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Introduction

Multiple sclerosis (MS) is a chronic and unpredictable, often disabling disease of the central nervous system, which is made up of the brain, spinal cord, and optic nerves. MS interrupts the flow of information within the brain and between the brain and the body. Symptoms range from numbness and tingling to blindness and paralysis. The progress, severity and specific symptoms of multiple sclerosis in any one person cannot yet be predicted, but advances in research and treatment are moving us closer to a world free of MS. More than 2.3 million people are affected by MS worldwide.

Research on multiple sclerosis was almost nonexistent in 1945, the year 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. 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 born and in 1947 the Society sponsored its first three research projects. Today, the National MS Society funds more MS research than any other MS organization in the world. Research sponsored by the Society and our many partners in government, other MS organizations around the world, and the private sector has led to major advances in our understanding and treatment of this complex disease.
Although the cause of MS is still unknown, thanks to global research efforts, we’ve already seen some immense successes. Society efforts have led to faster, more accurate diagnosis of MS, shortening the wait for answers, and offering earlier treatment, which may help prevent nervous system damage. Our breakthrough research has helped identify some of the genes that contribute to MS susceptibility — a key in understanding the cause and how to prevent MS. We’re at the forefront of entirely new areas of MS research including the discovery of nerve and myelin repair potential. And we’re making strides in the area of wellness and rehabilitation research, testing these solutions and others so that people with MS can live their best lives every day. During the last 70 years, the Society has been involved in virtually every major breakthrough in treating and understanding the disease.

Our goal is to drive scientific breakthroughs to end MS and identify everyday solutions that change the lives of people with all forms of MS. This brochure traces the comprehensive and holistic approach being taken to stop MS is its tracks, restore lost function and end MS forever.
What we know about MS drives research efforts

MS is an immune-driven disease

In MS, the body’s own immune defense system attacks myelin, the fatty substance that surrounds and protects the nerve fibers in the central nervous system. The nerve fibers themselves are also damaged. The damaged myelin forms scar tissue (sclerosis), which gives the disease its name. When any part of the myelin sheath or nerve fiber is damaged or destroyed, nerve impulses traveling to and from the brain and spinal cord are distorted or interrupted, producing the variety of symptoms that can occur. Destruction of nerve fibers is thought to lead to disease progression and disability.
Research into the immune processes and the damage they cause is providing insights and new targets to stop MS in its tracks; and understanding how nerves and myelin work and how they respond to damage is providing new leads in the quest to reverse the damage and restore function. This research also is driving wellness initiatives forward, as we begin to understand how gut bacteria or diet may affect the immune attack in MS, and how probiotic or other diet-related strategies might be employed to stop this attack.

What causes MS and its progression?

While the cause of MS is still not known, scientists believe that a combination of several factors may be involved in causing MS. MS is known to occur more frequently in geographic areas that are farther from the equator. Epidemiologists — scientists who study disease patterns — are looking at many factors, including variations in geography, demographics (age, gender, and ethnic background), genetics, infectious triggers and migration patterns, in an effort to understand:

- Why are women at a higher risk for developing MS than men?
- How do a person’s genes make them susceptible to whatever causes MS (but genes alone are not the only answer, since MS doesn’t appear to be directly inherited, and even identical twins don’t experience the same chances of developing MS)?
- What other factors in the environment trigger MS in people who are susceptible?
- Why do some people who have MS experience progressive disability and others do not?
- What are the factors that cause MS progression, and how can they be stopped?
Progress is being made in identifying possible MS triggering factors. Knowing the cause of MS and what drives progressive disability will lead to ways to stop the disease in its tracks and end it through prevention.

The National MS Society’s approach to research

Because MS is a complex disease that is different for every individual, we take a comprehensive approach that can propel knowledge, better treatments, healthcare policies, and new disease management therapies forward, faster. We drive research and collaborate worldwide to stop MS in its tracks, restore lost function, and end the disease forever — for every single person with MS.

The National MS Society drives progress through an expert research review process and funding of the most promising research across all areas, including the advance of basic understanding of the disease process and the translation of promising new therapies to accelerate commercial development. Through these efforts, we have:

- Recruited more than 900 new MS researchers to the field
- Provided early career support and funding to nearly every thought leader in MS research
- Set standards in diagnosis, symptom management, pediatric MS, complementary and alternative medicine, rehabilitation research, clinical trial strategies and stem cell research
- Established the MS field of nerve and myelin repair which resulted in trials for treatment
- Drove research uncovering genes contributing to MS susceptibility and new treatment avenues
- Paved the way for existing therapies; currently there are more potential therapies in the pipeline than at any other time in history

After an independent audit of our comprehensive research programs, Faster Cures (an independent nonprofit focused on speeding medical research) identified the Society as the “single organization serving as a catalyst for new research in MS.”

<table>
<thead>
<tr>
<th>YEAR</th>
<th>EVENT</th>
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<tr>
<td>1868</td>
<td>First correlation of MS clinical symptoms with central nervous system pathology; disease named “Sclerose en plaques” by Jean Martin Charcot.</td>
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<td>1933</td>
<td>Acute experimental allergic encephalomyelitis (EAE) developed as model for MS.</td>
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<td>1946</td>
<td>National MS Society USA launched.</td>
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<td>1950</td>
<td>National Institute of Neurological Diseases founded at National Institutes of Health through the work of the Society.</td>
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<td>1954</td>
<td>First Society fellowship programs to train MS scientists.</td>
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<td>1969</td>
<td>Society co-funds research of steroid ACTH, which becomes the first therapy shown to speed recovery from MS relapses.</td>
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<td>1981</td>
<td>First MRI pictures of a brain affected by MS are produced, revolutionizing MS diagnosis.</td>
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<td>1992</td>
<td>Society supports first comprehensive search for genes that make people susceptible to MS, initiating targeted research program in MS genetics.</td>
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1993  First MS therapy approved to treat underlying disease.

1998  Society targets study of gender differences to fuel potential for developing new therapeutic strategies.

1999  Society initiates first-ever longitudinal patient-focused database effort, the Sonya Slifka MS Longitudinal Study, providing socioeconomic and quality of life data.

1999  Society grantees first to isolate immature cells in the adult brain capable of developing into replacements for myelin-making cells destroyed by MS.

2001  Society task force develops new diagnostic criteria for MS, which shortens the time it takes a person to receive a firm diagnosis. These were updated in 2005 and 2010.

2005  International Nervous System Repair and Protection initiative launched by the Society.

2007  Society and MS International Federation convene a Stem Cell Research Summit of leading stem cell and MS experts to explore the potential of all types of stem cell research for MS and to set research priorities.

2007  Society launches Fast Forward to support commercial research to speed treatments to people with MS by partnering with industry to develop new therapies.

2008  MS activists secure a place for MS research in the Congressionally Directed Medical Research Program.

2010  First oral disease-modifying therapy for MS, approved for relapsing forms.

2010  First symptomatic therapy specific to MS approved, to improve walking ability in people with all types of MS.
2009–
2011  Society launches three clinical trials of nerve-protecting agents and a trial of vitamin D supplements.

2011  Nervous System Repair initiative garners millions of dollars in new funding to train promising young investigators; produces over 180 research papers and jump-starts this field of MS research.

2011  Society-supported global consortium doubles the number of MS risk genes identified.

2012  Launch of International Progressive MS Alliance to speed the development of therapies.

2012  Society task force launches effort to create a better tool to track benefits of therapies on disability in MS, leading to formation of the MS Outcome Assessments Consortium.

2013  Society leverages its groundbreaking support of clinical services for children with MS to launch the Network of Pediatric MS Centers, providing essential infrastructure to facilitate research on MS in its earliest stages.

2014  Large trial funded by NIH and Society begins recruiting participants with progressive MS to test whether ibudilast can protect the nervous system from damage.

2015  International initiative launched to focus on how having MS and other conditions (co-morbidities) influences disease course and treatment.

2015  A phase 2 clinical trial co-funded by the Society suggests a pill used to treat epilepsy (phenytoin) has the potential to slow the accumulation of disability in people with MS.

2015  Results of phase 2 trial of anti-LINGO suggest potential as myelin repair strategy.
Encouraging innovation

The Society fuels novel ideas, potential therapies, projects and technologies to discover and pursue every avenue that holds promise:

- Funding university-based research and clinical trials to feed the treatment pipeline and pursuing industry partnerships for therapy development.
- Exploring non-traditional research avenues, including: healthcare policy/delivery; quality of life; complementary and alternative therapies; and concepts initiated within the pharma/biotech industries.
- Funding investigator-initiated and Society-targeted research: we invite scientists to come to us with new ideas to be tested and we proactively target promising areas for exploration.
- Supporting the international Barancik Prize for Innovation in MS Research, the largest prize of its kind, established to spur progress toward stopping MS, restoring function and ending MS forever.

Another way the Society propels MS research forward is by funding high-risk, high-potential pilot projects to investigate new, untested ideas and attract new researchers to the field. These unique one-year grants allow researchers to quickly gather data needed to determine if their novel ideas are worth pursuing. A researcher who submits a pilot research proposal will receive fast-track reviews and approvals to speed the testing of new ideas.

Driving global collaboration

The National MS Society fosters large-scale coalitions between MS experts and experts from other fields and diseases to make rapid and meaningful progress. We are increasing global research
investment and collaboration leading to new knowledge and effective solutions for people living with all forms of MS.

- We engage thought leaders to identify new opportunities, help set priorities and to serve as peer reviewers and advisors. Our centralized peer review and funding process helps us avoid geographic and political bias and identify the best research projects in which to strategically invest our resources.

- We helped found and continue to provide leadership as a Managing Member of the Progressive MS Alliance, an international coalition working together to connect resources and experts around the world to find answers and develop solutions to end progressive MS.

- We leverage support from other organizations, agencies and industry to propel MS research. The Society-led MS Outcome Assessments Consortium leverages data from $2 billion in clinical trials to create a robust outcomes measure that will address the critical need for a more sensitive way to detect the benefit of potential treatments that slow or reverse progressive disability in people with MS.

- We convened over 60 international workshops and meetings over the past 45 years, playing a pivotal role in building collaborations and moving knowledge forward in critical areas. Many of these workshops have been springboards for crucial leaps forward in research approaches to MS. For example, the Society held a wellness strategy meeting to identify key research questions to be answered in areas such as diet, exercise and emotional issues in MS.

Another way we foster collaboration is through our Collaborative MS Research Center Awards, providing flexible funding for intensive laboratory studies combined with expansive clinical investigations. These five-year awards provide flexible funding, bringing together scientists and physicians from diverse fields to nurture cross-fertilization of ideas and techniques to propel progress in promising avenues of MS research.
Funding research and training

The National MS Society supports and funds research activities spanning ALL research stages, including early discovery research, translational research that brings promising ideas forward into actual therapeutic solutions for testing, and clinical trials. Our unique approach drives the pursuit of all promising avenues that can positively impact people living with multiple sclerosis.
We are expanding and increasing the scientific workforce focused on MS. To move toward a world free of MS, the National MS Society provides grant funding, tools, and information resources to support the brightest scientists and physicians exploring questions underlying MS. We offer a spectrum of funding opportunities and resources to support MS investigators at virtually every stage of their careers — from training promising young scientists to furthering the work of established leaders in the field.

**Driving commercial research**

Getting treatments to people with MS requires bold leadership, tenacity and investment at every stage of the research process. Often, the biggest hurdle in moving potential treatments forward is securing the necessary early investments and resources for commercial development — when the potential return of those investments is largely unknown. The Society continues to propel promising new therapies by breaking down barriers to commercial development through Society mechanisms like Fast Forward. We drive connections of all the resources necessary to ensure that promising treatments don’t languish on a dusty shelf. The Society is boldly closing the gap between promising discoveries and the commercial development necessary to get new treatments to people with MS.
Stop, restore, end

Freeing the world from MS requires a comprehensive approach to research — research that will STOP MS in its tracks; research that will RESTORE what’s been lost; and research that will END MS forever.

STOP MS in its tracks

A variety of therapies exist for people with relapsing forms of MS. For some, these treatments reduce the number and severity of attacks and slow disease activity, but more must be done to stop disease progression for everyone affected by MS — including those with progressive forms.

We must stop the disease in its tracks and prevent further loss for people by speeding the development of new disease-modifying therapies and symptomatic treatments, including alternative and complementary therapies. We need to:

- Better understand the role the immune system and inflammation play in the cause of MS and in ongoing disease activity and progression
- Support clinical trials testing new therapies to stop damage and progression of disability
- Explore wellness strategies that might help to stop inflammation or progression
- Ensure that we understand healthcare issues and gather data to advocate for policies that enable everyone with MS to access quality care and treatment
- Understand the mechanisms that cause tissue injury and that drive disease progression
Driving progress

We are making significant progress toward stopping MS:

- The International Progressive MS Alliance funds research worldwide and removes barriers to the development of treatments for progressive MS.
- Research is beginning to uncover modifiable factors that increase a person’s risk for developing progressive MS, including smoking and obesity.
- A trial funded in part by the MS Societies of the U.S. and the U.K. showed that an oral epilepsy therapy may protect against optic nerve damage, often the first symptom of MS. The results need confirmation in a larger study, but raise the possibility of “repurposing” a therapy already on the market with a long track record of successful use. The Society also has joined with National Institutes of Health (NIH) to launch a therapy trial of the repurposed therapy ibudilast in primary-progressive and secondary-progressive MS.
- Wellness strategies may help stop inflammation or progression in MS. Reports by Society-funded researchers suggest that dietary salt may speed the development of an MS-like disease in mice, providing new insights on immune system activity in MS. A comprehensive analysis of gut bacteria in people with MS is ongoing to determine factors that may drive progression and develop probiotic strategies for stopping progression.
- Several of the Society’s commercial funding partnerships are advancing treatment strategies aimed at protecting the nervous system from damage and targeting progressive MS.
RESTORE what’s been lost

Just a few short years ago, there was little belief that nervous system repair was even possible. Through the tireless efforts of the National MS Society and other funding partners and researchers around the world, a whole new field has emerged to pursue strategies to repair the nervous system and restore function to people with MS.

We must find ways to repair damage through nervous system and myelin repair and help people regain function through rehabilitation, and physical and cognitive therapies. Here’s how:

- Understand how nerves and myelin work normally and how to stimulate repair when they are damaged
- Aggressively pursue clinical trials of new cell therapies and other therapeutic approaches to rebuild the nervous system
- Ensure that innovative wellness and rehabilitation techniques are developed to maximize function and develop better ways to reduce MS symptoms, including mood and cognitive symptoms
- Provide data on optimal health care delivery and policy to fuel advocacy efforts to improve quality of care and quality of life

Driving progress

We are making significant progress in efforts to restore function to people with MS, particularly in our priority areas of nervous system repair and lifestyle/wellness:

- Society-sponsored researchers at the University of Rochester and in Milan, Italy have shown recent success transplanting stem cells in mice, promoting recovery of function.
A Society-supported team at the University of California, San Francisco has identified compounds approved by the FDA for various disorders that might also stimulate myelin repair. This work has already led to a clinical trial of one of these compounds.

Strong evidence that cognitive rehabilitation improves learning and memory has been published by the Kessler Foundation in New Jersey, where new rehab researchers receive training through the Society’s mentor-based fellowship program. Effects of cognitive rehabilitation in the study lasted for 6 months after training ended and also benefited quality of life. In addition, the Society is funding a clinical trial to determine whether aerobic exercise can improve cognitive impairment in people with MS.

Commercial partnerships geared to restore function include the development of an adult stem cell platform for the treatment of MS and a partnership to test a novel “Medical Food” for MS cognitive impairment.

END the disease forever

The uncertainty of MS affects everyone with a diagnosis; uncertainty about what tomorrow might hold. But it also demands urgency to ultimately bring an end to this disease for everyone — forever. Prevention for future generations means we need to find the cause of MS, what triggers it, and what may protect against it. Here’s how:

- Aggressively pursue studies to identify all of the MS-related genes, because genes make people susceptible to MS — so that we can answer how it is triggered and how it could be prevented
- Better understand what factors in the environment influence whether a person gets MS
- Identify possible infectious triggers for MS
Driving progress

Progress has been made to identify factors that may increase a person’s chances of developing MS, such as specific genes, infections and lifestyles. We know that none of these is a single cause of MS, that not everyone with MS has been exposed to these factors, and that people exposed to them will not necessarily develop MS. However, they may provide clues to disease prevention. For example:

- With funding from the National MS Society and others, the International MS Genetics Consortium has identified more than 150 new MS risk genes that better define the biological pathways leading to MS and that may inform ways to prevent the disease and to enhance treatment design.

- Researchers funded by the Society and others have developed a new approach to understanding how subtle changes in genes may increase the risk of developing MS and other immune diseases.

- The Society launched the MS Prevalence Initiative to better understand who and how many people are affected by MS in the United States.

- An expanded Network of Pediatric MS Centers, supported by the Society, collects research data that advances our understanding of MS in both children and adults. One example is a study of what triggers MS in children.

- Studies funded by the Society increasingly indicate that MS may be experienced more severely by African Americans. These studies are crucial to better understand MS progression, to plan and conduct clinical trials, and to find solutions for African Americans living with MS.
Our commitment

**Our vision is simple: a world free of MS.** We will expand investments and worldwide collaboration to accelerate research. Scientific breakthroughs will propel the knowledge to end MS and identify everyday solutions that change the lives of people with all forms of MS.
The National Multiple Sclerosis Society ("Society") is proud to be a source of information on multiple sclerosis related topics. The information provided is based on professional advice, published experience, and expert opinion, but does not constitute medical or legal advice. For specific medical advice, consult a qualified physician. For specific legal advice, consult a qualified attorney.

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Early and ongoing treatment with an FDA-approved therapy can make a difference for people with multiple sclerosis. Learn about your options by talking to your healthcare professional and contacting the National MS Society at nationalMSsociety.org or 1-800-344-4867.

The Society publishes many other resources about various aspects of MS. Visit nationalMSsociety.org/brochures or call 1-800-344-4867.

Other popular resources include:
- Disease-Modifying Therapies for MS
- Participating in Clinical Trials: A Guide for People with MS
- Living with MS
The National MS Society’s mission is for people affected by MS to live their best lives as we stop MS in its tracks, restore what has been lost and end MS forever. To fulfill this mission, the Society funds cutting-edge research, drives change through advocacy, facilitates professional education, collaborates with MS organizations around the world, and provides services designed to help people with MS and their families move their lives forward.