



Multiple Sclerosis and Autoimmune Neurology

BENEFACTOR IMPACT





Philanthropy is vital to Mayo Clinic's efforts to find the cure for multiple sclerosis and other autoimmune neurological disorders. By helping us attract world-class research talent, harness the most advanced imaging technology, and translate discoveries from the lab to real patient benefit, benefactor gifts are unlocking answers that the world desperately needs. On behalf of Mayo Clinic, our patients and their families who are finding answers, thank you.



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A New Path

Muscle fatigue that immobilizes a young mom in the prime of her life. Seizures that strike a child without warning. A 45-year-old man's puzzling forgetfulness.

Today, patients who present these symptoms can receive appropriate diagnoses — multiple sclerosis (MS), epilepsy and early-onset dementia, respectively — and embark on standard treatment protocols to improve quality of life. But in cases triggered by the body's autoimmune response, modern medicine falls short of attacking these diseases at their root causes, offering only temporary relief rather than cures.

Mayo Clinic is forging a new path. As Mayo experts define the underlying autoimmune mechanisms that drive a host of neurological conditions including MS, they can diagnose conditions more accurately and earlier, discover new targets for treatment, develop more effective therapies and find first-time cures.

This marks a turning point in the way we confront many neurological conditions. Now more than ever, benefactor support makes a difference.

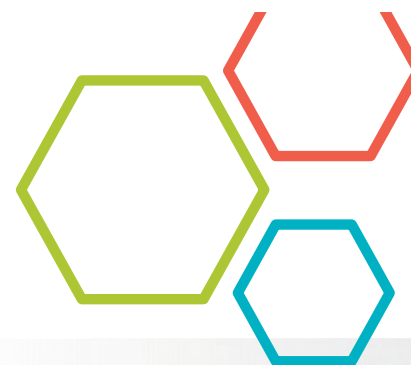


Leading the Way

Mayo Clinic's Center for Multiple Sclerosis and Autoimmune Neurology is the premier group for advancing knowledge and treating autoimmune neurological disorders such as MS and neuromyelitis optica (NMO). While seeing more than 3,500 adults and children with these conditions each year, the center has made groundbreaking progress, including the following.

- Identified four distinct types of MS lesions that differ among individual patients.
- Developed natural human antibodies that promote remyelination and neural repair, **healing the loss of myelin sheath around the nerves or the nerve itself.**
- Pioneered the use of plasma exchange therapy for the **treatment of acute attacks of MS and NMO.**
- Established the first Autoimmune Neurology Clinic in the United States in 2006. The clinic provides **state-of-the-art approaches to diagnosis and treatment of autoimmune neurological disorders** including epilepsy, dementia and movement disorders.
- Discovered the anti-aquaporin 4 antibody, the first diagnostic biomarker for any MS-like illness. The discovery that patients with NMO have an autoantibody that targets a water channel in astrocytes, a type of nerve cell in the brain, has changed the way we think about the development of demyelinating diseases and has **led to novel treatments, some of which are in phase III clinical trials.**
- Established a Neuroimmunology Laboratory to **test a diverse array of neural antibodies on blood samples from more than 150,000 patients.**
- Identified the role of a unique population of immune cells involved in the damage of nerve fibers, axons, that have lost their myelin sheath and discovered the mechanisms underlying such injury. This **discovery may ultimately provide a strategy for protecting axons and preserving neurologic function** in patients with MS.
- Designated as **one of six Pediatric MS Centers of Excellence** by the National Multiple Sclerosis Society.

At the Center for Multiple Sclerosis and Autoimmune Neurology, we see the whole picture, not just the individual neurological disorder.

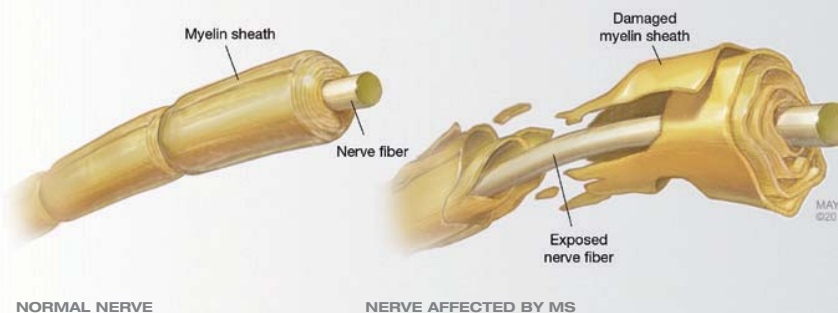


WHAT IS AUTOIMMUNE NEUROLOGY?

Autoimmune neurology is a rapidly evolving subspecialty driven by the discovery that the immune system can target virtually any structure within the central or peripheral nervous system. These conditions manifest as disorders previously thought to be independent and unrelated — some well-known, like MS, and others so rare that only a handful of known cases exist in the world.

While the subspecialty stretches far beyond MS, we apply newfound knowledge of these disorders to advance MS research. This continuous loop of discovery and application increases our ability to treat patients with a wide variety of autoimmune and demyelinating diseases, which are increasingly recognized as treatable and reversible.

To give patients the definitive cures they need, we must learn, at a cellular level, what mechanisms cause the body to attack itself and how we can both halt the process and repair damage.



In MS, the protective myelin sheath surrounding nerves becomes damaged, causing disease symptoms.



Pioneering Progress

MS

The Center for Multiple Sclerosis and Autoimmune Neurology focuses much of its effort on MS research and treatment because the disorder impacts so many people, nearly 400,000 in the U.S. and 2 million worldwide. The center continues Mayo Clinic's legacy as a leader in this field by caring for nearly 3,000 adults and children with MS every year.

The center's research involves a unique vision for modeling, understanding, treating and curing MS. This vision encompasses a new way of looking at axon injury as a critical therapeutic target in MS



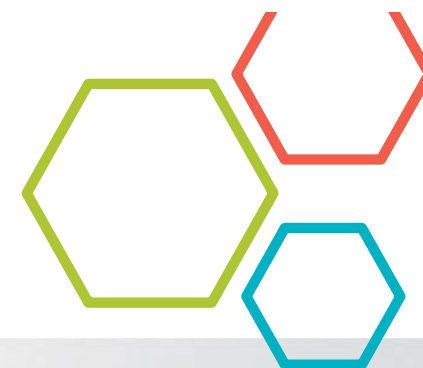
and emphasizes the importance of protecting the neuron from further injury or degeneration, also known as neuroprotection. Mayo Clinic researchers have found that preserving functional pathways is an essential step for new remyelinating and immunomodulatory therapies to take effect.

The MS Team

The vision for MS research at Mayo Clinic is the result of a unique blend of clinical and basic science investigators coming together to push the boundaries of our current understanding of this complex disease.

The MS research community at Mayo Clinic is committed to repairing and restoring neurologic function in patients via the application of cutting-edge tools in imaging, regenerative medicine, stem cell biology, individualized medicine, drug discovery, pathology, genetics, engineering and computational biology. Our researchers span a broad spectrum of disciplines, ranging from neuroscience, neurology, neuropathology and neurosurgery to bioengineering, radiology and immunology. This comprehensive approach is what sets the center apart and epitomizes the Mayo Clinic Model of Care.

Our vision also highlights the unique nature of the disease of each patient. While we uncover new knowledge from analyses that model aggregate aspects of MS, we understand that curing MS may require individualized approaches tailored to each patient.



“The glory of medicine is that it is constantly moving forward, that there is always more to learn.”

– William J. Mayo, M.D.

To treat MS patients, Mayo Clinic engages in groundbreaking research that spans human studies, animal models, cell-based assays and molecular analyses. The studies include:

- Defining the pathological substrate and therapeutically targetable pathogenic cascades underlying MS disease progression. Novel technologies and imaging modalities applied to the analysis of human MS lesions will **provide insights into the mechanisms that drive disability**, thereby accelerating our ability to track and ultimately treat disease progression.
- Identifying clinical, imaging, molecular and serological biomarkers of distinct MS pathological subtypes. A better understanding of MS disease heterogeneity is critical to the identification of **new treatments that can be tailored to an MS patient's specific disease subtype**.
- Establishing a discovery platform that allows us to **generate neurons, axons and oligodendrocytes from patient-derived stem cells for identification of individualized approaches** to patient care.
- Continuing to build on Mayo Clinic's innovative use of monoclonal antibodies that have **successfully stimulated cell regeneration and repaired myelin**
- **in mouse models of MS.** These therapies may help nerves recover normal signaling functions and improve movement and cognition in patients with MS and other autoimmune neurological disorders.
- Investigating environmental triggers for MS and other autoimmune neurological disorders in children. Trials assessing the safety and effectiveness of disease-modifying treatments for children are underway. The insights from these trials will contribute to our **understanding of how to best treat pediatric MS.**
- Identifying enzymes that target specific proteins that contribute to the development of central nervous system immune responses, demyelination and axon injury. These **enzymes, called proteases, may provide a novel, previously untapped target for protective and reparative therapies.**
- Developing **robotic devices for patients with impaired limbs** to help them regain strength and function in those limbs.





Neuromyelitis Optica

Mayo Clinic is recognized as a center of excellence for neuromyelitis optica (NMO) diagnosis, treatment and research. Our experts are committed to discovering the cause of this disease and developing new and better treatment strategies for patients. Advances in research and technology provide patients with hope. Recent progress includes:

- Establishing NMO spectrum disorders as a way to classify and unify a variety of related disorders to help focus research and treatment approaches. Experts can now identify the best treatment therapies for individuals more effectively and efficiently.
- Detecting the first antibody biomarker for NMO and developing a diagnostic test to distinguish the disease from MS. This discovery, using samples from our biorepository, enabled scientists to positively diagnose NMO and initiate appropriate treatments.
- Launching phase III of a worldwide clinical trial testing eculizumab, a drug typically used to treat blood disorders, shown in previous studies to successfully halt and prolong the time between NMO attacks. If the trial is successful, it will result in application to have eculizumab approved for NMO treatment.
- Discovering novel mechanisms of injury and cellular stress induced by the NMO antibody and identifying molecular pathways that are targetable by current drugs.
- Developing new tools for screening the molecular and cellular effects of the pathogenic antibodies present in NMO patients and establishing methods for predicting disease progression based on laboratory models.

Autoimmune Neurological Disorders

Across the Center for Multiple Sclerosis and Autoimmune Neurology experts collaborate to understand, at the cellular level, what mechanisms cause the body to attack itself. For the spectrum of autoimmune neurological disorders, where an early and accurate diagnosis is paramount, we focus our research efforts on diagnostic tests and treatment options.

The center's experts build on previous successes and groundbreaking research to increase our understanding of autoimmune disorders that cause disabling symptoms for our patients, including:

- Vision loss.
- Spinal cord disorders.
- Movement disorders.
- Dementia, epilepsy and encephalopathy.
- Paraneoplastic (cancer-related) neurological disorders.
- Nerve, muscle and neurotransmission disorders (neuropathy, myositis and myasthenia gravis).
- Intestinal disorders (AGID – autoimmune gastrointestinal dysmotility).

Our core belief is that understanding the basic mechanism of disease will lead to new therapies. We continue to pioneer new techniques to treat and provide hope for all our patients with autoimmune neurological disorders.

“The best interest of the patient is the only interest to be considered, and in order that the sick may have the benefit of advancing knowledge, union of forces is necessary.”

– William J. Mayo, M.D.

WHAT MAKES MAYO CLINIC UNIQUE

At the Center for Multiple Sclerosis and Autoimmune Neurology, we see the whole picture, not just the individual neurological disorder. Our experts work across the continuum of research, practice and education to provide exactly the care each patient needs. To advance Mayo Clinic's tradition of groundbreaking progress, the center must continue to perfect the delivery of care and deploy critical infrastructure necessary to support translational innovations.



Patient Care



Education



Research

THE MAYO CLINIC MODEL OF CARE

The center's collaborative approach **breaks down traditional borders of neurological subspecialties** such as neuro-oncology, stroke, epilepsy, behavioral neurology and movement disorders, allowing us to find connections across a broad spectrum of disease and target common underlying mechanisms.

We bring all of Mayo Clinic's resources to bear to advance answers and achieve the Mayo Clinic Model of Care, including neurology, immunology, radiology,

physical medicine and rehabilitation, pediatrics, genetics, pathology, biochemistry and laboratory medicine.

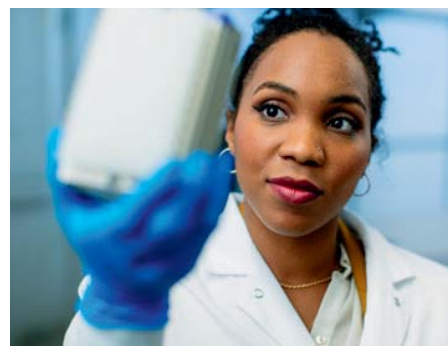
The diversity of conditions and number of patients we see with autoimmune neurological conditions are **unmatched in the world**, making the center a highly sought-after destination for patient care and trusted resource for physician consultation.

Critical Infrastructure

Biorepository

The Center for Multiple Sclerosis and Autoimmune Neurology biorepository enables experts to collect, process and store biospecimens — including DNA, tissue samples, plasma, serum and cerebrospinal fluid (CSF) — from individual patients and volunteers. These biospecimens fuel critical research to identify biomarkers for earlier diagnosis and treatment targets.

Expanding and enhancing this biorepository will accelerate new and innovative treatments by allowing faster access to a wider range of samples for use in research and for sharing results among investigators. Mayo Clinic currently has the United States' largest biorepository of brain tissues, serum and CSF samples from patients with inflammatory demyelinating disorders and autoimmune neurological disorders. These biospecimens continue to fuel our ground-breaking discoveries.



Bioinformatics Infrastructure and Personnel

Now in the era of "big data," new investigations require bioinformatics and statistical analyses to derive meaning from massive data sets. With the right tools and specialized talent available, Mayo experts can access the information they need more efficiently and effectively, ultimately benefiting drug discovery and human clinical trials.

Molecular Imaging

Using magnetic resonance imaging (MRI), Mayo Clinic scientists can detect the interactions of immune cells with central nervous system cells and better understand what mechanisms are at play in the destruction and repair of cells and tissues. Optimizing brain imaging technology is key to advancing research and measuring success in clinical trials.



Clinical Trials

Investigators are involved in numerous clinical trials focusing on translational diagnostic and therapeutic research programs across Mayo Clinic's three campuses — in Phoenix/Scottsdale, Arizona; Jacksonville, Florida; and Rochester, Minnesota — giving the center a broad geographic reach and diverse patient populations. These clinical trials afford Mayo patients the opportunity to be involved in breakthrough research.

World-Class Researchers

Our interdisciplinary model harnesses the collective knowledge of clinicians and scientists in neuroscience, bioengineering, radiology, immunology, physical medicine and rehabilitation, pediatrics, genetics and laboratory medicine. At the same time, we are devoted to training and nurturing the next generation of scientists and investigators who will make the next bold advances in our understanding of MS and autoimmune neurology.



Mayo Clinic's reputation for scientific discovery results from pairing talent with the right resources.



The Defining Difference

Mayo Clinic has a responsibility to provide whole-person care to everyone who needs healing. As a not-for-profit organization, we seek new medical knowledge and share discoveries with others to make a difference in communities near and far.

Your gift to the Center for Multiple Sclerosis and Autoimmune Neurology advances this cause by helping us imagine the unimaginable — and make it reality. On behalf of patients everywhere, thank you for your philanthropic interest.

For information on supporting neurological research at Mayo Clinic, please contact:

Department of Development
Mayo Clinic
Toll-free: 1-800-297-1185
www.mayoclinic.org/development