Historic Survey of MS Research Progress

In 1945, a small classified ad appeared in *The New York Times*:

**Multiple sclerosis.** Will anyone recovered from it please communicate with patient.

The ad was placed by Sylvia Lawry, whose brother Bernard had been diagnosed with MS, and whose family was frustrated by the lack of treatment options.

At that time, relatively little was known about multiple sclerosis. MS was still being misdiagnosed as “hysteria” or “chronic alcoholism”; some doctors mistakenly believed MS was contagious; there was no private or government agency charged with conducting research into multiple sclerosis.

In answer to the ad, no one came forth with a treatment. But many came forth with the need and desire to do something about this urgent problem. In 1946 the National Multiple Sclerosis Society was established, and in 1947 the Society sponsored its first three research projects.

Today, the Society has invested a total of some $420 million in biomedical research to solve the puzzle of MS, and is the largest private sponsor of MS research in the world. Although Sylvia Lawry died in 2001, her spirit and mission live on in the millions of researchers, health professionals, volunteers, donors and event participants we count on each year to contribute to our cause: To end the devastating effects of multiple sclerosis.
Searching for MS Therapies

Even before French neurologist Jean-Martin Charcot first described multiple sclerosis as a distinct disease in 1868, physicians were attempting therapy based on contemporary beliefs about its cause. Recognizing the neurologic characteristics of the disease, Charcot tried the arsenal of remedies then used to “treat” such disorders: gold chloride, zinc sulfate, silver nitrate, strychnine, electrical stimulation, belladonna, ergot and hydrotherapy, all “without favorable results.”

When MS was attributed to overexertion (1880s), attempted treatments included bedrest and electrical stimulation. When a poison, toxin or metabolic abnormality were blamed (early 1900s and later), treatments included purgatives, cathartics, stimulants, various enzymes and even tonsillectomy.

Infectious agents have been suspected over the years (1920s, today), giving rise to treatments including antisyphilis drugs, fever therapy (by regular injections of typhoid vaccine), vaccines, antibiotics and blood transfusions. The preponderance of MS brain lesions near blood vessels led to speculations that MS was caused by poor circulation of blood in the brain and blood clots (1930s-40s), thus anticoagulants were prescribed.

Allergy was thought to play a role in MS for two decades (1950s-70s); treatment centered on antihistamines, vitamins and steroids. From the late 1970s to the present, MS has been thought to be an autoimmune reaction (in which the immune system turns on the body’s own tissues), possibly triggered by an infectious agent(s). Treatment now focuses on curbing destructive immune responses with steroids and immune-system regulators.

Importance of Controlled Trials

Multiple sclerosis is unusual in that its symptoms often abate spontaneously. So the task of determining whether a given treatment is responsible for a remission or improvement has been difficult. That’s why well controlled trials, usually involving hundreds of patients, in which neither the physician nor the patient knows who is receiving which treatment (“double blinded”), are vital to identifying genuine therapies for multiple sclerosis.

Looking Ahead

As more and more is uncovered about the disease mechanisms at work in MS, treatments become more specialized, and we have a greater chance of treating the underlying cause of the disease. There are now more than 100 clinical trials of potential treatments in various stages of testing around the world. Therapies now being tested include:

♦ custom-designed molecules that can turn off only the specific destructive immune forces active in an individual’s body by actually blocking or providing decoy mechanisms for damaging immune events;
<table>
<thead>
<tr>
<th>If you had multiple sclerosis in...</th>
<th>1890</th>
<th>1910</th>
<th>1940</th>
<th>1960</th>
<th>2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>The cause was thought to be...</td>
<td>suppression of sweat</td>
<td>unknown toxin in blood</td>
<td>blood clots and poor circulation</td>
<td>allergic reaction</td>
<td>autoimmune reaction, possibly linked to infection</td>
</tr>
<tr>
<td>You probably be treated with...</td>
<td>herbs and bedrest</td>
<td>purgatives and stimulants</td>
<td>drugs that improve circulation</td>
<td>vitamins and anti-histamines</td>
<td>steroids, immune regulators</td>
</tr>
<tr>
<td>Your life expectancy after diagnosis...</td>
<td>5 years</td>
<td>10 years</td>
<td>18 years</td>
<td>25 years</td>
<td>essentially normal for most</td>
</tr>
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Life expectancy from time of diagnosis increased over time as management and control of complications improved. (Chart based on research by Loren A. Rolak, MD, neurologist and medical historian, Marshfield MS Center, The Marshfield Clinic, Marshfield, Wisconsin.

♦ agents that can stop destructive immune cells from crossing the blood-brain barrier, in attempts to prevent inflammation and nerve tissue destruction before they start;
♦ drugs that can manipulate “messenger” signals to actually turn aggressive immune cells into peacekeeping immune cells, halting the immune response in its tracks;
♦ agents that may stimulate the repair of brain and spinal cord tissue that has been damaged in MS, or procedures that infuse replacement cells, which could be given once the destructive process has been halted; and
♦ drugs to fight specific infectious agents that may directly or indirectly trigger MS.

MS History Fact

1400s- The earliest written record of someone with MS was Lydwina of Schieden, Dutch patron saint of iceskaters
Timeline of MS Research Progress

This timeline highlights a selection of major landmarks in research into multiple sclerosis, over a backdrop that charts the National MS Society’s total cumulative research investment of $420 million. These are only a few of thousands of advances in basic and clinical research which have laid the foundation for the rapid progress we’re seeing today.

1946 National Multiple Sclerosis Society formed by Sylvia Lawry.

1947 Society sponsors first 3 research projects.

1948 Dr. Elvin Kabat, first Society grantee, discovers “oligoclonal bands” in MS spinal fluid, leading to an important diagnostic test.

1949 Society convinces US Congress to create a new national institute devoted to researching neurological diseases.

1950 Society funds first major survey of MS in the US and Canada.

1955 Dr. John Kurtzke develops first scale to categorize the severity of MS; a later version (EDSS) is still in use today.

1965 Society-convened panel of experts develops precise criteria for diagnosing MS.

1967 Multiple Sclerosis International Federation is formed.

1969 Society co-sponsors research of ACTH, which becomes the first drug shown to speed recovery from MS attacks.

1974 Society convinces US Congress to appoint commission on MS; resulting report increases federal funding for MS research.

1960 NMSS launches epidemiology studies of MS in Australia, Norway, Israel and Iceland; later grantees would explore “Clusters” of MS in the Faeroe and Orkney islands.

$3.2 million
**1980** Society funds first large trial of any form of interferon (interferon alpha), stimulating interest in interferons for treating MS.

**1981** Society sponsors international conference establishing double-blind, placebo-controlled clinical trials as gold standard for MS.

**1981** First MRI pictures of a brain affected by MS are produced, revolutionizing MS diagnosis.

**1982** Society supports first comprehensive search for the genes that make people susceptible to MS.

**1987-88** Society launches research programs in health care delivery and health policy, as well as patient management, rehabilitation, and psychosocial aspects of MS.

**1988** Society initiates targeted research into gender differences in MS and establishes the Sonya Slifka Longitudinal MS Study, a research-oriented nationwide patient database.

**2000** Novantrone approved in US for worsening forms of MS.

**2001** Society task force develops first new diagnostic criteria for MS in 20 years.

**2002** Society launches Collaborative MS Research Centers program to enhance cross-pollination of ideas and attract new scientists to MS research.

**2003** Over 150 MS clinical trials going on worldwide, including tests in primary- and secondary-progressive MS, trials of oral medications, and combination therapies.

**1993** Betaseron approved by FDA as first drug to alter the underlying course of relapsing-remitting MS.

**1996** Avonex and Copaxone approved by the FDA for relapsing-remitting MS. Zanaflex, an oral drug to fight spasticity, also approved.

**1998** Society initiates targeted research into gender differences in MS and establishes the Sonya Slifka Longitudinal MS Study, a research-oriented nationwide patient database.

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**2002** Rebif approved in US for relapsing MS.

**2003** Over 150 MS clinical trials going on worldwide, including tests in primary- and secondary-progressive MS, trials of oral medications, and combination therapies.

**2004** $420 million

**2001** Society task force develops first new diagnostic criteria for MS in 20 years.

**2000** Society launches The MS Lesion Project to correlate patterns of tissue loss with clinical disease and MRI.

**2000** Novantrone approved in US for worsening forms of MS.

**1996** Avonex and Copaxone approved by the FDA for relapsing-remitting MS. Zanaflex, an oral drug to fight spasticity, also approved.

**1993** Betaseron approved by FDA as first drug to alter the underlying course of relapsing-remitting MS.

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Stimulating MS Research: Yesterday, Today and Tomorrow

From the beginning, a role of the National MS Society has been to fund research seeking clues to the cause, treatment and cure of multiple sclerosis, and to spark MS research efforts around the world:

Increasing Federal Research Spending

In 1950 the National MS Society successfully convinced the U.S. Congress to create a new national institute devoted to neurological and related diseases. What is now the National Institute of Neurological Disorders and Stroke was born, becoming partners with the Society in supporting basic and clinical research into MS.

Worldwide Network

In 1967, Society founder Sylvia Lawry established what is now known as the Multiple Sclerosis International Federation, a worldwide association of nearly 40 organizations devoted to carrying on important MS research and services. In 2000, the Society committed substantial support to MSIF’s Sylvia Lawry Centre in Munich. One goal of the Centre is to collect and analyze data from major natural history studies and clinical trials of treatments for MS to create “virtual” placebo groups – statistical portraits that researchers could use to more quickly evaluate new MS therapies.

Attracting Top Minds

To attract promising young investigators to the field of MS, in 1955 the Society developed a postdoctoral research training program. This program has trained many of the country’s leading MS investigators, and ensures that top-notch minds will always be focused on the problems of MS until a cure is found.

MS History Fact

1919- Abnormalities in the spinal fluid were discovered in MS, but their significance remained puzzling for decades

Seed Money

The National MS Society often plants research “seeds” from which great things grow. Long before pharmaceutical companies became interested, the Society was supporting clinical trials of drugs to treat MS. One of the earliest grants the Society gave, in 1950, was to conduct preliminary tests of the steroid ACTH in MS. This drug was proved (with Society funding) to be the first to speed recovery from MS exacerbations.

The Society was the first to fund a large-scale clinical trial of any type of interferon - alpha interferon - in the early 1980s, spurring industry interest in this immune-system regulator. Ultimately, in 1993 Betaseron was approved as the first drug to alter the underlying course of MS. Today there are five drugs approved in the U.S. for treating different forms of the disease.
Cross-Fertilization

MS involves diverse fields: basic and clinical immunology, neurophysiology, virology, genetics, rehabilitation, and many others. To facilitate cross-fertilization of ideas among researchers from different realms, the Society supports scientific workshops on topics relevant to MS. Over the years, many of these workshops have been springboards for crucial leaps forward in our approach to MS.

In 2002, the Society launched a Collaborative MS Research Center program to further stimulate interaction of researchers from diverse fields and to attract new scientists to MS research.

Harvesting New Ideas

Since 1987, the Society has used special pilot research grants to cultivate novel or high-risk research ideas and attract new investigators to the field of MS. These low-cost, short-term awards allow quick determinations as to whether a new idea merits full-scale exploration.

With a cumulative investment of some $350 million to fund and stimulate MS research, the Society has laid a foundation of basic and clinical knowledge upon which all advancements are built, and planted the seeds for tomorrow’s breakthroughs.

Top 10 Events: History of MS

1. Disease described by Jean-Martin Charcot (1868).
2. Discovery of myelin’s role in nerve conduction by Louis Ranvier (1878). Later researchers discovered the cell that makes myelin (oligodendrocyte).
3. Detailed microscopic description of diseased brain tissue by James Dawson (1916) revealed the basic processes at work in MS.
4. Development of an animal disease resembling MS by Thomas Rivers (1935), ultimately suggesting an autoimmune basis for the disease, with myelin in the central nervous system as the target.
6. Discovery of oligoclonal bands in the spinal fluid by Elvin Kabat and others (1948), providing a diagnostic test suggestive of MS and further linking it to the immune system.
7. Definite criteria for the diagnosis of MS developed by an expert committee gathered by the NMSS (1965).
8. ACTH proved to treat MS exacerbations (1969-70). This was the first careful, controlled trial of a successful treatment for MS, using standardized diagnostic criteria and rating scales for evaluating MS patients.
9. MRI invented, with the first images of an MS patient (1981). MRI revolutionized the diagnosis of MS and established the concept of MS as a constantly active disease rather than a relapsing one.
10. Interferon beta 1-b (Betaseronr) approved as the first drug to alter the course of MS (1993).

- by Loren A. Rolak, MD, neurologist and medical historian, Marshfield MS Center, The Marshfield Clinic, Marshfield, Wisconsin
Improving Diagnosis

Over the years, hundreds of researchers have tried to identify a test that could determine quickly whether or not a person has MS:

♦ In the 1920s, post-mortem tissue studies were the only reliable way of saying that a person had definite MS.
♦ In the 1930s came the “hot bath test,” wherein someone suspected of having MS was placed into a hot bath and observed for symptom changes.
♦ In the late 1940s, Dr. Elvin Kabat and others discovered abnormal immune-system antibodies, called “oligoclonal bands,” in MS spinal fluid. Although not exclusive to MS, this finding became the basis of an important new diagnostic test.
♦ In 1981, diagnosis was changed forever with the introduction of magnetic resonance imaging (MRI). Although it cannot be used alone to diagnose MS, MRI in combination with other tests has been invaluable in speeding the diagnosis of MS.
♦ In 2001, a National MS Society task force developed the first new diagnostic criteria for MS in 20 years, incorporating MRI and other benchmarks to help speed diagnosis. People get answers much faster than they did even a decade ago, enabling them to have access to disease-modifying drugs faster.

MS History Fact

1920s- Men were thought to be more susceptible to MS than women. Why? Because women were often mistakenly diagnosed with “hysteria”

The National MS Society is proud to be a source of information about MS. Our comments are based on professional advice, published experience and expert opinion, but do not represent individual therapeutic recommendation or prescription. For specific information and advice, consult your personal physician. For more information about MS research, call: 1-800-FIGHT MS, or visit our Web site: www.nationalmssociety.org.

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