Introduction

Multiple sclerosis 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 may be mild, such as numbness in the limbs and tingling or severe, such as blindness or paralysis. The progress, severity and specific symptoms of multiple sclerosis (MS) 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 2.1 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 is a driving force of MS research, and global research efforts are underway.
Research sponsored by the Society and its many partners in government, other MS societies, 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, clear clues are emerging on factors that influence the risk of developing MS. We have better and faster ways of diagnosing MS, and there are therapies that can reduce MS attacks and delay progression for many, with more potential therapies in the pipeline than at any other time in history.

This brochure traces the comprehensive and holistic approach being taken to stop MS progression, to restore function that has been lost, and to end MS forever.

What We Know About MS Drives Research Efforts

**MS is thought to be an autoimmune disease**

MS is thought to involve “autoimmune” processes. 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 can also be 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.
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.

Other Factors

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 causes, and migration patterns, in an effort to understand why:

■ We know that women are more susceptible to developing MS than men.
■ We know that a person’s genes can 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).
■ We know that something in the environment can trigger MS in those who are susceptible.

Progress is being made in identifying possible MS triggering factors. Knowing the cause of MS will lead to ways to end the disease by preventing it.

The National MS Society’s Approach to Research

The complexity of MS necessitates a comprehensive approach when it comes to research — employing multiple strategies that can propel knowledge, better treatments, health care policies, and new disease management therapies forward, faster.

The National MS Society drives progress through research review and funding, including a variety of Society programs, and our Fast Forward initiative, focused on advancing the transition of promising new therapies to rapid commercial development and understanding mechanisms underlying the disease.

Research funded by the Society, the National Institutes of Health, and other funders around the world has built a foundation that is driving progress today. Generous funding, extensive collaboration and our commitment to research have resulted in immense progress, including:
- Accurate and effective means to diagnose MS, enabling earlier treatment.
- The development of disease-modifying therapies available for treatment and reducing disease progression.
- Breakthroughs in identifying genes that are involved in MS.
- More potential therapies in the pipeline than at any other time in history.

**HISTORY IN MS RESEARCH**

- **1868** First correlation of MS clinical symptoms with central nervous system pathology; disease named “Sclerose en plaques” by Jean Martin Charcot.
- **1933** Acute experimental allergic encephalomyelitis (EAE) developed as model for MS.
- **1946** National MS Society USA launched.
- **1947** First research grant to Elvin A. Kabat, MD.
- **1950** National Institute of Neurological Diseases founded at National Institutes of Health through the work of the Society.
- **1954** First Society fellowship programs to train MS scientists.
- **1969** Society co-funds research of steroid ACTH, which becomes the first drug shown to speed recovery from MS relapses.
- **1981** First MRI pictures of a brain affected by MS are produced, revolutionizing MS diagnosis.
- **1992** Society supports first comprehensive search for genes that make people susceptible to MS, initiating targeted research program in MS genetics.
- **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 quality of life and socioeconomic 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 may shorten 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 as part of Society’s Promise: 2010 campaign.
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 impact those living with multiple sclerosis.

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.

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 speed treatments to people with MS by partnering with industry to develop new drugs.

2008  MS activists secure a place for MS research in the Congressionally Directed Medical Research Program, plus $5 million restricted to MS research.

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-  Society launches 3 clinical trials of nerve-protecting agents and a trial of vitamin D supplements in line with efforts to stop MS.

2011  First symptomatic therapy specific to MS approved, to improve walking ability in people with all types of MS.

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We are finding expeditious ways to conduct research, forge relationships, bridge barriers and garner resources to propel research forward:

- Fast-tracking high-risk pilot grants to quickly test novel ideas.
- Evaluating urgent research opportunities with special peer review panels.
- Sharing resources to enhance discovery, including MS tissue banks and DNA banks.

We foster coalitions worldwide with experts in other fields and diseases to make rapid and meaningful progress:

- Offering special funding for collaborative teams.
- Engaging thought leaders to identify new opportunities and help set priorities and to serve as peer reviewers and advisors. Our centralized peer review and funding process helps us avoid geographic and political biases, and identify the best research projects in which to strategically invest our resources.
- Leveraging support from other organizations, agencies and industry to propel MS research.

We fuel novel ideas, potential therapies, projects and technologies to discover and pursue every avenue that holds promise:

- Offering special funding to test innovative ideas.
- Funding university-based research and clinical trials to feed the drug pipeline, and pursuing industry partnerships for drug development.
- Exploring non-traditional research avenues, including: health care policy/delivery; quality of life; complementary/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 their new ideas to be tested, and we also proactively target promising areas that are ripe for exploration.
- We have convened over 50 international workshops and meetings over the past 40 years, playing a pivotal role in fostering collaborations and moving knowledge forward in critical areas. Many of these workshops have been springboards for crucial leaps forward in research approaches to MS.
- In 2002 the Society launched a Collaborative MS Research Center program to stimulate interaction of researchers from diverse fields and to attract new scientists to MS research.
- In 2010, after an exhaustive audit of our research programs, Faster Cures (an independent nonprofit focused on speeding medical research) lauded the Society’s efforts, identifying us as the “single organization serving as a catalyst for new research in MS.”
Fast Forward

Fast Forward, founded by the National MS Society, focuses on expediting the drug development process, bridging the gap between promising discoveries and the commercial expertise and funding to move them forward. Fast Forward provides critical funds to academic groups and emerging biotechnology and pharmaceutical companies involved in drug research and development. By connecting people, ideas, and resources, promising drug treatments can now break through barriers, move through the pipeline, and enter clinical trials faster.

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

There are more potential MS therapies in development today than at any other time in history, and a variety of therapies exist for those with relapsing forms of multiple sclerosis. 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.

Stopping MS involves understanding the role the immune system plays in the cause of MS and ongoing disease activity; conducting clinical trials of promising therapies; understanding mechanisms that cause tissue injury and drive disease progression; and efforts to ensure we understand health care issues and can gather data to advocate for policies that enable everyone with MS to access quality care and treatment.
Driving Progress

- The National MS Society supported early studies that eventually led to most of the disease-modifying therapies available today.
- Our funding led to the identification of 4 types of MS lesion patterns, changing the way researchers view MS.
- Society efforts drove the development of “Gold Standards” for the design of MS clinical trials, opening a path for FDA approvals.
- Our research initiative on gender differences led to the first clinical trials of sex hormones to treat MS.
- Society initiatives have led to faster, more accurate means of diagnosing MS, shortening the wait for answers, and offering earlier treatment, which may help prevent future nervous system damage.

Recent Breakthroughs

Decades of basic research into immune mechanisms involved in MS, and the underlying processes that cause injury to the brain and spinal cord, have increased our understanding of what goes wrong in the disease and continues to provide new therapeutic targets for stopping MS attacks and protecting the nervous system from harm.

Recent milestones in this field include:

- More evidence emerging to suggest that getting on MS therapies early after disease onset, or even before a definite diagnosis, can pay off later by delaying disease progression.
- Results suggesting that smoking cigarettes increases the risk of developing MS, and may also make MS progress more quickly.
- The first oral disease-modifying therapy approved for reducing relapses and delaying the accumulation of physical disability in relapsing forms of MS.
- Clinical trials of other oral therapies and therapies with infrequent dosing regimens are in late-phase clinical trials in all types of MS including progressive forms, offering hope that new treatment options may soon be available for people with MS.
- New interest and clinical trials aimed at “neuroprotection” — to protect the nervous system from damage and stop MS in its tracks.

Current Approaches to Stopping MS

Understanding the immune system:

- Studies focusing on the mechanics of the immune system, and its cells such as T cells, B cells, and how nervous system tissues become targets of MS attacks.
- Research focusing on immune molecules involved in launching attacks, and on natural molecules that can put a stop to them.
- Studies exploring the genetic markers of MS, which may hold the key to understanding how the MS immune attacks are triggered and may provide new avenues for stopping the attacks.
Clinical and pre-clinical trials:
- Clinical trials of new approaches including vitamin D supplements, the antioxidant lipoic acid, and repurposing drugs approved for other disorders.
- Investments aimed at pre-clinical studies of new approaches to stopping immune attacks.
- Studies focusing on detecting and measuring disease activity using advanced imaging techniques and new clinical assessments to enhance and speed clinical trials of therapies that can stop MS immune activity and protect against further injury.
- Early trials to test the potential of a special type of adult stem cell found in the bone marrow, called mesenchymal stem cells. Although these cells have the potential for both turning down MS immune attacks and stimulating nervous system repair, it’s still too early to know whether this approach will prove safe and beneficial.
- Clinical trial testing the idea that infection with intestinal parasites may reduce immune attacks in MS. This relates to the “hygiene hypothesis,” the idea that MS may be less common in underdeveloped regions because early exposure to common infections stimulates immune responses that help offset the attack on the brain and spinal cord in MS.

Gathering data on health care issues:
- Studies focusing on standards and indicators of good MS medical care, on modeling medical costs, and on impediments to care faced by people with MS.
- Investigations of issues such as long-term care, housing needs and caregiver issues.

Understanding mechanisms that cause tissue injury and progression:
- Studies exploring mechanisms that drive injury to the brain and spinal cord to expose new potential therapeutic targets along the injury pathways that may stop the damage.
- Advanced imaging and laboratory studies seeking to define and track the full measure of MS disease activity, MS lesions, and atrophy in the brain and spinal cord.
- Studies of people with MS designed to identify factors that contribute to the risk of MS progression, and may lead to ways to predict and prevent disease worsening.
- Studies focusing on CCSVI (chronic cerebrospinal venous insufficiency) to determine its role in the MS disease process.
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, there is not just belief, but a whole new field that has emerged to pursue strategies to repair the nervous system and restore function to people with MS.

The MS immune attacks on the brain and spinal cord cause extensive damage to nerve fibers and their protective myelin coating. Without their myelin coating, nerve fibers fail to conduct signals properly, leading to symptoms of MS. When nerve fibers and their nerve cells are damaged, long-term disability can result.

Restoring what’s been lost in MS requires a better understanding of how nerves and myelin work normally, and how repair can be stimulated. It requires clinical trials of new cell therapies and other therapeutic approaches to rebuild the nervous system. It requires innovative rehabilitation techniques and better ways to reduce MS symptoms. And it requires data on optimal health care delivery and policy to fuel advocacy efforts to improve quality of care and quality of life.

Driving Progress

- The National MS Society funded the first study showing that natural repair occurs in MS lesions, paving the way for a whole new field of inquiry.
- Society researchers discovered that human adult brains have replacement cells for myelin, and showed that transplanting those cells could restore function in mice.
- We funded early trials on a therapeutic approach that led to the first approved medicine to improve walking in MS.
- Society grantees pioneered research on cognition problems in MS as well as rehabilitation strategies to address them.
- The Society funded the first study showing that aerobic exercise could fight fatigue in MS, changing doctors’ age-old advice to “take it easy.”
- Thanks to stimulus funding from the Society, as well as support of other related projects, the field of nervous system repair and protection is exploding. This initiative trained scores of promising young investigators, produced over 180 research papers, forged new international collaborations, and leveraged millions of dollars in new funding.
- The Society supports a unique fellowship program to increase the quality and quantity of MS rehabilitation research by training talent in best practices for this type of approach.
Recent Breakthroughs
Progress is being made toward finding ways to repair nervous system damage and toward improving quality of life and specific MS symptoms through exercise, meditation, rehabilitation and medications.

Recent milestones in this field include:

- Several new molecules have been identified which are key to myelin regeneration; these may serve as targets for new therapies aimed at stimulating myelin repair.
- Two symptom management treatments specific to MS were approved.
- Novel imaging technologies can specifically detect myelin and nerve fiber damage and track it over time.
- Researchers are discovering the biological basis of depression in MS, linking it to specific areas of damage in the brain. This offers an important clue to a symptom that can interfere greatly with the quality of life of people with MS.
- Several clinical trials are getting underway to test whether adult stem cells, such as cells in the bone marrow (called mesenchymal cells) can both turn off the immune attacks in MS and stimulate natural myelin repair processes.
- A large study showed that mindfulness-based meditation may improve health-related quality of life, depression, and fatigue in people with all types of MS.

Current Approaches to Restoring Function
Nervous System Repair:

- Understanding how myelin and nerve interactions support nerve messaging and what goes wrong as myelin and the underlying nerve fibers are damaged.
- Finding ways to repair damaged myelin by identifying signaling molecules active during natural repair processes, which can then be tested for their potential for stimulating the body’s natural ability to rebuild itself after injury. Many believe that re-wrapping healthy nerve fibers with protective myelin will guard against further damage.
- Studies exploring the repair potential of different types of stem cells in pre-clinical models of disease, and ways to enhance the survival of repair cells in the inflamed and scarred nervous system of people with MS.
- Efforts focusing on high-tech imaging tools to better measure nerve tissue damage and assess nerve protection and repair without having to wait possibly years to observe a person’s disease progression.
- Investigations to design new ways of conducting clinical trials and to develop better outcome measures to speed up the testing of promising repair strategies.
Rehabilitation, Treating Symptoms, and Ensuring Access to Care:

- Studies in health care delivery and policy provide data needed to fuel advocacy efforts to improve quality of care and quality of life for people with MS.
- Research investigating complementary and non-traditional therapies to combat specific symptoms.
- Tests of innovative rehabilitation techniques to improve walking, strength and balance.
- Studies focusing on exercise and other non-pharmaceutical strategies to enhance wellness and combat painful spasticity (extreme muscle tightness) and MS fatigue.
- Research on thinking and memory problems, and the best therapies and coping strategies to address them.

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.

Ending MS forever requires studies to identify all common MS-related genes, because genes make people susceptible to MS. It requires better understanding of what factors in the environment influence whether a person gets MS, and identifying possible infectious triggers for MS.

Driving Progress

- Over the years, the Society has supported research that informs what we now know about who gets MS around the world, which has led to clues about possible risk factors.
- The Society provided seed money that launched the International MS Genetic Consortium, helping identify which genes contribute to MS susceptibility — a key to understanding the cause and how to prevent MS.
- We supported early studies showing how immune cells might be triggered to attack myelin by encounters with infectious agents.
- Society funding created a data hub for studies of kids with MS, whose young immune systems may offer clues to MS triggers.
Recent breakthroughs

Studies focusing on who gets MS are called epidemiology studies. These and gene studies are helping us understand who gets MS and why, and identify and explain areas with high or low rates of the disease. Ultimately, these approaches will help pinpoint the cause or causes of MS and ways to prevent the disease.

Recent milestones in this field include:

- Researchers are beginning to explore activity of MS susceptibility genes that have been identified, providing new and deeper understanding of the disease. For example, new gene studies suggest that all forms of MS have similar susceptibility genes.
- Society-supported studies grantees identified clinical and genetic differences between African Americans and caucasians with MS — suggesting the disease may be more severe in African Americans.
- Links have been identified between the Epstein-Barr virus, which causes infectious mononucleosis and MS; ongoing research continues to explore the meaning of this relationship.
- Growing evidence focuses on the relationship between vitamin D intake, blood levels of vitamin D, and the risk of MS.
- Society grantees and others have reported the possibility that cigarette smoking increases susceptibility to MS and also increases the risk of MS disease progression.

Current Approaches to Ending MS Forever

- Massive screening studies have identified over 50 susceptibility genes common among people who have MS, and further work is delving into specific MS genes to uncover plausible paths through which they influence the disease process.
- DNA banking to support the efforts of researchers around the world seeking clues to MS susceptibility.
- Population studies examining factors such as vitamin D intake, sun exposure and smoking, to uncover exposures that may increase risks for the disease — or protect against it.
- Studies exploring complex interactions between environmental factors and genes to better understand how MS might be triggered.
- Studies tracking factors that influence disease worsening, which may also influence its onset.
- Studies exploring patterns of infectious agent exposures in people with MS and people without MS.
- Explorations of underlying mechanisms through which immune cells respond to viruses and the potential for misguided immune attacks.
- Studies that investigate models in which infections trigger the immune system to turn against the body’s own nervous system, for clues to similar mechanisms that may be active in MS.
Our commitment moving forward

We are committed to freeing the world of multiple sclerosis. Our research objectives established by our 5-year Strategic Plan, the Society’s Strategic Response 2011-2015, are:

- To better understand the mechanisms that lead to disease progression and we accelerate the development of new therapies.
- To pursue new avenues to discover how nerve cells are damaged and potentially repaired.
- To pursue new rehabilitation techniques and symptomatic treatments to restore neurological function and enhance quality of life.
- To identify risk and triggering factors that cause MS, and understand the biological interactions that lead to its development so that MS can be prevented.
- To expand and strengthen the quantity and quality of MS research worldwide to accelerate new discoveries and treatments for people with MS.

We will achieve our goals by:

- Pursuing all promising avenues.
- Engaging the best and brightest minds.
- Connecting people, resources and ideas.
- Speeding development of treatments.
- Identifying and filling gaps.

We will be everywhere at once with a focus on all the most promising opportunities. One path unexplored is one too many left behind. We will stop the progression of MS and restore everything people have lost. Anything less is not far enough. And now, we will end MS forever, so that every mother, father, son and daughter is safe in the future.
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 health care professional and contacting the National MS Society at nationalMSsociety.org or 1-800-344-4867 (1-800-FIGHT-MS).

The Society publishes many other pamphlets and articles about various aspects of MS. Visit nationalMSsociety.org/brochures to download them, or call your chapter at 1-800-344-4867 to have copies mailed to you.

**Some of our popular pamphlets include:**

- The MS Disease-Modifying Medications
- Participating in Clinical Trials: For People with MS
- Living with MS
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