Interferon beta-1a wird eingeführt

ARTICLES

Randomised double-blind placebo-controlled study of interferon β -1a in relapsing/remitting multiple sclerosis

Lancet 1998; **352**: 1498–504

*PRISMS (Prevention of Relapses and Disability by Interferon β -1a Subcutaneously in Multiple Sclerosis) Study Group**

EXPEDITED PUBLICATIONS

Intramuscular Interferon Beta-1a for Disease Progression in Relapsing Multiple Sclerosis

Lawrence D. Jacobs, MD,* Diane L. Cookfair, PhD,† Richard A. Rudick, MD,‡ Robert M. Herndon, MD,\$ John R. Richert, MD,¶ Andres M. Salazar, MD,** Jill S. Fischer, PhD,‡ Donald E. Goodkin, MD,†† Carl V. Granger, MD,‡‡ Jack H. Simon, MD, PhD,\$\$ John J. Alam, MD,¶¶ David M. Bartoszak, MD,** Dennis N. Bourdette, MD,*** Jonathan Braiman, MD,** Carol M. Brownschidle, PhD,* Michael E. Coats, MD,** Stanley L. Cohan, MD,¶ David S. Dougherty, MD,** Revere P. Kinkel, MD,‡ Michele K. Mass, MD,\$ Frederick E. Munschauer, III, MD,* Roger L. Priore, ScD,† Patrick M. Pulicino, MD, PhD,* Barbara J. Scherokman, MD,††† Bianca Weinstock-Guttman, MD,‡ Ruth H. Whitham, MD,*** and The Multiple Sclerosis Collaborative Research Group (MSCRG)

Ann Neurol 1996;39:285–294



Geschichte der MS

1996 – Zulassung von Glatirameracetat

Copolymer 1 reduces relapse rate and improves disability in relapsing-remitting multiple sclerosis:

Results of a phase III multicenter, double-blind, placebo-controlled trial

K.P. Johnson, MD; B.R. Brooks, MD; J.A. Cohen, MD; C.C. Ford, MD; J. Goldstein, MD; R.P. Lisak, MD; L.W. Myers, MD; H.S. Panitch, MD; J.W. Rose, MD; R.B. Schiffer, MD; T. Vollmer, MD; L.P. Weiner, MD; J.S. Wolinsky, MD; and the Copolymer 1 Multiple Sclerosis Study Group*

Article abstract—We studied copolymer 1 (Copaxone) in a multicenter (11-university) phase III trial of patients with relapsing-remitting multiple sclerosis (MS). Two hundred fifty-one patients were randomized to receive copolymer 1 ($n = 125$) or placebo ($n = 126$) at a dosage of 20 mg by daily subcutaneous injection for 2 years. The primary end point was a difference in the MS relapse rate. The final 2-year relapse rate was 1.19 ± 0.13 for patients receiving copolymer 1 and 1.68 ± 0.13 for those receiving placebo, a 29% reduction in favor of copolymer 1 ($p = 0.007$) (annualized rates = 0.59 for copolymer 1 and 0.84 for placebo). Trends in the proportion of relapse-free patients and median time to first relapse favored copolymer 1. Disability was measured by the Expanded Disability Status Scale (EDSS), using a two-neurologist (examining and treating) protocol. When the proportion of patients who improved, were unchanged, or worsened by ≥ 1 EDSS step from baseline to conclusion (2 years) was evaluated, significantly more patients receiving copolymer 1 were found to have improved and more receiving placebo worsened ($p = 0.037$). Patient withdrawals were 19 (15.2%) from the copolymer 1 group and 17 (13.5%) from the placebo group at approximately the same intervals. The treatment was well tolerated. The most common adverse experience was an injection-site reaction. Rarely, a transient self-limited systemic reaction followed the injection in 15.2% of those receiving copolymer 1 and 3.2% of those receiving placebo. This reaction was characterized by flushing or chest tightness with palpitations, anxiety, or dyspnea and commonly lasted for 30 seconds to 30 minutes. This rigorous study confirmed the findings of a previous pilot trial and demonstrated that copolymer 1 treatment can significantly and beneficially alter the course of relapsing-remitting MS in a well-tolerated fashion.

NEUROLOGY 1995;45:1268-1276

