



Neuromyelitis Optica

NMO

What You Need to Know

A guide for patients, their families and caregivers

THIRD EDITION

EDUCATION • RESOURCES • RESEARCH • AWARENESS

Providing information and support for those living with NMO



You may have NMO –
but NMO does not have you.





Welcome. You are not alone...

You have taken the first step with us by saying yes to a cure.

When Ali was diagnosed with NMO in 2008, there was next to no information available for anyone facing what at that time was a poorly understood autoimmune condition. When we learned how little was being done to advance basic and clinical science toward solving NMO, The Guthy-Jackson Charitable Foundation was formed. We said yes to funding the research needed to better understand, treat, and ultimately cure NMO. We gathered the best and brightest experts in many disciplines and they said yes—to leading us on a life-saving path of progress.

In preparing this 3rd Edition of our **NMO Patient Guide**, we are more inspired than ever by all the members of our NMO community—especially the scores of patients who have said yes to sharing your stories and your clinical data. Together we have made great strides on our mission to solve NMO. From the new diagnostic criteria that improve the speed and accuracy of NMO and NMOSD diagnosis, to exciting clinical trials studying new drugs to prevent relapses, we are making a difference. When patients participate in formal clinical trials, they are helping to develop safe, effective and approved treatments. And when patients and families donate blood to the CIRCLES program, they are helping to unlock the mysteries to solving NMO.



To date, over 15,000 readers have eagerly reached for prior editions of our **NMO Patient Guide**. We gratefully receive many thoughtful words of appreciation, along with reports that convey a global connection among those who live with NMO. Together we continue to raise awareness of this rare disease. Together we say yes to breakthroughs that will unlock solutions for NMO patients, and for patients suffering from autoimmune diseases, who number as many as 30 million in the U.S. alone, and hundreds of millions worldwide.

Our **NMO Patient Guide** is intended to inform and inspire all those who have been affected by NMO.

With love and hope,
Victoria Jackson and Ali Guthy, Founders





You Are the Cure

A decade ago, only a handful of specialists had even heard of NMO—this rare and orphan condition in which many patients are often first diagnosed as having multiple sclerosis or other diseases. That all changed with The Guthy-Jackson Charitable Foundation and its mission to cure NMO.

Together with countless patient heroes, their families and a laser-focused NMO research consortium, the Foundation united a global team of problem-solvers to decode the mystery of NMO. From state-of-the-art laboratories to leading drug companies, these efforts have forever changed the landscape of NMO science and medicine. These steps from molecules to miracles are told in **The NMO Story** and **NMOtion** features.

Many patient-inspired milestones have been achieved on this mission to cure NMO, including:

- NMO research publications have risen from less than 550 as of 2007 — to over 4,000 as of 2017
- Today, the GJCF international clinical consortium links 79 members from 24 countries worldwide
- We now know NMO is due to autoreactive T and B cells, autoantibody, complement and leukocytes

- In 2015, the International Panel for NMO Diagnosis (IPND) rewrote the book on NMO diagnosis
- Based on IPND criteria, NMO is now estimated to be 50 percent more common than previously known
- New diagnostic criteria have improved diagnostic speed & accuracy for NMO and related diseases
- NMO is now clearly differentiated from MS in terms of causes, effects, diagnosis and clinical care
- Two distinguishable forms of NMO have been characterized: AQP4-reactive and MOG-reactive
- Gender, race, geography and other factors are now known to contribute to NMO epidemiology
- CIRCLES, the largest multi-center NMO study, is on its way to its goal of 1,000 NMO patients enrolled
- Key genes that appear to influence NMO risk have been identified and are now being investigated
- Biomarkers are emerging as predictive signals of pathogenesis, relapse and treatment outcomes
- Today, multiple clinical trials are underway to find safe and effective new treatments for NMO
- Over 10 drug targets have been discovered in NMO, creating a pipeline for next-gen treatments
- The Foundation is now catalyzing a bold new science of tolerization to cure NMO permanently



There is more to do to solve NMO—and only patients can provide the X factors for cures. They hold the keys—their courage and optimism inspire us to find them. Like patients, we have made ending NMO personal.

Combining rare hearts with rare minds is how every patient, advocate, researcher and industry and regulatory partner has helped the Foundation revolutionize the field of NMO—it is a model that is redefining how information can be shared, answers can be found and lives can be saved.

Breakthroughs made to help solve NMO have also sparked a bold new movement to solve other diseases—rare and not so rare. From multiple sclerosis, diabetes, lupus and like autoimmune diseases—to cancer, heart disease, infection, wound healing, transplantation and aging—secrets of the immune system learned from NMO shine a bright new light to help meet the greatest challenges in human health.

Extraordinary people inspire extraordinary achievements. Whether through clinical trials, research, advocacy, sharing your story or raising funds, everyone can participate in the cure for NMO. **You Are the Cure.**

With heartfelt thanks to every NMO patient, family, caregiver, researcher, clinician and stakeholder —

Dr. Michael Yeaman
Chair, GJCF Advisor Team









Using This Book

This guide may be a companion, a mentor, a compass, a friend – all meant to support you on your journey with neuromyelitis optica (NMO) and/or neuromyelitis optica spectrum disorder (NMOSD). Refer to section 1.7 for more information about the distinction between NMO and NMOSD. While certain sections address NMO and NMOSD specifically, for simplicity in this guide, the abbreviation NMO will be used to include both NMO and NMOSD. Whether you are a patient, a caregiver, a family member, a friend, or someone who just wants to learn more about NMO, we hope that you can find some answers to unanswered questions, a helping hand where there was no help. Perhaps its contents will encourage patients and all stakeholders to gain comfort and knowledge from the resources in this guide and in the foundation's online community. Because this book offers a great deal of information, we encourage you to pace yourself. In navigating the world of NMO, we hope this guide may serve as an interactive tool that will aid living with NMO until there is a cure. You may have NMO – but NMO does not have you.

To address primary concerns of NMO patients, their families and caregivers, information is presented in a format to best assist newly diagnosed as well as established patients. The content lists at the beginning of each section aim to assist in finding specific information.

This book provides information intended to help everyone best meet the unique challenges of living with an uncommon disease. Ask your doctor for advice regarding questions that arise as you read this book.

Valuable companions to this guide include:

- The Guthy-Jackson Charitable Foundation website: **guthyjacksonfoundation.org**
- **NMO Resources**, the free smartphone app for NMO and NMOSD **smarturl.it/nmoresources**

There you will find ways to help cure NMO by educating yourself about or participating in NMO clinical trials, joining the CIRCLES study and biorepository, learning of the latest scientific discoveries, and engaging to the NMO community through social media like Facebook and Twitter. Patients and caregivers may gain from these opportunities by connecting with others who are living with NMO. Other helpful resources include:

- **NMOTV** – a library of videos and multimedia tools to understand NMO in many different ways

- **Spectrum** – a library of published NMO studies that highlight the exciting new discoveries emerging from NMO research
- **Connect the Docs** and **Mapping NMO** – assist in locating NMO clinicians and our community of NMO Advocates
- **NMOtion** – (pronounced “in motion”) tools and resources targeting NMO advocacy, education, and raising general awareness about NMO
- **LEAD** – an educational program empowering patients to educate themselves about NMO and opportunities to participate in the cure
- A link to our **donation page** for those who are able to contribute to NMO research. Any donation amount is welcome and appreciated on our mission to cure NMO. **The Guthy-Jackson Charitable Foundation allocates 100 percent of all donations directly to NMO research.**





The Guthy-Jackson Charitable Foundation is proud to facilitate awareness and education about NMO. It is important to note that information provided in this resource guide should not be used or considered as clinical advice, therapeutic recommendations, or medical treatment. For specific information and medical advice, consult your physician. The Guthy-Jackson Charitable Foundation does not endorse or recommend specific products, services, manufacturers, or assume any liability whatsoever for the use or content of this or any product or service mentioned.



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Preface

A diagnosis of neuromyelitis optica (NMO) and/or neuromyelitis optica spectrum disorder (NMOSD) can be confusing and frightening for patients and loved ones. Many newly diagnosed patients may feel overwhelmed, powerless, and afraid. The resources contained in this guide are intended to empower all those affected by NMO — and help NMO patients and their families understand that you are not alone — others travel this road with you. While certain sections address NMO or NMOSD specifically, for simplicity in this guide, the abbreviation NMO will be used to represent both NMO and NMOSD.



How many people have been diagnosed with NMO? This answer remains difficult to know precisely. However there is emerging evidence that the number of cases is considerably higher than known to date. This situation may be due to a previous lack of awareness of the disease, limited test methods that did not allow accurate diagnosis, and similarities that NMO shares with other autoimmune and neurologic conditions. Current studies indicate that the **incidence** (number of new cases) and **prevalence** (total number of known active cases) of **NMO are significantly greater than originally estimated**. Importantly, NMO is now becoming more effectively diagnosed thanks to new diagnostic methods, laboratory tests, and special imaging methods. Many of these tools have emerged in just the past several years, so the current estimates of NMO disease almost certainly do not reflect the actual incidence and prevalence of NMO worldwide.

Historically, the prevalence of NMO was estimated to be approximately 1-4 per 100,000. Today, due to improved awareness and advances in clinical diagnosis, research data estimate that NMO afflicts up to **10 in 100,000** persons. **This rate suggests nearly 15,000 NMO patients in the U.S. alone, and hundreds of thousands of patients worldwide**. Interestingly, the prevalence of NMO appears to vary in different regions and among distinct populations around the world. Because such population effects may result from heritable or environmental factors, this observation may provide new insights into the genetic contributions to NMO.



NMO is one of roughly **7,000 rare diseases** that affect about **30 million people in the U.S. alone**, and up to **700 million individuals worldwide**, according to the **National Institutes of Health (NIH)** and **World Health Organization (WHO)**. Each rare disease touches a relatively small population, making it difficult to recover research costs of developing treatments. Rare diseases are often called **orphan diseases** because they have not been adopted by the pharmaceutical industry as a focus for drug development. **However, NMO is special even among rare**

diseases, because there is a simple blood test that can enhance diagnosis and aid potential therapeutic development. This test is called the **NMO-IgG assay**, which determines whether an individual has detectable autoantibody in their blood or cerebrospinal fluid that targets the **aquaporin-4 (AQP4)** protein. In this guide, details are provided about this test, and where it can be accessed.

While a diagnosis of NMO can be challenging, it can also reveal great strengths. When faced with their teenage daughter's diagnosis of NMO, the Guthy-Jackson family set out on a mission on behalf of all those affected by this uncommon disease: to catalyze groundbreaking research to accelerate treatments and cures. By forming The Guthy-Jackson Charitable Foundation, research was launched to facilitate prevention, diagnosis, treatment, and quality of life for NMO patients and caregivers. To do so, the Foundation brought together scientists and clinicians, pharmaceutical and biotech companies, governmental agencies, as well as patients and families to explore ways to cure this disease.

The Guthy-Jackson Charitable Foundation (GJCF) is a non-profit 501(c)(3) organization dedicated to funding breakthrough research, increasing public health education, and bringing physicians and researchers together to develop safe and effective treatments and ultimately find a cure for NMO.

To facilitate these goals, the GJCF has assembled leading scientific and medical teams that have published the latest scientific and clinical guidelines. The Foundation

has also established expert clinical centers for NMO research (called CIRCLES sites; refer to Chapter 5). The GJCF has also directly funded innovative basic and clinical science to better understand causes and effects of NMO, and in turn, improve NMO diagnosis and treatment. The GJCF promotes collaboration among scientific, clinical, industry, and regulatory partners to accelerate new medical solutions and end NMO once and for all.

NMO patients and their blood relatives are invited to talk to their clinicians and caregivers about the possibility of volunteering to participate in clinical research.

Everyone can play a role in curing NMO.



NMO Explained

NMO Explained

- I.1 What is NMO?
- I.2 What is the NMO-IgG biomarker?
- I.3 Are there different types of NMO?
- I.4 What causes NMO?
- I.5 What are the symptoms of NMO?
- I.6 What can I expect in the course of disease?
- I.7 How is NMO diagnosed?
- I.8 Diagnoses Other Than NMO
- I.9 Recognizing an NMO Relapse (Attack)
- I.10 Areas of the Body Commonly Affected by NMO
- I.11 How does NMO affect the body?
Mechanisms of Damage

I.1 What is NMO?

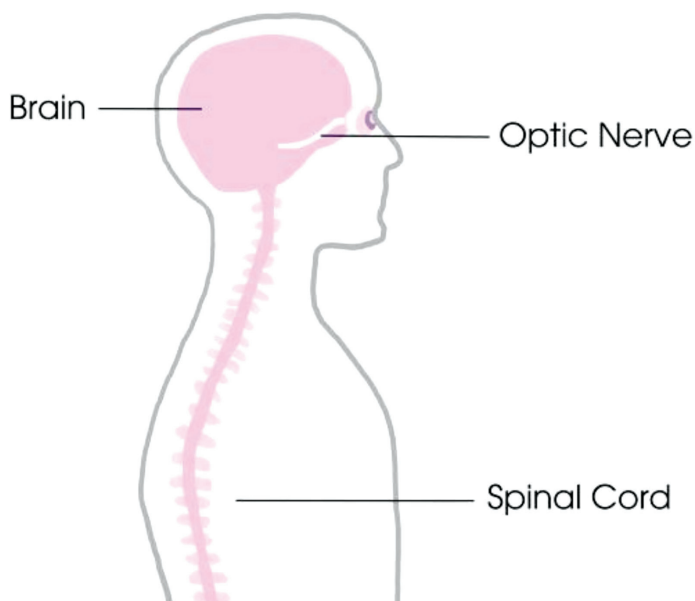
Once thought to be a type of **multiple sclerosis** (MS), **neuromyelitis optica** (NMO) and **neuromyelitis optica spectrum disorder** (NMOSD) are variants of a distinctive but rare autoimmune disease. Today, NMO and NMOSD occur when the immune system mistakes normal tissues of the **central nervous system** (CNS) as being foreign. As a result, the immune system attacks these tissues, making proteins (called **antibodies**) and recruiting immune system cells that can harm otherwise

healthy parts of the CNS. Often, because CNS tissues are rich in a protein called aquaporin-4 (AQP4), **the initial attack targets the nerves of the eyes and other parts of the CNS, which include the brain and spinal cord.**

QUICK READ

Neuromyelitis optica (NMO) and **NMO spectrum disorder (NMOSD)** are diseases that damage tissues of the **central nervous system (CNS)**. These conditions likely result from dysfunction in the immune system such that it reacts to otherwise healthy, “self” tissues. This mistaken identity causes injury and swelling (**inflammation**) of the optic nerves (**optic neuritis or ON**) and/or spinal cord (**transverse myelitis or TM**). The first symptoms of NMO are often changes in vision (light perception or acuity), eye pain, loss of balance, and/or numbness or weakness of the feet, legs, arms, or hands. These symptoms may improve, but can reappear (**relapse**) and may worsen over time.

NMO is an inflammatory disease of the CNS characterized mainly by attacks (**relapses**) of swelling and damage in the optic nerves (optic neuritis or ON) and spinal cord (transverse myelitis or TM). Normally, nerve cells (neurons) depend on special cells called **astrocytes** for survival and function.



When astrocytes are injured by autoantibody directed against the AQP4 protein, as occurs in NMO, the nearby neurons can also be damaged directly or due to inflammation. In turn, injured and inflamed neurons can lose function, causing vision impairment or loss (ON), as well as imbalance, incontinence, weakness, numbness or paralysis of limbs or other body parts.

Astrocyte and neuron damage can also cause **demyelination**. This process erodes the protective **myelin sheath** covering that insulates nerve cells. Damage to myelin slows or stops nerve impulses traveling to or from the brain which may affect many physical systems. Some patients diagnosed with NMO may have attacks that affect certain parts of the brain, especially at the connection point of the spinal cord to the brain itself, a location called the **brainstem**.

1.2 What is the NMO-IgG biomarker?

A **biomarker** is a type of cell or molecule that is used to diagnose or predict a disease, or monitor how well a drug may be working to prevent a relapse or treat the disease. **In NMO, the immune system creates an autoantibody that targets the astrocyte water channel protein called aquaporin-4 (AQP4), a unique biomarker.** This special biomarker is called anti-AQP4 immunoglobulin G, or more simply **NMO-IgG**.



The GJCF is funding research to seek other important biomarkers to help prevent, treat or even cure NMO. Biomarkers may be found in some places in the body but not others. For example, certain types of cells and molecules pass through the **blood brain barrier** (BBB) and into the **cerebrospinal fluid** (CSF), while

others do not. So, particular biomarkers may be present in the CSF, while others are found only in the **peripheral bloodstream** (e.g. circulating blood as may be drawn from a vein in the arm). Some biomarkers change in concentration or location in the body over time. This fact may afford the opportunity to discover biomarker(s) to help guide safe and effective therapy, or perhaps even **predict when a relapse is going to occur**. If proven to reliably indicate or predict the diagnosis, disease status or severity, or a response to therapy, **NMO biomarkers can be important tools in preventing, treating or curing NMO**. Proving that a biomarker is specific to NMO or a key signal of the disease is a process called **validation**. This process must be carefully performed, and eventually approved by regulatory agencies for a biomarker test to be certified for use in the clinic.

To date, **the NMO-IgG test result is positive in ~75% of patients diagnosed with NMO**.

Because **serum** is most often used to test for the presence of NMO-IgG antibody, a positive result is termed **seropositive**, while a negative result is termed **seronegative**. Among the ~25% of patients who are

To date, the NMO-IgG test result
is positive in ~75% of patients
diagnosed with NMO.

seronegative, there may be several reasons for such a result, including:

- the type of test (called an **assay**) used to detect the antibody was not effective (did not detect the antibody even though it may be present)
- the type of biospecimen tested (e.g. blood vs. CSF) did not contain any detectable NMO-IgG
- no NMO-IgG exists, suggesting an autoimmune process and/or auto-antigen different from NMO-IgG. For example, in some cases autoantibodies other than anti-AQP4 may be present (see below).

Although uncommon, **the assay results for NMO-IgG may change over time in some individuals.** For example, certain types of therapies may affect the ability of laboratory tests to detect NMO-IgG. Likewise, as assays improve, **NMO-IgG may be detected in some patients who have tested negative in the past.** This area of research is rapidly advancing, and may help uncover the causes and cures of NMO.

**Anti-MOG antibody may be a
new biomarker candidate in some
NMOSD patients.**

Do You Know...

The NMO-IgG test can be ordered by any qualified clinician. Today, there are many reference laboratories that can perform the test and report results within days.

Learn more about the NMO-IgG test and access the updated NMO diagnostic criteria on the GJCF website at:

guthyjacksonfoundation.org/diagnosis

One area of recent focus in NMO research is that of seronegative patients. New evidence suggests that antibodies to antigens other than AQP4 may exist in this group of patients. For example, antibody targeting **myelin oligodendrocyte glycoprotein (MOG)** appears to be present in some patients in whom NMO-IgG cannot be detected. This pattern suggests that **anti-MOG** antibody may be **a new biomarker candidate in some NMO patients.**

The GJCF supports breakthrough research to improve assay accuracy and reliability, understand where biomarkers are best found in the body, and explore **immune pathways** that may drive NMO disease regardless of whether it involves AQP4, MOG or other autoantibodies or targets of autoimmunity.

The NMO-IgG antibody test can be requested by any qualified clinician in the United States and many countries around the world. **The availability of the test is increasing globally due to collaborations in clinical research, and the launch of clinical trials evaluating drug candidates intended to achieve safe and effective treatment for NMO.** Individuals are encouraged to ask their doctor about the NMO-IgG test, as well as NMO clinical trials. For more information, please refer to section 1.7.



**Learn More On
NMO Resources.**

*Download the app for free on
your Android or iOS device today!*

Available on the
App Store

ANDROID APP ON
Google play

Historically, NMO was most commonly diagnosed when both the spinal cord and optic nerves were affected, leading to vision problems along with limb weakness or paralysis. Yet, NMO may include more limited presentations that involve attacks of just one area (e.g. either ON or TM) with or without the AQP4 antibody. Research is quickly advancing, making it likely that diagnostic and therapeutic approaches to NMO will be further refined. Other conditions might also be considered as being within the definition of NMO. For example, inflammation of the brainstem that leads to **uncontrollable hiccups and nausea or vomiting**

that last for extended periods of time may be caused by NMO. The classification and diagnostic criteria regarding NMO are anticipated to evolve as new insights are gained and applied to improve patient care.

For simplicity throughout this guide, the abbreviation NMO is used to mean both NMO and NMOSD.

1.3 Are there different types of NMO?

QUICK READ

There are two forms of NMO based on recurrence:

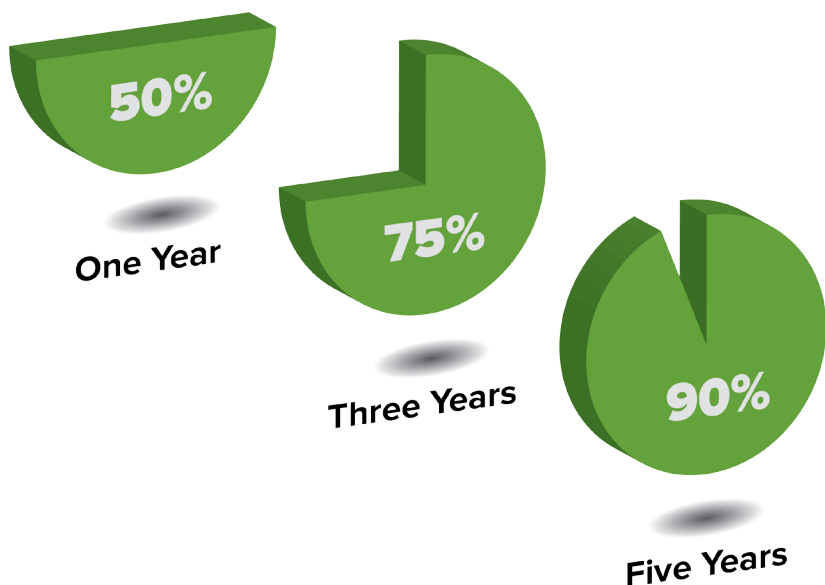
1. Relapsing NMO
2. Monophasic NMO

- **Relapsing NMO** is most common and identified by recurrent attacks separated by months or years. Attacks are usually followed by partial or complete recovery during periods of remission. **This relapsing form of NMO appears to affect women 4 times more commonly than men.** Unfortunately, in some severe cases of relapsing NMO, recovery may not occur following a relapse, causing permanent disability.

- **Monophasic NMO** is less common and is usually characterized by a single, severe attack over a short period of time (days or weeks). As a rule, relapses do not occur in monophasic NMO. This form of NMO typically affects optic nerve(s) and the spinal cord. Interestingly, women and men tend to be equally affected by this form of NMO.

When a patient is first diagnosed with NMO, it is unclear whether they will experience a monophasic or relapsing course. In either scenario, accurate and rapid diagnosis of relapses is a key to minimizing severity and promoting recovery.

***Probability of recurrence
among patients with relapsing NMO:***



1.4 What causes NMO?

QUICK READ

The exact cause of NMO is unknown. As with many autoimmune conditions, NMO is likely caused by a combination of factors, and may be caused by different factors in different patients. Some of the factors being studied for potential contributions to NMO include:

- Genetics
- Co-existing Autoimmunity
- Infection or Vaccination
- Metabolic Disorders
- Endocrine Disorders
- Allergies
- Other Environmental Factors
- Combinations of the above

It should be emphasized that none of the above factors are known to cause NMO. Experts also do not know the causes of NMO relapses. The factors listed here, and detailed in the following pages, are among those on which research is being focused for their potential roles in this disease.

Genetics: Changes in structure or function of one or more genes may contribute to NMO disease. Such genetic changes may be present at birth, or

acquired over the course of one's life. Recent studies suggest that compared to Caucasian populations, people of Asian or African ancestry have a higher tendency to develop NMO. However, current research does not suggest heritability as a primary cause of NMO, nor is NMO significantly more common among relatives of NMO patients. It is estimated that 3 percent of patients have one or more family members affected by NMO, usually just a single individual. Although rare, NMO is more common than might be predicted by chance occurrence. This observation may suggest some genetic influences in the development of NMO. Careful research is being conducted to uncover new insights into possible genetic causes of NMO.

Co-Existing Autoimmunity: NMO is an autoimmune disorder. This means that the body's own defense system (**immune system**) attacks its own tissues and organs. In other words, the immune system turns on the body itself and causes disease. In NMO, the immune system is believed to target the **aquaporin-4**

Sometimes patients with one kind of autoimmune disease also develop other autoimmune diseases. This situation is termed co-existing autoimmunity, and may occur in NMO.



protein (AQP4) that is enriched on cells called **astrocytes** in the **central nervous system** (CNS). Currently, researchers believe that astrocyte injury and inflammation leads to loss of the myelin sheath that protects nerves (a process called **demyelination**), and results in CNS symptoms commonly present in NMO. Sometimes patients with one kind of autoimmune disease also develop additional autoimmune diseases, and this may be true for NMO. Approximately one-quarter of patients with NMO, especially those with a positive blood test for AQP4 autoantibodies (see section 1.7), also have one or more other autoimmune diseases, such as systemic lupus erythematosus, Sjögren's syndrome, autoimmune thyroid disease or myasthenia gravis.

Infection or Vaccination: The causes of NMO are currently unknown, and at present no infection or vaccine is known to cause NMO or relapses.



Hypothetically, there are many possible **triggers** of NMO, but **there is no clear evidence to prove any specific causes**. NMO researchers are open-minded to all possibilities for understanding how NMO begins and relapses occur in patients. Interestingly, it is possible that the initial causes of NMO and the triggers of NMO relapse may not be identical, and may be different from patient to patient. Some patients report having what they believe to be a respiratory, urinary tract, or flu-like infection prior to a relapse. While it is possible that

infection or vaccination may influence relapse, there is no proof of any cause-and-effect relationship in this regard to date. The causes of NMO and relapses are likely complex, and could involve many factors, including patient genetics, diet, hormone status, microbial flora (the **microbiome**), emotional stresses and many other factors. Furthermore, different factors may contribute to NMO onset or relapse in different patients. Studying the potential causes of NMO in a careful and evidence-based manner is the most responsible way to find meaningful answers and is a key mission of the GJCF.

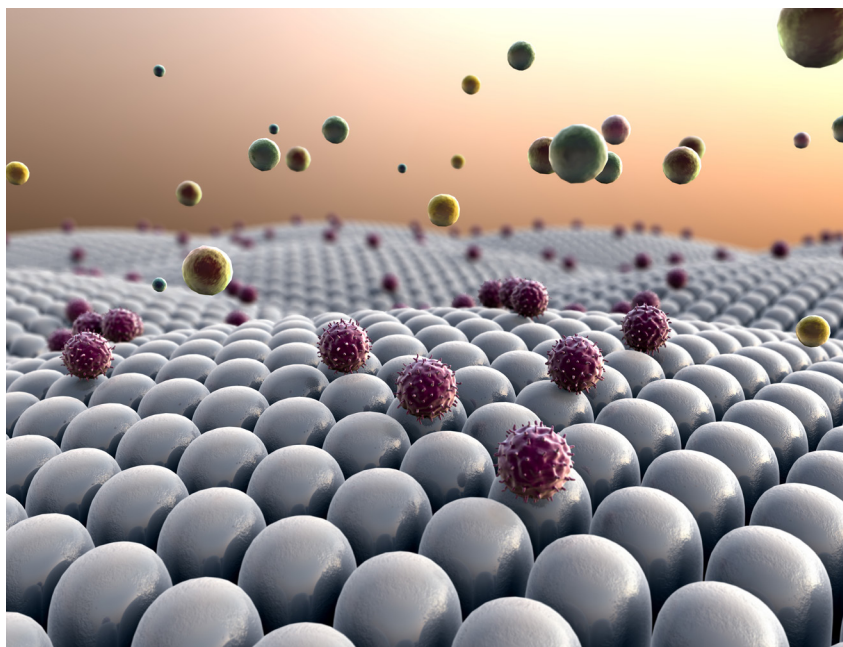
It is important to note that vaccination remains among the most effective ways to prevent many serious medical conditions, and to date the benefits of immunization programs far outweigh any known risks. Even so, it is best to consider vaccines carefully with respect to the specific needs, medical history and potential risk factors in each individual. **As with all information in this guide or elsewhere, NMO patients or anyone considering vaccination should consult with their physician or NMO specialist to assess the potential benefits or risks of vaccines that may be recommended.**

Metabolic Disorders: In recent years, certain autoimmune conditions have been suggested to be associated with metabolic disorders. For example, type-1 diabetes (T1D) is due to an autoimmune process in which the immune system attacks cells in the pancreas that make insulin. As a result, T1D can affect the

metabolic status of the patient. While unknown, it is possible that NMO may arise from a process that involves **metabolic dysfunction**, and NMO may contribute to such dysfunction. Some researchers believe that certain foods, including high-salt or sugar-rich diets can contribute to a general increase in **inflammation in the body**, or perhaps autoimmune diseases. One interesting area of current research focuses on food components as they may affect the microbiome of a person as potentially contributing to NMO or other autoimmune diseases.

Endocrine Disorders: NMO and most autoimmune diseases occur at a **much higher frequency in women than men**. This fact suggests there are unique aspects of gender that may contribute to autoimmune diseases, including NMO. For example, **hormones that differ in females and males** can influence the immune system, particularly during child-bearing years in women. Likewise, pregnancy can alter immune system function, and influence NMO onset or relapse frequency or severity. Research is in progress to better understand potential relationships among gender, hormones, pregnancy (refer to section 3.4), and NMO causes or relapses as compared to other related autoimmune conditions.

Allergies: Excessive or misdirected immune system responses are involved in allergies, as they are in autoimmune diseases. It is possible that there may be a common factor connecting these two conditions, which may contribute to NMO onset or relapse. This area of



research is a focus of studies that are currently ongoing. One exciting area of research involves treatments to reset the immune system in NMO and other autoimmune diseases, similar to methods used to solve allergies. For NMO, this strategy is called **tolerization therapy**. If successful, restoring immune tolerance in NMO has the **potential to solve the disease**, without the need for long-term immunosuppressive therapy. Minimizing or eliminating the need for long-term immunosuppression is important to reduce risks of infection, cancer or other conditions associated with such treatments.

Other Environmental Factors: Environmental factors may also contribute to the risk of NMO onset, relapse or severity. For example, the potential roles

of smoking, stress (physical and emotional), fatigue, temperature, geography, environmental pollutants or toxins, and other factors are being explored for potential impact on NMO through clinical science called epidemiology. In such studies, many different variables may be examined for potential correlations to NMO risk or relapse.

1.5 What are the symptoms of NMO?

QUICK READ

Common symptoms of NMO may include:

- Eye pain or an “eye headache”
- Changes in vision (light, color, or clarity) due to optic neuritis (ON)
- Numbness or weakness in limbs due to transverse myelitis (TM)
- Imbalance, dizziness, or pins-and-needles sensations
- Loss of bowel or bladder control

The symptoms of NMO can vary from person to person in disability, duration and severity.

However, NMO is most commonly characterized by **optic neuritis (ON)** that affects eye function, and/or **transverse myelitis (TM)** that affects limb function.

Generally, NMO symptoms begin rapidly. After the initial attack, **NMO follows an unpredictable course, and time to remission can vary.** Recurring episodes of optic neuritis and/or transverse myelitis can be weeks to months in duration, and in some very unusual cases can last years. However, much more often these symptoms are temporary and resolve fully or partially, usually after a course of treatment.

Symptoms and signs of optic neuritis (ON) may include:

- Rapid onset of eye pain or “eye headache” that is worsened by eye movement
- Impaired or complete loss of vision usually in one eye, but in some cases in both eyes
- Reduced light perception, color vision, visual clarity, and/or depth perception

Symptoms of transverse myelitis (TM) include:

- Pain in the neck or back
- Tightness or corset-like sensations in the abdomen, as well as arms or legs
- Sensitivity to touch, cold and heat
- Feeling of numbness, tingling, coldness, itching or burning, often spreading to large parts of the body over a period of minutes, hours or occasionally days



- Weakness in arms or legs ranging from mild to complete paralysis in one or multiple limbs
- Urgent need to urinate or difficulty urinating; urinary incontinence (unintentional passing of urine)

- Constipation leading to vomiting, abdominal bloating, pain and inability to pass stool or gas; or bowel incontinence (unintentional passing of stools)
- Muscle spasms that may last for several minutes accompanied by arm or leg pain
- Fever in some cases

In cases of brainstem or brain involvement symptoms may include:

- Prolonged hiccups, nausea, vomiting or dizziness
- Mental confusion

1.6 What can I expect in the course of disease?



QUICK READ

NMO patients may experience any of the following:

- Acute attacks of ON or TM
- Rapid development of symptoms
- Potential plateau of symptoms
- Symptoms may improve over weeks and/or months with treatment

NMO is considered an acute disease because it **comes on suddenly, lasts a short time** and **may enter a remission**. Progressive disability developing over months and years is unusual. However, individual attacks may not be recoverable leaving severe neurological disabilities that are permanent.

NMO symptoms may develop quickly — **even within a few hours** — increase over the course of a few days and then plateau. Symptoms may improve over weeks and months with treatment. Lasting signs and symptoms of NMO may differ in each patient, and vary according to many factors, including:

- The severity and degree of recovery from the first attack
- The number and frequency of subsequent relapses
- The effectiveness of therapies

- Other co-existing conditions or autoimmune disorders, if they are present or develop
- Gender
- Age
- Pregnancy
- Other factors

Depending on the response to maintenance therapy, some patients will experience multiple attacks of ON and/or TM throughout their lives. **Some measure of improvement may occur, but patients may experience residual symptoms or disabilities that persist.** Based on current data, among patients with relapsing NMO, roughly **50 percent** will have one relapse in the first year after the initial episode, **75 percent** by the third year and **90 percent** by the fifth year. **The intervals between relapses are highly variable and unpredictable, but might**

The intervals between relapses are highly variable and unpredictable, but may be managed by adjusting medications that may help to prevent or delay relapses.

be managed by adjusting medications that may help to prevent or delay relapses. Relapses can be spaced months or years apart. Although the majority of patients facing NMO have a relapsing form of the disease, early diagnosis and treatment may reduce the relapse rate and/or lessen the severity of relapses should they occur.

While uncommon, patients with monophasic NMO tend to have a more severe initial attack than those with relapsing NMO. Approximately **20 percent** of patients with monophasic NMO have permanent vision loss, and **30 percent** have permanent paralysis in one or both legs. **In order to be classified as monophasic, no relapse may occur after the initial episode of optic neuritis and/or myelitis.**

New diagnostic criteria have provided specific definitions for NMO and NMOSD that facilitate consistency in defining disease and clinical care of patients. In this new diagnostic process, potentially confusing terminologies have been clarified so that a more accurate diagnosis can be made and appropriate treatment begun more quickly for most patients.

The fact that **monophasic NMO patients** have only one attack suggests that their immune systems may find a way to correct the dysfunction that caused disease. If so, **these patients may hold discoveries that could be key to understanding NMO and finding ways to stop it.** All NMO patients are encouraged to consider participating in research,

learning more about clinical trials to help find cures, and donating blood and clinical information to research programs like the **CIRCLES NMO Biorepository** (refer to Chapter 5 for more information).



1.7 How is NMO diagnosed?

QUICK READ

NMO can be diagnosed by a combination of methods, including:

- Blood test: NMO-IgG
- Magnetic Resonance Imaging (MRI)
- Neurological examination
- Lumbar puncture (spinal tap)
- Eye tests
- Optical Coherence Tomography (OCT)

Core Clinical Characteristics of NMOSD

Most common:

1. Optic neuritis (ON)
2. Acute myelitis
3. Area postrema syndrome (APS): episode of otherwise unexplained hiccups or nausea and vomiting

Less common:

4. Acute brain stem syndrome
5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
6. Symptomatic cerebral syndrome with NMOSD- typical brain lesions

Supporting MRI Requirements for NMOSD without AQP4-IgG

1. **Acute optic neuritis:** brain MRI normal or demonstrating only nonspecific white matter lesions; OR optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium-enhancing lesion extending over >1/2 optic nerve length or involving optic chiasm
2. **Acute myelitis:** spinal cord MRI showing attack-associated lesion extending ≥ 3 contiguous segments (LETM); OR ≥ 3 contiguous segments of focal cord atrophy in patients with prior history of acute myelitis
3. **Area postrema syndrome:** dorsal medulla/area postrema MRI lesion
4. **Acute brain stem syndrome:** peri-ependymal brain stem lesions

2015 IPND Neuromyelitis Spectrum Disorder (NMOSD) Diagnostic Criteria

In 2015, a global team of experts working with The Guthy-Jackson Charitable Foundation published new guidelines for improved diagnosis of NMO. This team, known as the **International Panel for NMO Diagnosis** (IPND), created what is now known as the 2015 IPND diagnostic criteria for NMO and NMO spectrum disorder (NMOSD). Clinical research using these new criteria is already showing significant improvements in speed and accuracy of NMO and NMOSD diagnosis. These advances help patients receive the most appropriate care more quickly, and also help patients who do not have NMO in the same way.

The IPND was comprised of 18 expert members from around the world.

Core Clinical Characteristics

Most common:

- Optic neuritis (ON)
- Acute myelitis
- Area postrema syndrome (APS): episode of otherwise unexplained hiccups or nausea and vomiting

Less common:

- Acute brainstem syndrome (e.g. intractable hiccups, nausea, vomiting, dizziness or confusion)
- Symptomatic narcolepsy or acute diencephalic* syndrome with typical diencephalic MRI lesions
- Symptomatic cerebral syndrome with typical brain lesions

**The diencephalon is an associated group of structures in the brain, including the hypothalamus, thalamus, epithalamus (including the pineal gland) and the subthalamus. Collectively, these structures comprise the diencephalon, which serves key functions, including controlling many roles of the autonomic nervous system. The autonomic nervous system works automatically (known as unconscious function) to regulate critical body functions, such as heart rate, breathing, pupil response in the eyes, urination and bowel activity, and many other functions. The autonomic nervous system is often considered to have two components: the sympathetic nervous system (e.g. “fight or flight” response) and the parasympathetic nervous system (e.g. “digest and rest” effects). In these ways, the autonomic nervous system controls many unconscious functions and instinctive behaviors that can be affected by NMO.*

NMO when NMO-IgG Test Positive (Seropositive for Anti-AQP4 Antibody)

- At least 1 core clinical characteristic (see above), **and**
- Positive test for NMO-IgG*, **and**
- Exclusion of alternative diagnoses**

NMOSD when NMO-IgG Test Negative or Unknown (Seronegative for NMO-IgG Antibody)

- At least 2 core clinical characteristics (see above) resulting from 1 or more clinical attacks, **and**
- At least one of the following: optic neuritis (ON), acute myelitis with LETM, or area postrema syndrome PS, **and**
- Dissemination in space (≥ 2 different core characteristics), **and**
- MRI requirements, if applicable (see below)
- Exclusion of alternative diagnoses**



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In addition to the above clinical signs and symptoms, **magnetic resonance imaging (MRI)** may also be used to establish or rule out other features that may be associated with NMO, such as inflammation of the optic nerve(s) (e.g. in optic neuritis [ON]), longitudinally extensive transverse myelitis (LTEM; meaning a lesion on the spinal cord spanning more than 3 continuous vertebral segments), area postrema syndrome (lesions in the medulla and adjacent areas of the brain that may cause intractable hiccups, prolonged nausea / vomiting or like conditions), and other features consistent with NMOSD.

* Using best available detection method (cell-based assay strongly recommended)

** Evaluation for alternative diagnoses guided by “red flags”

Wingerchuk DM, et al. International consensus criteria for neuromyelitis optica spectrum disorders. *Neurology* 2015;85:177-189.



Why were the new diagnostic criteria necessary?

In just the last few years, quantum leaps have been made in understanding what NMO is, and what it is not. For example, it is now clear that NMO and multiple sclerosis are very different diseases in terms of immune system causes and effects. In addition, previous diagnostic criteria were not as good at recognizing NMOSD or varying forms of NMO. For these reasons, new criteria were needed to recognize these advances so that diagnosis of NMO could be made more quickly and more accurately, enabling the most appropriate medical care as soon as possible.

How were the new criteria developed?

The GJCF catalyzed much of the research that led to better understanding of NMO basic science and evidence-based clinical diagnosis. It did so by bringing

scientists and clinicians together to think in new ways to recognize NMOSD. One of the special groups organized by the GJCF was the International Panel for NMO Diagnosis (IPND). In collaboration with GJCF and its advisors, the IPND worked for nearly two years to carefully review all the available scientific and clinical data to develop the new diagnostic criteria. Data reviewed included cases, experiences, MRI and other imaging results, and laboratory testing such as serology. **In 2015, the IPND Diagnostic Criteria were officially published, and have greatly increased the speed and accuracy of NMO and NMOSD diagnosis.** It is also important to note that the 2015 IPND criteria have also benefitted patients with diseases that might otherwise be misdiagnosed as NMO, and vice versa. In this way, GJCF efforts have helped patients with NMO as well as patients who have other related autoimmune diseases.

What are the key improvements in the new criteria?

The 2015 IPDN Diagnostic Criteria for NMO offer many advances to improve the accuracy of NMO diagnosis, including:

- The new criteria address NMO Spectrum Disorder (NMOSD), an umbrella term for NMO and variants encompassed under the expanded spectrum of NMO signs and symptoms
- NMOSD patients can be further specified based on NMO-IgG status, or the presence of other autoantibodies (e.g. anti-MOG-IgG)

- Diagnosis can only be made in symptomatic individuals with compatible clinical presentations
- Clinical presentation is defined based on 6 core clinical characteristics that focus on neurologic features and their locations in the central nervous system (CNS)
- Only one core clinical characteristic is required in patients seropositive for NMO-IgG
- Criteria for NMO-IgG seronegative NMOSD are similar to those for seropositive patients, but include additional requirements for greater accuracy
- “Red flags” are also included in the 2015 IPND criteria, which indicated signs or symptoms that may suggest a diagnosis other than NMOSD. For example, clinical findings, imaging results and/or laboratory tests may raise concerns about NMOSD diagnostic accuracy and identify conditions that could be mistaken for NMO
- The new criteria also offer greater clarity in interpretation of NMO-IgG test results
- The criteria are more applicable to children, although there are special considerations for all pediatric cases. For example, caution is required regarding longitudinally extensive transverse myelitis lesions, which may also occur in children who have MS

Access the complete, open-source publication on the GJCF website at: guthyjacksonfoundation.org/diagnosis

What steps are involved in using the new diagnostic criteria?

A diagnosis of NMO begins with medical history, questions about signs and symptoms and a neurological examination. Key elements of diagnostic testing include:

- **Neurological Examination:** A key step in the process of diagnosing NMO is a thorough examination by a qualified neurologist or specialist in neurological diseases. The neurologist examines a patient for two types of signs and symptoms: 1) cognitive functions such as thinking, logic, memory and speech; and 2) sensory functions such as vision (acuity, depth perception, light perception, color, etc.), sensations such as touch, taste or smell, muscle strength, balance, reflexes, and coordination. An eye specialist (called a **neuro-ophthalmologist**)



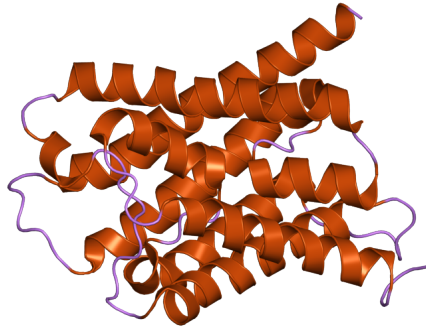
may also be involved in the examination to look for swelling or inflammation in the optic nerves or damage to the retinas.

- **NMO-IgG Blood Test (Anti-AQP4 Antibody Assay):** In approximately 75 percent of NMO patients, a specific **autoantibody** (a type of protein produced by **B cells** of the immune system) is present in the blood. This antibody can attack the **aquaporin-4** water channel protein normally present on healthy astrocyte cells of the central nervous system (brain, spinal cord, optic nerves). The blood test detects this **anti-AQP4 antibody**, which is known as **NMO-IgG** (NMO immunoglobulin G). **The detection of NMO-IgG strongly supports a diagnosis of NMO.**

However, not all patients with NMO have a positive NMO-IgG test. Someone may test



negative for NMO-IgG, but still have NMO or NMOSD. For example, it is possible that NMO-IgG may not be detectable with the test used, or the test may not be available in some places in the world.



Aquaporin-4 (AQP4)

Photo Source: By Jawahar Swaminathan and MSD staff at the European Bioinformatics Institute - Public Domain, <https://commons.wikimedia.org/w/index.php?curid=7137858>

Also, some patients may have undetectable antibody levels due to treatment they are receiving. Recently, tests have been developed that have higher rates of detecting the NMO-IgG antibody (**sensitivity**) and accuracy to reduce the chance of false positive or negative results (**specificity**). It is possible that some NMOSD patients may be **seronegative** for NMO-IgG, but have a different autoantibody that may produce similar effects as NMO-IgG. For example, **anti-MOG antibody** may be present in certain NMOSD patients.

The **NMO-IgG test** can be requested by any **qualified physician** and is generally ordered by a neurologist or other specialist evaluating a potential case of NMO, NMOSD, or other related neurological condition.



- **Magnetic Resonance Imaging (MRI):** MRI is an important tool in diagnosing NMO. This **generally safe and painless test** uses strong magnetic fields and radio waves to produce a detailed **image of the brain and spinal cord**.

In a typical MRI scan, patients are placed on a table that slides into a tube which houses strong magnets. Some centers have open MRI scanners (no tube) that are helpful for patients with claustrophobia. An MRI scan lasts approximately 30 to 60 minutes and requires the patient to be still the entire time. Often

a water-based dye (called contrast) is injected into an arm vein (through an IV or intravenous catheter) just prior to the scan. This dye allows for more specific pictures of the **lesions** or sites of inflammation in the brain, optic nerves and spinal cord and lasts in the body for only a few hours. In NMO patients, MRI test results often show lesions indicative of inflammation in the spinal cord, optic nerve(s) and occasionally in the brain. **However, brain lesions observed in NMO follow a different pattern and are not as common as in other diseases, including MS.**



- **Lumbar Puncture (Spinal Tap):** In some cases, a neurologist may request a lumbar puncture to sample **cerebrospinal fluid (CSF)** that bathes the spinal cord and brain. For example, if a patient has signs and symptoms of NMOSD, but has a negative blood test for NMO-IgG, diagnosis can be more accurate if CSF is tested for this or other autoantibodies.

In NMO, the cerebrospinal fluid (CSF) may show elevated white blood cell counts during first episodes or relapse attacks.

The lumbar puncture allows the neurological team to test the CSF for levels of immune cells, proteins and antibodies. In NMO, the spinal fluid may show elevated white blood cell numbers during attacks, which are greater than typically seen in other autoimmune diseases. In special tests to distinguish NMO from similar diseases, CSF is tested for **oligoclonal bands** (certain types of antibody groups), which are commonly detected in MS patients, and usually but not always absent in NMO patients.

- **Ophthalmological Tests:** To help obtain a correct diagnosis, patients may be referred to an ophthalmologist or neurological eye specialist known as a neuro-ophthalmologist. These experts may perform the following eye tests:

A routine eye exam will check visual clarity (acuity), the ability to perceive different colors, and depth perception.

Ophthalmoscopy examines the structures at the back of the eye such as the retina by shining a bright light into the area and using special lenses to view the structures. This eye test evaluates the optic disk

and fovea, which is the area where the optic nerve enters the retina in the back of the eye. The optic disk becomes temporarily swollen in about one-third of people with optic neuritis (ON). Patients who have had previous ON due to NMO may have a permanently pale optic disk, but the same signs may be present in patients with MS and other conditions that target the optic nerve. For these reasons, this finding is not specific for NMO.

Pupillary light reaction (PLR) tests the eyes to see how the pupils respond when exposed to bright light. After shining a bright light in a healthy eye, the pupil of the eye affected by ON often incorrectly dilates, likely due to inflammation or damage of the autonomic nervous system.

Optical coherence tomography (OCT) is a non-invasive image technique to study the retina.



OCT is a simple high-resolution scan used to measure the thickness of the retinal nerve fiber layer (RNFL). The RNFL may be decreased in NMO patients with optic neuritis.

1.8 Diagnoses Other Than NMO



QUICK READ

NMO can have signs and symptoms similar to:

- Multiple sclerosis (MS)
- Acute disseminated encephalomyelitis (ADEM)
- Sjögren's syndrome
- Systemic lupus erythematosus (SLE)
- Mixed connective tissue disease (MCTD)
- Infective inflammation
- Sarcoidosis
- Other neurological illnesses

With many signs and symptoms that are similar to those of multiple sclerosis (MS) or other neuroinflammatory conditions, misdiagnosis of NMO can be a missed opportunity to treat the disease in its earliest form and with the most appropriate medications. Conditions commonly confused with NMO that can produce optic neuritis and myelitis include:

- **Multiple sclerosis (MS):** an inflammatory condition of the central nervous system (CNS) affecting movement and balance. Like NMO, **optic neuritis and myelitis are common in MS, although generally less severe than in NMO.** In addition, MS usually has a slower, longer course of disability than NMO. **Unlike NMO, to date there is no blood test to diagnose MS.**
- **Acute disseminated encephalomyelitis (ADEM):** a short-term condition affecting the brain and spinal cord, which can also cause optic neuritis and myelitis.
- **Sjögren's syndrome:** an autoimmune condition typically affecting the salivary and tear glands.
- **Systemic lupus erythematosus (SLE):** an autoimmune condition causing joint pain, fatigue, rashes, kidney disease and sometimes inflammation in the CNS.
- **Mixed connective tissue disease (MCTD):** inflammation of the connective tissue associated with joint pain, muscle weakness, and in some cases damage to internal organs.

- **Infective Inflammation:** inflammation caused by an infection of the central nervous system (CNS).
- **Sarcoidosis:** a type of inflammation that may target multiple organs including the optic nerves, brain and spinal cord. Sarcoidosis that affects the CNS is called neurosarcoidosis.

FACTS ABOUT NMO AND MS

Until recently, NMO was thought to be a type of MS. However, recent discoveries have provided evidence indicating that NMO and MS are distinct diseases with distinct diagnostic criteria and treatment plans.

With so many symptoms in common, NMO can sometimes be confused with MS or other diseases. However, these diseases are treated in different ways and early detection and treatment help ensure best outcomes.

NMO symptoms may include:

- Severe, rapid onset attacks causing significant disability
- Episodes of prolonged nausea, vomiting or hiccups
- Usually normal MRI brain scan early in disease
- Distinctive lengthy spinal cord lesions
- NMO-IgG presence in blood and/or CSF



It is important

to emphasize that **some MS medications do not help NMO patients**, and may actually **cause more severe attacks** and complications in NMO.

Likewise, **off-label treatments used for NMO may not benefit patients with diseases other than NMO.**

These facts underscore the need for rapid and accurate diagnosis of NMO, as well as other similar diseases.

For more information, visit:
guthyjacksonfoundation.org/ms-nmo

MS symptoms may include:

- Initial attacks that are usually slower to emerge and relatively milder than NMO
- MRI which usually shows brain abnormalities in a recognized pattern
- Presence of oligoclonal bands in CSF of most MS cases but relatively few NMO cases; no NMO-IgG

1.9 Recognizing an NMO Relapse (Attack)

Mimicking the initial or onset episode, NMO patients can experience a recurrence of similar symptoms due to inflammation of the optic nerves and spinal cord as outlined in section 1.5. Such symptoms may also be after-effects of a prior episode, referred to as “ghost” or residual pain following an attack. It is important to determine whether such symptoms represent a new relapse, or the lingering effects of a previous attack.

Maintaining regular communication with your healthcare team, and seeing your physician or neurologist immediately if there are unresolved symptoms is best in this regard.



I.10 Areas of the Body Commonly Affected by NMO

QUICK READ

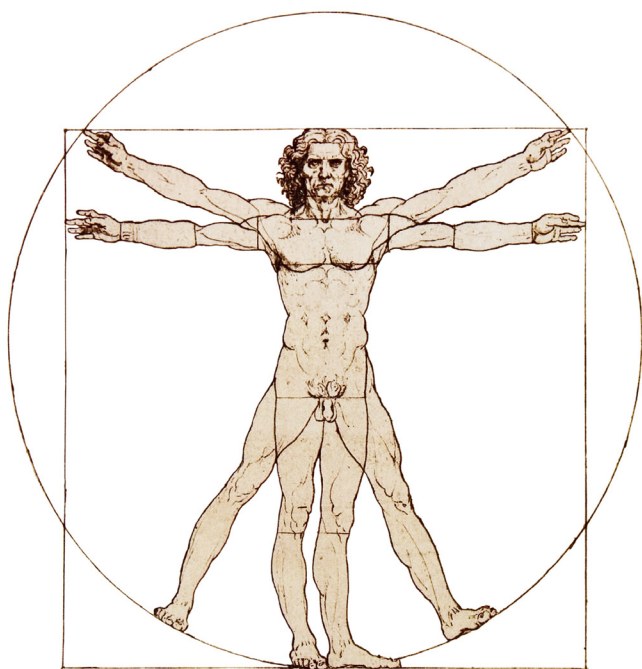
NMO occurs when the immune system (which normally protects against infection, cancer, and other disease) malfunctions. As a result, the immune system attacks healthy tissues, making antibody proteins and activating white blood cells that cause inflammation. In turn, these immune system factors damage the central nervous system (CNS) which leads to neurological problems.

Areas and systems of the body affected by NMO:

- Central nervous system (CNS)
- Peripheral nervous system (PNS)
- Blood brain barrier (BBB)
- Neurons
- Astrocytes
- Immune system

Nervous System

The nervous system regulates all body activity including memory, language, vision, mobility, and sensation. It includes the brain, spinal cord, optic nerves, and a circuitry of nerve cells (called **neurons**) responsible for transmitting information to and from all parts of the body. Other specialized cells known as **astrocytes** and **glial cells** structurally and nutritionally support the neurons.

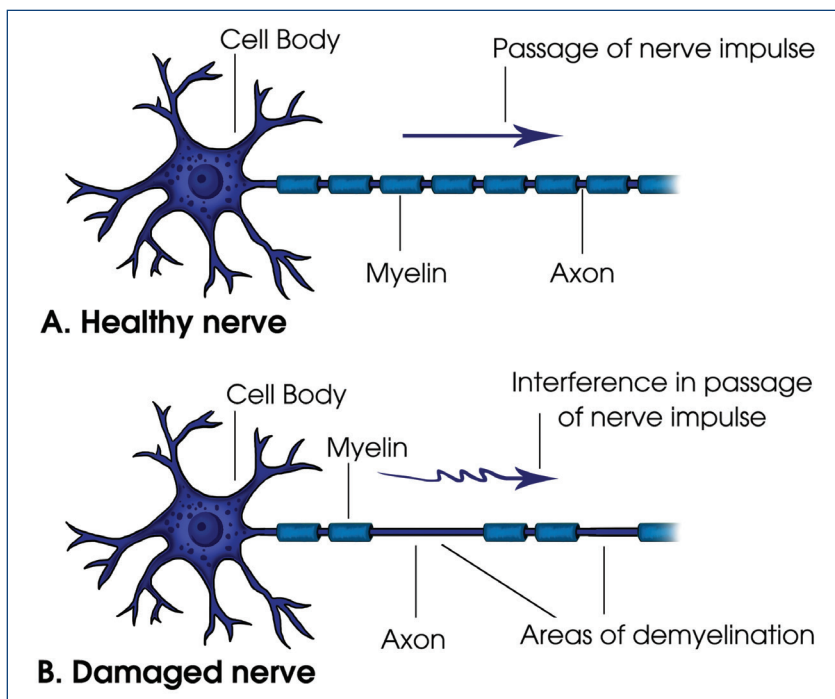


The nervous system is comprised of the **central nervous system (CNS)** and the **peripheral nervous system (PNS)**. The spinal cord, optic nerves and the brain make up the CNS. They coordinate the activities between the various parts of the body. The PNS is the portion of the nervous system outside the brain and spinal cord. The PNS carries incoming messages to the CNS from sensory organs (such as the eyes, skin, and ears), and carries messages from the CNS to muscles, sweat glands, blood vessels and many other tissues.

The spinal cord and optic nerves are the main sites of the nervous system affected by NMO.

The spinal cord controls movement, receives neuronal

signals and regulates bodily functions including excretions and secretions. The optic nerves carry visual information from the eyes to the brain. The CNS and PNS coordinate thought, logic, memory, balance, speech, bowel and bladder function, and many other essential bodily activities which can be affected by NMO.



Nerve Conduction

Neurons are the basic information processing units in the CNS. They receive, process and send information to other neurons through cable-like fibers called **axons** using special molecules called neurotransmitters.

Axons help process signals in the nervous system. For example, in the case of light stimulation, the eye collects the signal via the retina, which contains special sensors that convert light energy to neurotransmitter molecules. Next, these molecules activate neurons in the optic nerve, which in turn transmit the information to the brain. Similarly, in the case of pain stimulation, sensory information is carried from neurons in affected tissues to the spinal cord and brain.

Axons are coated by a fatty substance called the **myelin sheath**, which plays an important role in speeding and securing electrical transmission along axons. This sheath allows impulses to transmit efficiently along the nerve cells (like insulation in an electrical system), ensuring messages sent by axons are not lost en route to the spinal cord, muscles or internal organs. **If myelin is damaged or removed due to inflammation, a process called demyelination, the ability of neurons to transmit signals slows down or stops altogether.** This effect can result in vision loss, limb weakness due to limited transmission of nerve impulses to and from the brain, or other loss in neurological functions.

Blood-Brain Barrier (BBB)

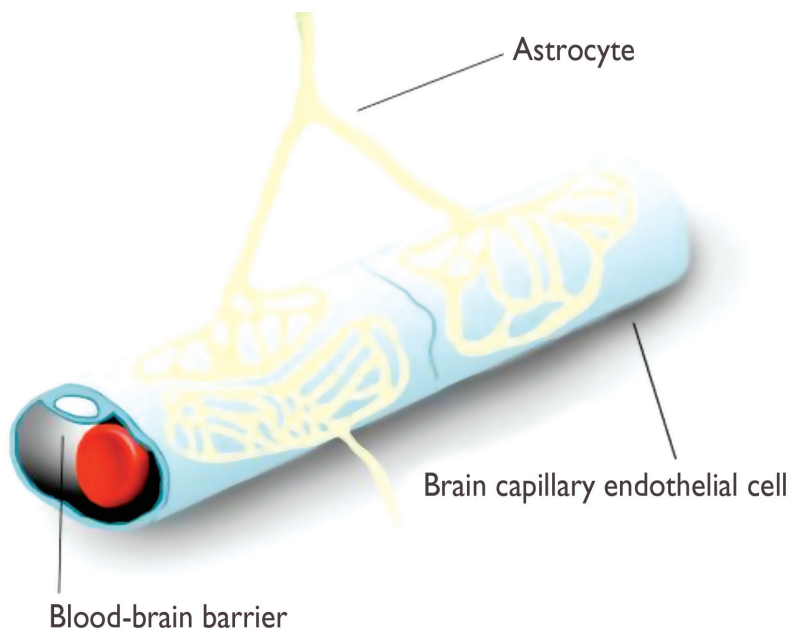
The Blood-Brain Barrier (BBB) is a complex of cells and specialized proteins that interact where the central nervous system (CNS) tissues meet the blood vessels (capillaries). The BBB creates a filter to the CNS, separating the circulating blood and its chemical and



cellular components from the CNS. The barrier prevents some drugs, chemical compounds, radioactive ions, and disease-causing microbes that may be present in the blood from passing into the CNS. **The BBB helps protect the CNS from potentially harmful factors, including autoantibodies, circulating in the blood.** Only special cells and substances that provide food and function to the brain are allowed through the barrier. Some parts of the BBB are naturally more permeable (or easy to pass through), and **the NMO-IgG antibody appears to have a particular tendency to attack the brain at these more vulnerable sites of the BBB.**

Certain conditions may lead to breakdown of the BBB. When this happens, substances normally kept out of the brain are able to pass into the brain, spinal cord, or other components of the CNS.

Astrocytes



Astrocytes are the most abundant cells in the CNS and play key roles in the function of the BBB as well as neuron health.

Astrocytes have several functions, including to serve as a framework guiding neurons to their proper locations during development, protecting and nourishing neuronal cells, and supporting the BBB to maintain a “privileged” environment unique to the CNS.

Astrocytes make other significant contributions to neuron activity including facilitating neurotransmission and signals for proper brain function and interaction with other CNS cells such as microglia.

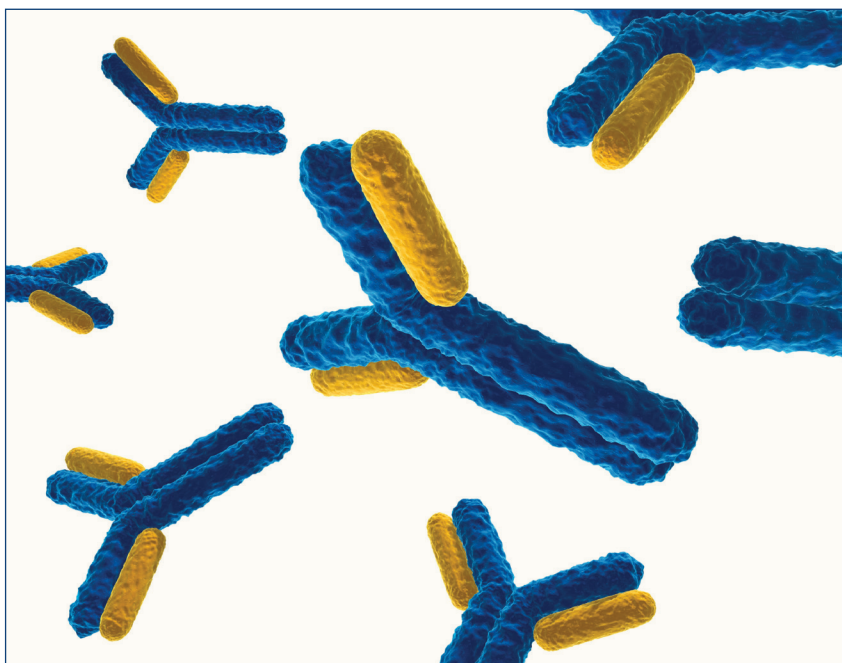
Astrocytes also support water transport in the CNS through a special protein that spans from the surface of the cell, through their cell membrane, into the cell interior. This protein, termed **aquaporin-4 (AQP4)**, is a water channel that creates arrays of pores through which water flows in the cell. **In NMO, AQP4 is the target of NMO-IgG antibodies.** By attaching to the water channel AQP4 protein on the astrocyte, the antibody activates immune reactions, such as complement activation, and attracts inflammatory cells. In turn, such inflammation can lead to many adverse consequences by injuring, disabling, or destroying some astrocytes and disrupting the normal functions of others. Water flow through tissues is impaired when AQP4 protein is attacked, demyelination can occur, and the accumulation of immune cells and other factors at sites of astrocyte injury cause swelling due to inflammation. **Together, these processes may produce the symptoms of an NMO attack.**



You can learn more about clinical trials on our website at:

guthyjacksonfoundation.org/clinical-trials

The Immune System



Antibodies

One of the most important functions of the immune system is to defend the body from external threats such as microbes, or internal threats such as cancer. The ability to tell the difference between healthy cells and tissues, and those representing infective or cancer threats is key. The ways in which the immune system achieves this goal are complex. Simply put, the immune system **T and B cells** (also called **lymphocytes**) are responsible for detecting “self” (normal) and “non-self” (abnormal or foreign) molecules or cells. **B cells** are named for their maturation in the **Bone marrow**, while **T cells** mature in the **Thymus**. When a foreign (e.g. infecting microbe) or abnormal (e.g. cancer) cell is detected by

T and B cells, immune reactions are triggered. This step leads to activation and reproduction of the specific type of T and B cells that first recognized the threat.

Over time, these T and B cell lineages lead a coordinated immune response to specifically remove the foreign or abnormal target, such as the invading microbe or cancer cell.

Most of the time the immune system is amazingly accurate in detecting foreign or abnormal cell threats and signals. However, in autoimmune diseases, this process goes wrong: T and/or B cells or other immune system cells mistake normal “self” tissues as foreign or abnormal.

NMO is believed to occur when the immune system attacks AQP4 and perhaps other “self” proteins, one’s own tissues, as if they were foreign. Components of the immune system include the thymus and spleen, in which T cells and antibody-producing B cells mature in structure and function before graduating to protect the body from infection, cancer, and other diseases. Normally in this process, immune cells with abnormal function that mistakenly react to normal cells or tissues are deleted to prevent autoimmune diseases. However, this is not a fool-proof editing system, and certain **autoreactive (or autoimmune)** immune cells may survive and contribute to autoimmune disease.

NMO is believed to occur when the immune system attacks AQP4 and perhaps other “self” proteins as if they were foreign.

The ability of the immune system to recognize and ignore “self” tissues as being normal is called **immune tolerance**. When this normal process to protect against autoimmunity breaks down, the immune system reacts to otherwise healthy cells or tissues, and mistakenly attacks the body. The result is known as an autoimmune disease, or a disease where the immune system mistakes tissues of the body itself for a foreign or abnormal threat.

Such misdirected immune responses and resulting autoimmune diseases can cause a broad range of illnesses. In addition to NMO, hundreds of other autoimmune diseases are known, and **at the core of each of these illnesses is a loss in immune tolerance**. For this reason, GJCF is focusing special efforts in the exciting science of **restoring immune tolerance, or tolerization therapy, to treat or perhaps even cure NMO**. Most NMO patients have antibodies in their blood that target an ordinary protein on astrocytes of the CNS, AQP4. In NMO, tolerization therapy has initially been targeted to inhibit immune

cells that mistake AQP4 as foreign. **Catalyzed by GJCF, clinical trials are already beginning** and others are planned to apply the power of the immune system to solve NMO in a new era of restoring immune tolerance. **And if tolerization therapy succeeds in NMO, the same methods might be adapted to help treat or even cure many autoimmune diseases such as multiple sclerosis, type-1 diabetes, lupus, and beyond.**

I.II How does NMO affect the body?

QUICK READ

In NMO, damage can affect the body if:

- The immune system mistakenly produces harmful AQP4 antibodies and inflammatory cells
- The Blood Brain Barrier becomes disrupted, allowing these factors to enter the CNS
- Complement proteins contribute to intense tissue destruction and attract other inflammatory components, such as white blood cells
- Inflammation leads to demyelination, which impairs functions of optic nerves, spinal cord and brain
- Further complications arise in the body, such as limb weakness or paralysis, bowel & bladder dysfunction, and other symptoms that are characteristic of NMO

In NMO, auto-antibodies targeting AQP4 and other self-proteins are mistakenly produced by the immune system.

Mechanisms of Damage

Inflammation

Inflammation is the first response of the immune system to tissue injury, infection, or other threat. For example, a cut to the skin will almost always result in inflammation, with its characteristic four signs: redness, swelling, pain, and heat. Inflammation is a vital defense mechanism essential for survival. Without inflammation, the body would not prevent blood loss at sites of injury, clear infection, remove harmful substances or allow normal tissue to rebuild. **In NMO, autoantibodies targeting AQP4 and other self-proteins are mistakenly produced by the immune system. These autoantibodies contribute to inflammation of the CNS that is a hallmark of NMO.**

Normally the blood-brain barrier (BBB) protects the CNS. However, if the BBB is disrupted or “opened” (see section 1.10), and AQP4 antibodies enter the CNS, they can attach to the AQP4 protein on the astrocytes. In

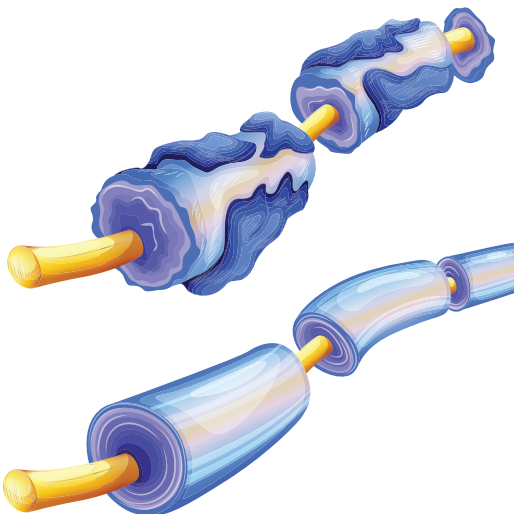
turn, this can send molecular messages to other white blood cells to attack the astrocytes. At the same time, another family of inflammatory proteins (called the **complement system**) is activated. Complement is a collection of over 20 proteins that work together and normally help immune system cells to clear infection, kill cancer cells, or promote wound healing. In the case of NMO, **complement proteins** can contribute to intense tissue destruction and attract other inflammatory cells, including special types of white blood cells called **granulocytes** (such as **neutrophils** and **eosinophils**) and **macrophages**.

Demyelination

When the AQP4 antibody interferes with the transfer of water in the brain, and activates immune system inflammation, water and immune cells and molecules accumulate near the astrocytes attacked in the CNS. In turn, the **myelin sheath** (protective insulation of neurons) can degrade, leading to **demyelination**.

*Demyelinated
Axon Sheath*

*Healthy
Sheath*

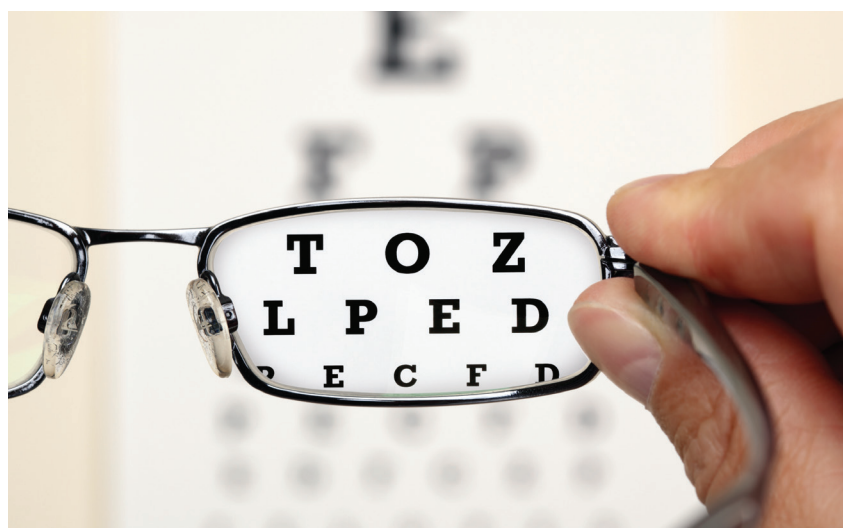


This process causes nerve conduction to slow or stop, leading to impaired vision, limb weakness or paralysis, and other symptoms common to NMO. Recent research suggests that myelin can be repaired and reversed, but only if the process of inflammation that caused the initial breakdown of myelin is arrested. This is why it is so important to recognize and diagnose NMO quickly and accurately, enabling treatment early in the course of disease that may minimize inflammation and demyelination.

Symptoms of Tissue Damage

Optic Neuritis

Optic neuritis (ON) is inflammation of optic nerves that shuttle visual information between the eyes and brain. In NMO, this process may involve one (unilateral ON) or both (bilateral ON) optic nerves. **Optic neuritis is**



the most common and often the first symptom in NMO. It is characterized by eye pain, vision loss and optic nerve dysfunction. Inflammation causes loss of vision usually because of swelling and injury of the myelin coated neurons in the optic nerves. The visual loss may be mild or severe, reversible or irreversible.

Transverse Myelitis

Inflammation across an extensive segment of the spinal cord is known as transverse myelitis (TM). The term **transverse** describes the position of inflammation along an extended length of the spinal cord. “Myelitis” refers to inflammation of the spinal cord. In NMO, TM



CIRCLES: AN NMO PATIENT STUDY

CIRCLES is the **C**ollaborative **I**nternational **R**esearch in **C**linical and **L**ongitudinal **E**xperience **S**tudy of NMO. Some of the goals include:

- Understand causes
- Improve diagnosis
- Address symptoms
- Prevent relapses
- Find cures

Blood samples and clinical data are vital for research in NMO. Many developments come from doctors and researchers analyzing blood samples and data.

If you or someone you know has been diagnosed with NMO, donating blood and clinical data to CIRCLES is a great way to contribute to the cure.

Learn more at:

guthyjacksonfoundation.org/biorepository

often extends to three or more spinal vertebrae in length (longitudinally extensive) over the spinal cord. The part of the spinal cord where the damage occurs determines which other parts of the body (e.g. limbs, bowel and bladder, etc.) may be affected.

- Nerves interacting with the **cervical** (neck) area of the spinal cord control signals to the neck, arms, hands and breathing muscles (diaphragm).

- Nerves interacting with the the **thoracic** (upper back) area of the spinal cord send signals to the torso and some parts of the arms.
- Nerves interacting with the **lumbar** (mid-back) area of the spinal cord control signals to the hips and legs.
- **Sacral** nerves interacting with the lowest segment of the spinal cord relay signals to the abdomen, groin, toes, and some parts of the legs.

Damage at one position of the spinal cord can affect function at and below that segment. **Pain in the lower back** is often a **symptom of TM**. By comparison, **demyelination usually occurs at the upper back thoracic level**, causing problems with leg movement, bowel and bladder control, skin numbness, tingling or pain.

Do you know?

NMO patients can join an email list or visit our Facebook and Twitter pages to receive information and learn the latest updates about NMO clinical trials.

See Sections 5 & 6 to find out more



History & Discovery



History & Discovery

- 2.1 Timeline and History of NMO
- 2.2 What are the differences between NMO and Multiple Sclerosis (MS)?
- 2.3 How common is NMO?
- 2.4 Who is affected by NMO?
- 2.5 2015 NMO Diagnostic Criteria
- 2.6 From Devic's Disease to NMOSD

2.1 Timeline and History of NMO



QUICK READ

- **1804:** Dr. Antoine Portal publishes an early case of disease consistent with NMO
- **1894:** Eugène Devic, M.D., coins the term “neuromyéélite optique,” or neuromyelitis optica
- **2004:** Vanda A. Lennon, M.D., Ph.D., and colleagues at the Mayo Clinic identify the NMO-IgG antibody as being correlated specifically with NMO disease
- **2006:** Updated NMO diagnostic criteria are published, distinguishing NMO from original term, Devic's disease
- **2015:** The International Panel for NMO Diagnosis (IPND) updates the 2006 diagnostic criteria for NMO and NMOSD



Eugène Devic

In 1804, **Dr. Antoine Portal** described a special case of optic neuritis (ON) with vision loss and spinal cord inflammation in the absence of brain pathology which may be the first report of “NMO” disease in the academic literature. In 1870, a British physician scientist named **Sir Thomas Allbutt** is given credit for initially describing a case of simultaneous optic neuritis and transverse myelitis. In 1894, a French neurologist named **Eugène Devic** published a case series of 16 such patients, and coined the term “neuromyéélite optique.” Devic’s clinical study of optic neuritis plus transverse myelitis became popularly known as Devic’s disease or Devic’s syndrome.

Devic's disease and NMO are different names for the same condition, with NMO being the contemporary term.

In 2004, Vanda A. Lennon, M.D., Ph.D., and colleagues at the Mayo Clinic in Rochester, Minnesota discovered a biomarker for NMO called the **NMO-Immunoglobulin G antibody, or NMO-IgG** (see section 1.7). This laboratory test, or newer versions that also test for NMO-IgG, allow clinicians to test people for the presence of this autoantibody as one criterion for NMO diagnosis.

In 2006, the diagnostic criteria were updated, and included other symptoms that were not originally characterized by Dr. Devic. **These 2006 criteria updated “Devic’s disease” to its more descriptive name, “neuromyelitis optica,” or NMO.** NMO and NMO spectrum disorder (NMOSD) are the terms used by modern researchers and clinicians. The 2006 diagnostic criteria helped diagnose patients with NMO.

In 2015, the GJCF and its advisory team organized a new effort to modernize the diagnosis of NMO, and expand the criteria to include NMOSD. The **International**

Since 2015, the estimated number of people who may be diagnosed with NMO or NMOSD has significantly increased.

Panel for Neuromyelitis Optica Diagnosis

(IPND), a panel of 18 international physician and scientist experts, updates the 2006 diagnostic criteria for NMO and NMOSD. As a result, the estimated number of people who may be diagnosed with NMO or NMOSD has significantly increased.

2.2 What are the differences between NMO and Multiple Sclerosis (MS)?

QUICK READ

NMO symptoms may include:

- Severe, rapidly disabling attacks
- Prolonged (e.g. weeks) episodes of nausea, vomiting or hiccups
- Usually normal MRI brain scan early in disease
- Lengthy lesions in the spinal cord
- NMO-IgG presence in blood or cerebral spinal fluid (CSF)

When NMO was initially described, it was considered to be a type of multiple sclerosis (MS). **However, over the past decade evidence from studies of the science and clinical features of NMO has established NMO as a distinct disease.** NMO is now recognized as a recurrent or relapsing disease that largely targets the spinal cord and optic nerves, but through a different immune system process than MS. Like MS, **NMO is now recognized as able to affect the brain as well**, but generally to a lesser degree than in MS. Other differences between NMO and MS include:

- The presence of NMO-IgG in NMO patients but not MS patients
- The types of white blood cells that accumulate in CNS lesions in NMO (granulocytes) but not MS
- Patterns of CNS lesions that can be seen by MRI in MS but not generally in NMO

MS symptoms may include:

- Generally more gradual initial attacks that are usually relatively milder
- MRI usually shows brain lesions early in disease and in a specific pattern
- The absence of NMO-IgG

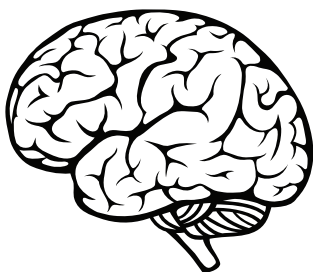
For more information, visit:
guthyjacksonfoundation.org/ms-nmo

- NMO and MS have different treatment regimens, and in some cases treatments for MS can be harmful to NMO patients.

These reasons emphasize why early detection and accurate diagnosis of both NMO and MS will benefit patients regardless of which disease they may have.

Do You Know...

NMO is now recognized as able to affect the brain, but generally to a lesser degree than in MS.



Research catalyzed by the GJCF in just the last few years has suggested that NMO and MS result from different immune system problems, target different tissues, can have distinct signs and symptoms, and patients benefit from different treatments. The primary differences between NMO and MS (detailed in Chapter 1) are summarized here:

■ Patients with NMO often experience:

- Initial symptoms that can have a rapid onset, and may become severe and disabling
- Relapse attacks that may result in cumulative long-term disability

■ **Patients with MS often experience:**

- Initial attacks that are usually comparatively milder than NMO
- Disability that often develops incrementally over time and not as a result of a single attack

■ About **10-20 percent** of patients with NMO may also have episodes of:

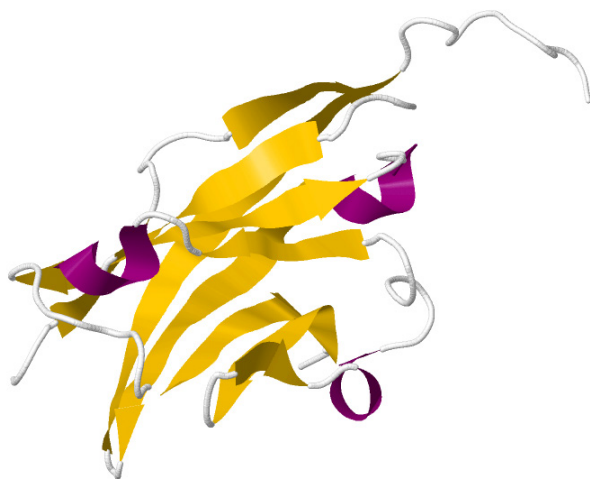
- Nausea, vomiting or hiccups lasting up to a month
- These symptoms are not specific to NMO, but are not commonly seen in MS

■ Patients with NMO can have normal magnetic resonance imaging (MRI) brain scans (see section 1.7) early in the course of the disease, while the brain scans of patients with MS usually show abnormalities with a classic pattern on MRI early in the course of disease. However, newer imaging techniques suggest brain tissue may be involved in NMO disease, and perhaps earlier in the natural history of disease.

**Some MS medications do not help
NMO patients and may actually
worsen disease or cause more severe
attacks and complications.**

- About **80 percent** of patients with NMO have distinct, long lesions in the spinal cord on MRI that are not typically seen in patients with MS.
- **An antibody, called NMO-immunoglobulin G (NMO-IgG), is present in the blood of approximately 75 percent of NMO patients, but almost always absent in MS patients.**

Therefore, patients appropriately diagnosed with MS do not usually test positive for NMO-IgG (see section 1.7). Approximately one-quarter of NMO patients who do not have detectable NMO-IgG have a different antibody targeted to **myelin oligodendrocyte glycoprotein (MOG)**, a myelin protein. This antibody appears to be associated with very similar symptoms as those of NMO. Such patients may qualify for a diagnosis of seronegative NMOSD (NMOSD without detectable NMO-IgG).



myelin oligodendrocyte glycoprotein (MOG)

Photo Source: Jmol Development Team -

Jmol, GPL, <https://commons.wikimedia.org/w/index.php?curid=1479194>

- Because they are both autoimmune diseases, NMO and MS are often initially treated with medications that work by generally suppressing the immune system, such as corticosteroids. However, specific treatments for NMO and MS often differ, or used in different ways to induce remission, manage disease in remission, or respond to relapses.

2.3 How common is NMO?

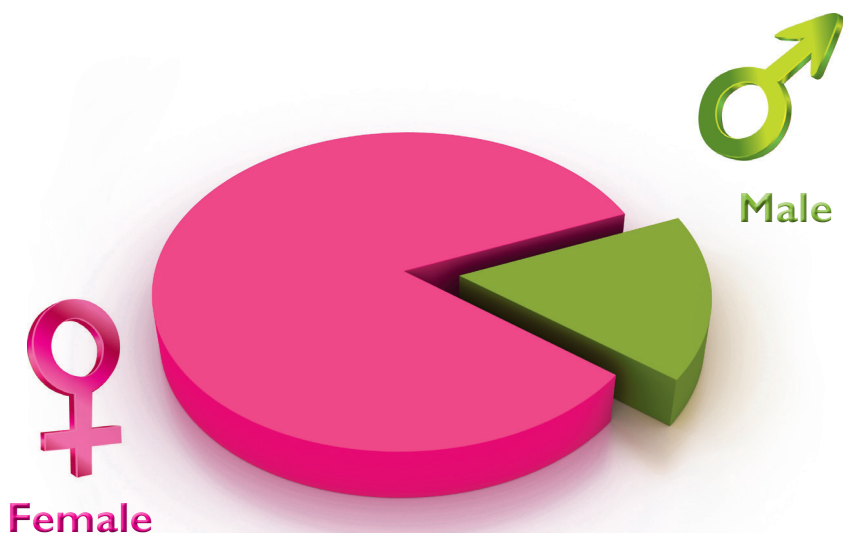
In the United States (U.S.), the National Institutes of Health (NIH) has historically considered NMO as a **rare orphan disease** (fewer than 200,000 people affected). While estimates may vary depending on several factors, currently in the United States NMO is estimated to affect approximately 4-10 per 100,000 people (previously published studies cited 1 in 100,000). **It is estimated that NMO affects up to 15,000 patients in the U.S. alone. Worldwide, NMO is projected to affect hundreds of thousands of patients based on prevalence rates that are emerging globally.**

Do You Know...

Worldwide, NMO is projected to affect hundreds of thousands of patients.



In addition, the IPND 2015 Diagnostic Criteria for NMO and NMOSD are already helping to diagnose more NMO patients more quickly and accurately, allowing the most appropriate treatment to begin rapidly. Additional population-based studies will assist in more accurately determining the **incidence** (new cases) and **prevalence** (total active cases) of NMO worldwide, how racial and ethnic factors may affect disease risk, and how to further enhance recognition of cases and accurate diagnosis (refer to section 1.7).



2.4 Who is affected by NMO?

NMO is more common in women than men, with a ratio of up to 7:1. NMO also appears to be more common among individuals having genetic ancestry including African, Asian, Pacific Island, Polynesian or Caribbean descent. However, all peoples can be affected by NMO and NMOSD.

The onset of NMO varies from early childhood to late adulthood. The **typical age of onset in women is 34-40 years** of age, based on reports from different regions of the world. However, NMO can strike much earlier in life, including pediatric cases, and occur in the elderly.

2.5 2015 IPND NMO Diagnostic Criteria

In 2015, the GJCF assembled an **International Panel for NMO Diagnosis (IPND)** to incorporate advances in NMO science and medicine into modern diagnostic criteria. The IPND consisted of **18 physician and scientist experts** from **nine different countries, along with GJCF advisors**. The members were from North and South America, Europe, Asia and Australia, each with differing expertise in NMOSD and related diseases. Regular face-to-face meetings of the IPND occurred in multiple countries over a two-year period, and **improved criteria** were informed by input from the GJCF **International Clinical Consortium (ICC)** for NMO.



The criteria were developed by careful review and comparison of the latest scientific and medical literature in NMO and NMOSD, as well as that of diseases that are often mistaken for NMO. Next, proposed diagnostic criteria were discussed in subgroups, and those criteria that met subgroup approval were advanced to review and critique by the full panel. For example, the panel analyzed imaging studies (e.g. MRI) and laboratory results (e.g. NMO-IgG serostatus) to ensure these findings could be best incorporated into the diagnosis.

The proposed NMO and NMOSD diagnostic criteria were then tested for accuracy by using the criteria to analyze hypothetical case examples. The actual diagnosis was known only to few members of the IPND (who did not take part in reviewing the cases).

The criteria were then refined to yield an international consensus on requirements for NMO and NMOSD diagnosis. In addition to the specific requirements for the diagnosis, the **IPND also identified “red flags” that could warn clinicians about potential for making an incorrect diagnosis.** They noted certain circumstances known to commonly mislead neurologists who might not be highly experienced in diagnosis of NMO or NMOSD.

Scientific and clinical advances incorporated into the 2015 IPND criteria have significantly improved the pace and accurate diagnosis of patients with NMO or NMOSD. For example, many patients with NMOSD have attacks of **hiccups or nausea and vomiting** or they have **brain MRI lesions** that follow distinct patterns. **These individuals were not recognized by the previous NMO criteria.** Experts also knew that most patients who presented with a first attack of optic neuritis or longitudinally extensive transverse myelitis (LETM), and who had a positive NMO-IgG (aquaporin-4 antibody)



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NMO Resources.**

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ANDROID APP ON
Google play

Patients are increasingly being diagnosed earlier in the course of disease, and more accurately, aiding in longer and healthier lives.

test, would almost always go on to develop all of the NMO criteria later on. **In these and other ways, the new 2015 IPND diagnostic criteria allow for such patients to be more accurately diagnosed at the time of the first attack.** Rapid and accurate diagnosis is a critical and exciting step toward the most appropriate treatment and an eventual cure for NMO. **These new diagnostic criteria also benefit patients facing other diseases that could have mistakenly been diagnosed as NMO, and NMO cases that could have otherwise been missed.** Because treatments for NMO and other diseases treatments differ, the improved 2015 IPND diagnostic criteria help all NMO patients, as well as patients who do not have NMO.

Refer to section 1.7 for details about the 2015 diagnostic criteria, and visit the GJCF website for the article about the IPND at:

guthyjacksonfoundation.org/diagnosis

2.6 From Devic's Disease to NMOSD

The 2015 IPND diagnostic criteria established NMO and NMOSD as being the contemporary terms used globally by leading clinicians and scientists. When Dr. Devic described the disease in 1894, it was characterized by clinical blindness, paralysis, and worse. **Now, quantum leaps are being made every day to better diagnose, treat and discover potential cures for NMO and NMOSD.** As a result, patients are increasingly being diagnosed earlier in the course of disease, and more accurately, which translates to reduced disease impact, with longer and healthier lives.

Patients and families can help make further strides in understanding and solving NMO through research studies and clinical trials if appropriate.

How can I make a difference?

NMO patients and their blood relatives can contribute to research breakthroughs to better prevent, diagnose, treat, and ultimately cure NMO by donating small samples of blood (from time to time) to the GJCF **CIRCLES NMO Biorepository**.

See Section 5 to find out how or visit:
guthyjacksonfoundation.org/blood-bank

Treatment & Management of NMO



Treatment & Management of NMO

- 3.1 Finding an NMO Specialist
- 3.2 Medical Treatment of NMO
- 3.3 Recovering from a Relapse
- 3.4 Pregnancy and Pediatrics
- 3.5 Creating a Healthcare Team
- 3.6 Managing Diet and Nutrition

OVERVIEW

Selecting a primary care physician, neurologist or related specialists, and other members of a clinical team is a personal decision that balances many factors unique to each patient and their caregivers. In addition, treatment regimens, lifestyle choices and other personal decisions such as pregnancy are for each individual patient to determine. The GJCF does not provide patient care or medical advice, and does not endorse any particular clinician, therapy or clinical trial. Rather, the following information offers resources that may be helpful in self-education and decision-making by NMO patients and their loved ones.

3.1 Finding an NMO Specialist

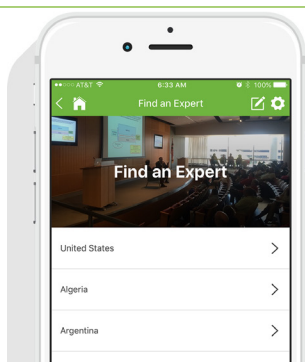
QUICK READ

Finding a clinician that you feel comfortable with and in whom you have confidence is an important personal decision.

There are several ways to locate NMO specialists. Physician referrals and word of mouth are two methods.

Another resource is **Connect the Docs**, an international directory of clinicians specializing in NMO diagnosis and/or treatment. Since 2008, the GJCF, along with the NMO patient community, has identified and collaborated with hundreds of clinicians around the world, mapping specialists including neurologists and neuro-ophthalmologists. **Connect the Docs** is available in this book and as an interactive, online directory.

To get started, refer to Chapter 7 or visit:
guthyjacksonfoundation.org/connect-the-docs



Find **Connect the Docs** on
NMO Resources.

*Download the app for free on
your Android or iOS device today!*



3.2 Medical Treatment of NMO

QUICK READ

Treatment of NMO requires careful diagnosis and consideration by a clinical care team. Usually, this team consists of a neurology specialist focusing on NMO, along with a primary care doctor to manage routine medical care, as well as other specialists such as may be indicated. Depending on the unique factors of a given case, different approaches may be used to manage different patients. Medical approaches used to help treat NMO can include:

- steroids
- plasma exchange (PLEX)
- immunoglobulin therapy (IVIG)
- immune suppression with medications
- alternative therapies

At present there is no regulatory-approved treatment and no identified cure for NMO. The GJCF is doing everything it can to help find answers, together with scientists, clinicians, industry, and regulatory partners around the world. The term “standard of care” describes treatment regimens or procedures that, while not specifically approved for treating NMO by regulatory agencies, involve medicines or interventions that are approved for other conditions, and which are generally considered potentially helpful in NMO.



Treatment options currently being used to treat NMO are considered **“off-label,”** meaning they have been **approved to treat conditions and diseases other than NMO**, but are being used in NMO treatment without formal clinical evidence that they are effective.

To obtain government approval, treatments must prove that they are safe and effective in carefully controlled and prospective clinical trials. **An utmost priority in the design of all clinical trials is patient safety.**

A therapeutic candidate must undergo rigorous testing in a well-defined population of patients using a clinical trial protocol that is approved in advance by a regulatory agency. Such clinical trials must also prospectively define the effectiveness goals of the drug candidate as part of the criteria upon which effectiveness and potential approval will be evaluated.

A **key mission of the GJCF** is to catalyze the discovery or development of treatments that advance to be proven safe and effective in NMO through clinical trials. **While just a few years ago there were none, the good news is that there are multiple**

now clinical trials in progress testing therapies in NMO. There is great hope that these clinical trials will progress such that one or more drugs may soon be approved to treat NMO.

While effective treatment is a common goal of clinical care, the specific best treatment regimen may differ in different patients. There are many factors that contribute to NMO treatment decisions made by NMO clinicians, patients, and their caregivers, including:

- Specific diagnosis and disease subtype (e.g. NMO vs. NMOSD)
- Safety and tolerability of a treatment in a given patient
- Disease status (e.g. early vs. advanced; maintenance vs. relapse)



- Disease severity (e.g. mild, moderate or severe)
 - Co-morbidities (simultaneous presence of two or more diseases) in a given patient
 - Management of associated symptoms (e.g. pain, bowel / bladder function, etc.)
 - Other factors that may benefit outcomes (e.g. nutrition, vaccination, etc.)
-

In some cases, the first sign of NMO may be eye pain or change in vision that comes on suddenly and worsens quickly.

Managing the First Episode of NMO

The first episode of NMO (termed the **“incident” episode**) can be a confusing and frightening experience. **Typically, this episode occurs completely by surprise**, with no known risk factors, warning signals, or prior history. Interestingly, recent research has suggested that some cases of **NMO may come after prolonged hiccups, nausea or vomiting**, or **other seemingly unrelated symptoms**. In some cases, **the first sign of NMO** may be **eye pain** or a **change in vision** (e.g. clarity, light perception, color)

that **comes on suddenly and worsens quickly**. In other cases, NMO **first appears as a loss of arm or leg strength or difficulty balancing**. In every case, **NMO can be a neurological emergency**, and quick actions offer best chances for good outcomes:

- Contact your doctor or neurologist immediately
- If necessary, seek care at the closest appropriate emergency room or urgent care center
- Remind the clinical staff to consider NMO as a possible cause of symptoms (called the ***differential diagnosis***)
- Be prepared for blood tests (e.g. NMO-IgG), imaging (e.g. MRI or CT scans), or perhaps a lumbar puncture (refer to section 1.7). These tests are generally extremely safe, and can be done relatively quickly.

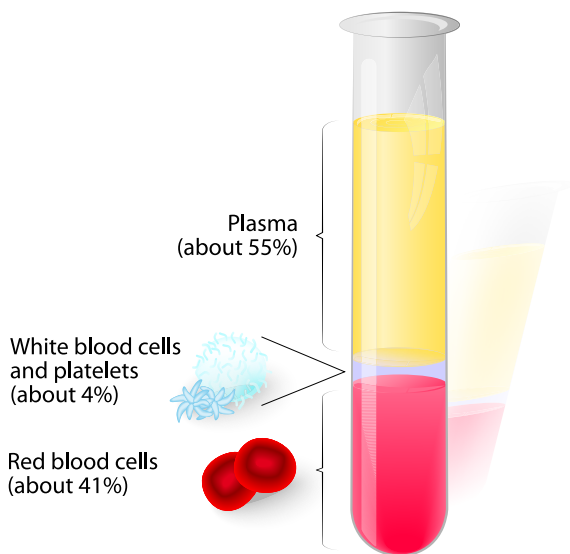


Once the initial episode has passed
and symptoms are under control,
individuals begin their journeys
living with NMO.

First episodes of NMO almost always come unexpectedly, and can be very serious. Managing this episode through calm, knowledge-based decisions may facilitate very positive outcomes in which recovery can be excellent.

If NMO or another inflammatory condition is detected in the optic nerves or central nervous system (CNS), **corticosteroids** (such as methyl-prednisolone) are normally one of the first medicines to be given. This medicine quickly reduces overall inflammation. For acute or severe cases, corticosteroids are administered through a vein (**intravenously or IV**). The neurologist may admit the patient into the hospital during an acute episode, to deliver IV medications, facilitate diagnostic tests, and provide close observation. Depending on results of blood or lumbar puncture tests, the clinical team may recommend other immediate treatment as well. For example, a process to remove harmful factors

such as autoantibodies from the blood may be used. This procedure is called **plasma exchange (PLEX)**, and involves the careful removal of plasma from the blood, with blood cells immediately returned to the patient bloodstream along with replacement fluid. In other cases, addition of potentially beneficial antibodies to the bloodstream may be used; such treatment involves **intravenous immunoglobulin (IVIG)**. The goals of



these strategies (described in more detail in the following pages) are to generally calm any acute inflammation that may be affecting the CNS, including the optic nerves, spinal cord or brain.

Ideally, a rapid response to symptoms of NMO may assist in the best outcome. Once the initial symptoms are under control, individuals begin their journeys living with NMO.

Managing Relapses in NMO

As in the first NMO episode, corticosteroids are often given as early as possible in the event of a relapse. Steroids work by generally suppressing the immune system and reducing inflammation in the central nervous system (CNS) and elsewhere in the body. Corticosteroids are usually given:

- Intravenously (through a vein; IV) for 3-5 days
- By IV followed by a course of oral steroids for several months or indefinitely as long-term therapy
- Steroid doses are initiated and adjusted in each individual patient based on disease status and severity, and/or side effects

What if corticosteroid treatment does not help?

Many episodes of NMO respond to corticosteroid therapy. However, **in some cases steroids do not provide clinical benefit**. When attacks progress or do not respond to this treatment, **other treatment options may be considered**. These include plasma exchange (PLEX), use of intravenous immunoglobulin therapy (IVIG), or other treatment regimens.

Plasma Exchange (PLEX) aims to remove harmful auto-antibodies (refer to sections 1.10 & 1.11) and other soluble inflammatory factors from the bloodstream. Using a specialized technique, blood is drawn out of the body



through an IV catheter, **cells are separated from the plasma and returned to the patient**, with the plasma being discarded and replaced. This procedure may be performed using catheters temporarily placed in arm veins, however some patients require a long-term catheter placement if PLEX is required on a regular basis.

Intravenous Immunoglobulins (IVIG) treatment is the administration of **a collection of antibodies** from a pool of thousands of healthy blood donations to the recipient patient. How IVIG therapy may work is not completely understood; it is believed to add beneficial antibodies and other factors from healthy individuals to act against any harmful antibodies or related factors within NMO patients. The result is that IVIG therapy may help to suppress inflammation overall, or interfere with disease-causing factors specific to NMO.



Long-Term Management of NMO

Long-term management of NMO **aims to reduce the frequency or severity, or prevent relapses** which can cause ongoing or worsening symptoms, and may lead to long-term or permanent damage. Individual neurologists use different agents and strategies for this goal, and the same neurologist may use different strategies in different NMO patients. Listed are a few of the common treatment options neurologists may consider on a case-by-case basis:

Low-Dose Steroids

In NMO, inflammation caused by the immune system leads to injury to the central nervous system (CNS) and disability in vision, limb use and other bodily functions. For this reason, medicines that broadly calm the immune system are often used to treat NMO. In this respect,

the term **“steroids”** is often heard in relation to NMO treatment. There are many kinds of steroids used in medical practice. In NMO, **corticosteroids** (also called glucocorticoids; often simply known as steroids in NMO treatment) are commonly used in treating acute NMO attacks and/or in long-term maintenance therapy. These steroids calm the immune system in a general way, or **non-specifically**, by suppressing molecular and cellular effectors of inflammation. Initial or relapse episodes of diagnosed NMO are often treated with IV steroids. Once the episode is under control, steroid therapy is typically changed to oral administration, and continued until other **maintenance treatments** are in place (see the following pages). In some patients, relapses may occur after steroid treatment is gradually stopped. If so, use of low-dose steroids over a long period of time may be appropriate to help reduce the frequency or severity of relapses. Ideally, a



clinical care team may identify a low-dose steroid regimen alone or in combination with other therapy as best for a specific NMO patient. If so, long-term/low-dose steroid treatment is often referred to as a **maintenance dose** in hopes of reducing the number or severity of relapses.



Corticosteroids are powerful medicines that suppress the immune system overall.

It is important to note that steroids are powerful medicines that suppress the immune system overall, including the ability of the body to fight infection and promote wound healing. In addition, steroids can have other **adverse side effects**, such as **weakening of the bones**, predisposition to **kidney stones** or **cataracts**, and **changes in metabolism**, including fluid retention, increased blood pressure or weight gain.

Other **long-term side effects** of steroid treatment may also include:

- **Acne/skin conditions**
- **Sleeplessness**
- **Indigestion**
- **Diabetes**

In some cases, **antacids** and **tablets for bone protection** (biphosphonates, calcium supplements, and vitamin D) may be helpful to **reduce the long-term, bone-thinning side effects of corticosteroids**.

It is also essential to be aware of signs of tapering off of corticosteroids too quickly. These signs may include:

- **Nausea**
- **Vomiting**
- **Joint aches** (hands and feet especially)
- **Weakness**
- **Fatigue**
- **Low blood sugar**
- **Weight loss**
- **Lack of appetite**
- **Dizziness with standing**
- **Low blood pressure**

Patients experiencing any of these symptoms while on a steroid tapering or low-dose regimen should notify their physician immediately.

Other Immune-Modifying Agents

Aside from corticosteroids, several other medicines may also be considered in managing the acute and long-term course of NMO. Many of these agents are intended to reduce the need to take steroids, which can have adverse effects over the longer term. For this reason, such treatments are called **steroid-sparing** regimens, meaning they intend to spare the patient from the potential long-term risks of corticosteroids. Some of these regimens are considered briefly in the following pages. **These drugs can powerfully modify the immune system, often in ways that suppress inflammation.** As a result, they all have **side effects that can range from mild to serious,**

including increased risks of infection and cancer. Most of these risks are generally well understood, and measures can be taken to minimize them. However, any such drug would need to be explained and carefully considered by your clinical team. **As always, NMO patients should consult with their physicians or neurologists before taking any medicine, and report any adverse events immediately.**



First-Line Agents

Medicines that are generally accepted by clinical experts as a primary or usual treatment for a given type and severity of disease are called **“first-line” agents**. In NMO, there are several first-line regimens that

may be considered, depending on specific factors of each individual patient case. First-line agents that are commonly used in NMO are listed below, in alphabetical order:

Azathioprine (Imuran®): because it inhibits DNA synthesis in rapidly growing cells, such as immune system B and T cells, azathioprine is a strong and relatively non-specific **immunosuppressant**. It is believed to **calm the immune system by reducing the ability of these cells to promote inflammation** involved in NMO and other autoimmune diseases. Because it can significantly and generally suppress immunity, **risks of azathioprine treatment** include infection, cancer and related issues. Azathioprine is available in tablet form for oral administration.



Mycophenolate Mofetil (CellCept®): like other first-line agents, mycophenolate mofetil is an immunosuppressing drug that inhibits the number

Do You Know...

Only through formal clinical trials can new agents be approved as safe and effective for use in NMO.



Learn more about clinical trials on our website at: **guthyjacksonfoundation.org/clinical-trials**

and function of immune system cells. Mycophenolate mofetil has a **more specific target** than azathioprine, namely **an enzyme that is enriched in T and B cells**. Because they have more of this enzyme target, mycophenolate preferentially inhibits these immune system cells. However, because of this action, mycophenolate mofetil also **reduces the ability** of the body to fight infections, and **increases the risk** of certain types of cancer especially if used at high-dose for many years. However, at low doses it may help prevent relapses and minimize long-term risks. Mycophenolate mofetil comes as a capsule, a tablet, a delayed-release tablet, and a suspension (liquid) to take by mouth. Some hospitals and physicians use another version of this drug (mycophenolate acid) called Myfortic®, which has the same activity against the immune system. Sometimes

this alternative version of mycophenolate is given to patients who experience gastrointestinal upset from the mycophenolate mofetil.



Rituximab (Rituxan®): rituximab is a **therapeutic monoclonal antibody**, and an example of the **biologic** (protein-based) class of drugs that may be considered in NMO treatment. It is an example of using an antibody to treat a disease. Rituximab works by targeting **B cells** (which make NMO-IgG) for removal from body by the immune system. This effect may help to prevent NMO relapses or increase the time between relapses. Rituximab is given through the bloodstream, usually as two intravenous (IV) infusions two weeks apart, followed by an approximate six-month break. In some cases, rituximab may be used alone or in combination with other methods to treat NMO cases that are refractory to corticosteroids, PLEX and/or IVIG therapy.

Second-Line Agents

If first-line agents such as those previously discussed do not control NMO or are not well-tolerated, a patient and their clinical team may consider different agents that may have more benefits in some patients. Medicines used when first-line agents fail or are contraindicated are called **“second-line”** agents. Such medications may be used alone or with other treatments. Each medication suppresses the immune system in a powerful way – and as with all such medicines – **the effects can come with unwanted side effects.**



Cyclophosphamide (Cytosan®): this drug is another well-established agent that is known to generally suppress the immune system. When activated by the liver, cyclophosphamide calms the immune system by **preventing the function of DNA and RNA** needed in production of new immune system cells. This drug

When immune-suppressive agents are used to treat NMO, careful monitoring of the immune system is important to address potential risks.

is non-specific, and can have significant adverse effects. While there are **many known side effects** of this drug, there is little evidence supporting its use in NMO.

Methotrexate (Trexall®): Methotrexate inhibits the production of a vitamin-like factor called **folic acid**. Because immune system cells that cause inflammation reproduce quickly, they require high levels of folic acid for normal growth. For this reason, methotrexate is used to calm the immune system by inhibiting the generation of new immune system cells. This drug is non-specific, and like other immune-suppressive agents **can lead to increased risk of infection**, as well as metabolic and other side effects. Methotrexate is commonly used to treat many other autoimmune diseases, and in high doses it is used to treat cancer. In some cases, vitamin supplements rich in folic acid (vitamin B9) may be used to help minimize side effects of methotrexate. Any such supplement should be discussed with a clinical expert prior to use.

Mitoxantrone (Novantrone®): originally developed as an anti-cancer agent, mitoxantrone inhibits the generation and function of many types of immune system cells, including T and B cells, as well as other white blood cells involved in NMO, including **macrophages** and **neutrophils**. This treatment reduces the activity of the immune system overall, thereby reducing inflammation. It is also commonly used in multiple sclerosis (MS) and other autoimmune diseases, and at high doses in cancer treatment. Mitoxantrone **side effects may include** increased risk of infection, hair loss, nausea and other symptoms.



Important Reminder: All treatments that reduce the activity of the immune system can have side effects, some of which can be serious or even life-threatening. If you and your clinical team choose to use such agents, **careful monitoring of the immune system is**

important to address these potential risks. For example, blood tests such as a **complete blood count (CBC)** and **white blood cell (WBC)** count may be performed routinely, with **kidney and liver function also routinely monitored in most cases.** Some patients require preventive vaccines against pneumonia, influenza, or other infections before using immune-suppressing drugs, and may also be prescribed preventive low doses of antibiotics for a period of time. Following some agents such as rituximab, previous vaccinations may be rendered ineffective. In any case, it is imperative to ask your doctor what may be the best treatment and preventive plans in your particular case.

Also, if you develop any side effects, have fevers or other signs and symptoms of infection, it is important that you contact your medical care team immediately.

None of the agents previously described are regulatory-approved to treat NMO. One of the exciting recent **advances in NMO science and medicine** is the initiation of **several clinical trials** to evaluate specific new treatment candidates for safety and efficacy in NMO. Importantly, many of the drug candidates being tested are believed to have more specific cellular or molecular targets than the existing first- or second-line agents. Therefore, if proven safe and effective in clinical trials, **these new agents may have fewer risks or side effects than the general immunosuppressive agents currently used.**

To learn more about **NMO** clinical trials, refer to section 5.1.

3.3 Recovering from a Relapse



QUICK READ

Recurrent episodes of NMO attacks are called **relapses**. It is not known what causes relapses in NMO, and they can come on suddenly and without warning. Relapses and recovery times vary from patient to patient. Likewise, recovery can depend on many factors, including the severity and duration of the attack, the time to confirmed relapse diagnosis and the effectiveness of therapy. Some relapse events can be long-lasting, while others more quickly resolve either partially or completely.

NMO Relapses Require Immediate Action

Regaining function after a relapse can vary greatly from patient to patient. After symptoms are evident, conditions may worsen over hours or days. **Because rapid diagnosis and treatment are crucial to enhance chances for best outcomes, it is important to notify your physician immediately if you sense a relapse.** Eventually, with appropriate treatment over time, many patients may regain some if not all the functions affected during the relapse. **Monitoring symptoms and staying in close communication with your team of clinicians is essential for treating relapses and ensuring a best chance for good outcomes in recovery from a relapse.**

Managing Symptoms of NMO

NMO is a disease that can have very different symptoms in each patient. Many symptoms may improve over time, **especially if treatment is received early.**

However, the effects of relapses may be cumulative, and each attack may lead to additional injury to the nervous system. If nerve fibers have been permanently damaged, long-lasting changes in **strength, balance, vision, bowel or bladder, or other bodily functions may result.** The following discussion considers a few of the more common symptoms that NMO patients may experience:

- **Neuropathic (nerve) pain** in NMO results from acute injury or chronic damage to nerve fibers. While it often associates with peripheral sites in the body (abdomen, limbs, fingers and toes) nerve pain (also called **neuropathy**) can vary quite a bit from patient to patient. For example, **some patients experience numbness in affected areas.** For others, the pain is described as a **burning sensation.** It can be described as a “**sharpness**” or

If nerve fibers have been permanently damaged, long-lasting changes in strength, balance, vision, bowel or bladder, or other functions may result.

a **brief “shooting” pain**, as well as a **“tingling,” “crawling,”** and/or **“electrical” sensation**.

Your clinical team may consider the many different medications that may effectively control neuropathic pain in order to recommend the treatment suited for you.



- **Problems in muscle tone** are called **dystonia**, and can occur in NMO when communication between the brain and spinal cord is affected. Without normal transmission of signals from the brain or spinal cord, nerves can send incorrect signals causing muscles to relax or contract in an uncontrolled manner. Generally, **two basic types** of dystonia may occur: **hypertonic** and **hypotonic**.
- In **hypertonic dystonia**, muscles become more tight or rigid due to spasms that may last minutes to hours. **Spasms** occur when there is too much nerve stimulation to muscle, causing excessive contraction.

- In **hypotonic dystonia**, muscles become more flimsy or flexible and limbs may seem weak. Muscle **weakness** occurs when there is too little nerve signal reaching the muscle.

Too much or too little muscle tone can reduce strength or endurance, and may be accompanied by pain or cramping. In addition, dystonia can contribute to **ataxia**, a condition in which muscular control is limited or poorly coordinated. Ataxia can make balancing or walking difficult. An exercise or stretching plan designed with your clinical team may help improve muscle tone and function.



- **Joint stiffness** is a symptom often caused by changes in muscle tone and/or inflammation. The result is reduced mobility of a joint, such as a knee, elbow, or shoulder. Oftentimes, joint stiffness may be

worse early in the morning or late in the evening.

Exercise or **stretching** can help manage stiffness and pain. Sometimes **medication** or **external treatments** (heat or cold application, or physical therapy) may be needed. Your physician or physical therapist can help determine the best way for you to manage or treat joint stiffness.

- **Bladder symptoms** can occur in NMO, and may include **urgency, frequency, hesitancy** or **difficulty initiating urination**. Other symptoms such as **nocturia** (awakening at night because of the need to urinate) and **retention** (unable to pass urine) may occur due to spinal cord injury. In more difficult cases, catheterization may be required to relieve urinary retention. For conditions of urinary incontinence, medicines may be prescribed by your doctor.
- **Bowel symptoms** may also occur in NMO, and can include constipation and loss of bowel control. Urgency may also be experienced, due to changes in spinal cord and nerve function. **If recommended by your clinical team, a high-fiber diet, fluids, laxatives, stool softeners, and abdominal massage may be part of a care plan to help manage symptoms** (refer to section 4.4 for more).
- **Sexual dysfunction** in NMO may result from changes in nerve function, resulting in a lack of sensation or numbness. Men may experience difficulty in achieving erection, and women or men may have difficulty reaching orgasm. Managing symptoms

often varies from patient to patient. Medications or alternative therapies such as **biofeedback therapy may be helpful** if indicated and prescribed by your clinical team.

- **Osteoporosis** (brittle bones) may result from long-term use of steroid medication or lack of weight-bearing activities or exercise. If practical, **an exercise plan approved by your physician can be a natural way to strengthen bones.** Adding **vitamin D** or **calcium supplements** to your diet may also be important considerations to discuss with your doctor (refer to section 3.6). If appropriate, medicines to help strengthen bones or prevent bone loss may be useful in some patients.

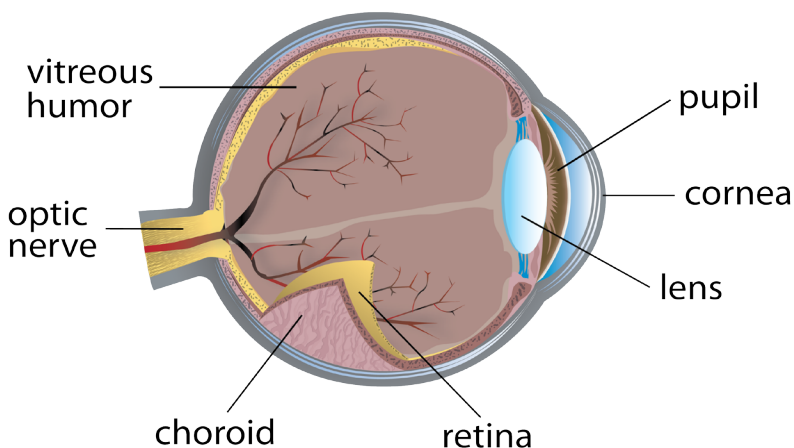


- **Depression** can be a natural and normal symptom associated with NMO and other chronic diseases. Symptoms may occur for many reasons, such as **changes in quality of life, loss of vision,**

mobility or **sensation**, or **stress**. The causes, symptoms and effects of depression can be brief, intermittent or chronic. Treatment for depression often consists of **counseling**, **medication**, or both. It is important to discuss your feelings with your clinical team to consider the best ways to manage any emotional impact of NMO.

- **Visual symptoms** in NMO may include **eye pain** that is worsened by eye movement, **vision loss** over hours or days, changes in the field of view (such as loss of **peripheral vision**) or perception of colors and depth. Such symptoms most commonly result from inflammation in the optic nerves (**optic neuritis**) that connect the **retina** of the eyes to the brain. With appropriate treatment, many NMO patients experience improved visual symptoms following a first attack or relapse, especially when treatment is started early.

Parts of the Human Eye



Be part of the cure.

Collaborative
International
Research in
Clinical and
Longitudinal
Experience
Study of NMO



Consider participating in the
CIRCLES NMO Study.

To learn more, refer to Chapter 5.

Managing Long-Term Effects of NMO

Creating a Holistic Care Plan

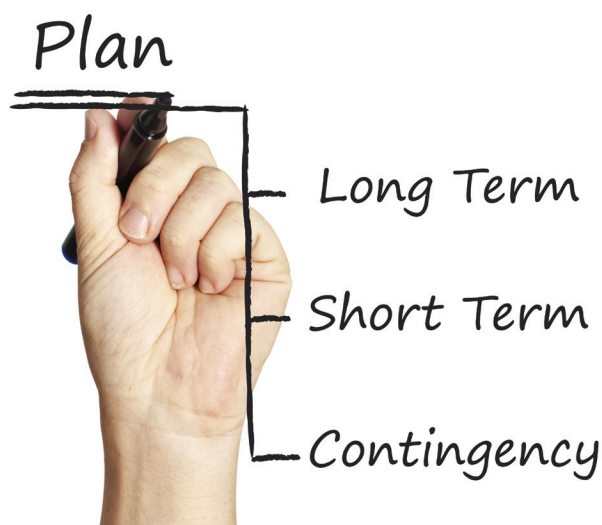
Symptoms experienced in NMO can persist over long periods of time, overlap with other symptoms, or have indirect effects on day-to-day functions and quality of life. For example, pain interferes with activities such as housework, employment or exercise. In turn, these effects can have negative impacts on self-esteem, mood, sleep, and personal or professional relationships. Although each problem may be addressed individually, many NMO patients find it helpful to manage their overall health through a multi-faceted approach, including **holistic** care.

In an effective holistic care plan, honest and regular communication occurs among the patient, doctors, nurses, and team of health specialists including:

- Alternative medicine (e.g. meditation, acupuncture)
- Psychological support or counseling
- Social integration
- Physical therapy
- Spiritual health experts

Importantly, such a holistic medicine team creates a coordinated plan to manage the unique healthcare process of each NMO patient. In addition to regular clinical evaluations and treatment as appropriate, vision or mobility aids (e.g. **walkers** or customized **wheelchairs**), home health care (e.g. **visits by healthcare professionals to your home**), or **custom home remodeling** can be part of a multidisciplinary management plan and may improve quality of life.

As in many autoimmune diseases, NMO can cause a broad spectrum of symptoms that may vary widely, with every patient affected differently.



Can long-term symptoms improve significantly?

It is possible that long-term symptoms may improve or resolve over time. **Researchers are learning more about NMO every day, and clinical trials are in progress to find treatments that arrest or reverse the disease process.** However, based on current knowledge it is rare for symptoms that have existed for years to resolve quickly or entirely. It is for each of us to do our best with every day we have.

Modifications to patient residence, mobility aids (e.g. walking aids or wheelchairs), and lifestyle modifications (e.g. change of job, move to a single-story home) may best be planned in advance. This way, time and resources can be focused on improving quality of life, rather than trying unproven or potentially dangerous approaches, which can be very costly. Consulting with your clinical

team – including a qualified occupational therapist – as early as possible can be important to help guide your planning, and may be covered by medical insurance (refer to Chapter 4 for more information).

How severe can NMO be?

As in many autoimmune diseases, NMO can cause a broad spectrum of symptoms that may vary widely, with every patient affected differently. **Disease symptoms can range from mild** – such as only one relatively benign attack of optic neuritis with a near-complete recovery and no further relapses – **to severe** and can include lasting effects such as blindness and/or paralysis. Some of the more severe effects may include loss of vision in one or both eyes, a degree of paralysis in limbs due to damage of the spinal cord, breathing difficulties due to spinal cord or other neurological issues, and even premature death.



You can learn more about clinical trials on our website at:
guthyjacksonfoundation.org/clinical-trials

Although the factors that predict severity of disease are not yet known, research moves forward every day to help find these answers.

And, with early diagnosis and effective treatment, many of the consequences of NMO can be managed, allowing people to better live their daily lives.



What about Alternative Therapies?

Alternative and complementary therapies can be used to **target a specific physical, mental, emotional or spiritual problem caused by NMO**. They can also be used as preventative measures or purely for relaxation, and may increase your feeling of well-being. Although this guide makes no recommendations for clinical care, reflexology, massage, Reiki or acupuncture may help sleep patterns, relieve pain, or reduce stress and tension. **Consult your physician and care team for more information or specific recommendations.**

Clinical research has yet to adequately study how effective any of these treatments may be. Therefore, **it is generally recommended that they not replace the medical treatments** that your neurologist, primary care physician or other healthcare professionals prescribe. However, alternative therapies may **complement the effects of traditional medicines when added to your overall care plan as appropriate**. For example, **stress reduction** methods have been reported in the scientific literature to help stabilize some autoimmune diseases, especially when part of a long-term medical treatment plan.

Physical therapy and rehabilitation medicine tend to be very customized to each specific patient case. The goal of these activities is to improve function and coordination of movement and strength, and reduce pain that may be associated with nerve inflammation. Specialized techniques and devices can be very helpful in this way, as part of an integrated treatment plan with your health care team.

Alternative and complementary therapies can be used to target a specific physical, mental, emotional or spiritual problem caused by NMO.



3.4 Pregnancy and Pediatrics

NMO and Pregnancy

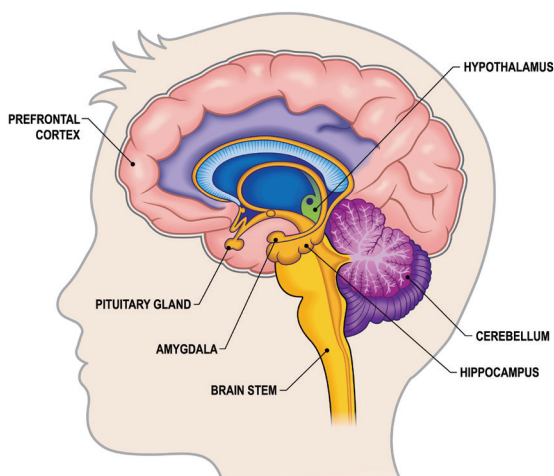
The hormonal changes during pregnancy can affect disease course in several autoimmune conditions such as multiple sclerosis (MS), systemic lupus erythematosus, and Sjögren's disease. Similarly, **relapse rate may be influenced by pregnancy in neuromyelitis optica (NMO)**. Like MS, several studies from different geographic populations suggest NMO relapses increase in the months immediately following childbirth. In addition, there may be an **increased chance** for initial NMO symptoms to occur during the **post-partum period**. Some studies suggest that **relapses may increase during pregnancy** as well, signifying that pregnancy may not confer the same protective properties to disease course in NMO as in MS. However, every NMO case may be different with respect to the effects of pregnancy. Because of the potential severity

of relapses and the unique considerations of pregnancy, your clinician may advocate continuing treatment or changing to a different treatment during pregnancy. **This is an important discussion to initiate with your care team early in the process of considering pregnancy so that a plan can be made ahead of time.** Currently, there is no consensus on the most appropriate treatment options during pregnancy. It is known that some therapies may have higher risks on fetal development than others. Furthermore, there is greater acceptance for the need to monitor closely and if needed treat aggressively during the post-partum period because of a higher risk of relapse. Larger studies are needed to determine if the incidence of pregnancy-related complications, miscarriage, or infertility differ in NMO from the general population.



NMO in Children

The **pituitary** gland is called the “master gland.” It is located in the center of the head, near the base of the brain and behind the eyes. The pituitary gland **governs many endocrine functions, including the thyroid gland, adrenal glands, ovaries and testes.** The pituitary gland also helps regulate the amount of salt and water in blood. **Growth hormone from the pituitary gland promotes growth and development in children.**



The pituitary gland is governed by a special region in the brain, called the **hypothalamus**. The hypothalamus connects to the pituitary by a thin stalk of vessels (known as the **infundibulum**) that **allows direct communication from the hypothalamus to the pituitary.** The hypothalamus is **rich in aquaporin-4 (AQP4; a key autoantigen in NMO), so an NMO attack on the hypothalamus can disrupt pituitary function.**

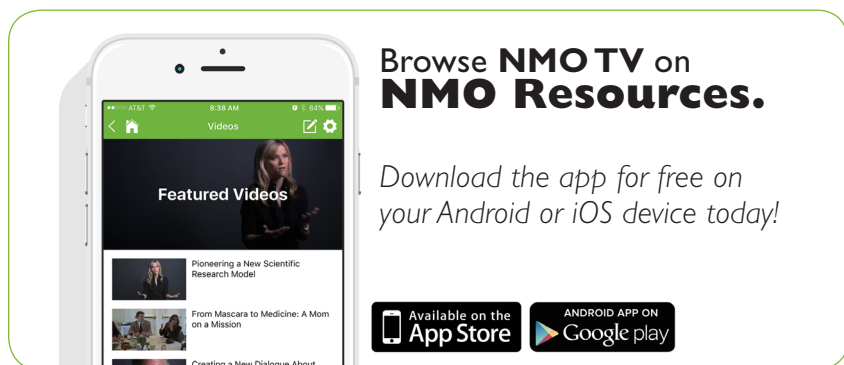
Although most NMO cases are diagnosed in adults aged 30-40 years, NMO can emerge at any age. The development of the immune system is active during childhood, and is influenced by many different interactions with the environment. While the disease processes that lead to NMO may be similar in children as adults, the symptoms and treatments may be very different in children. Likewise, pediatricians may have special experience and insights into diagnosis and care for children facing NMO.



Epidemiology of Pediatric NMO

Current data suggest that approximately 3 percent of all NMO patients experience their first symptoms in childhood or adolescence. **Patients as young as 16 months have been reported with NMO.** The average age for NMO diagnosis in children is 10 years

old. **Both boys and girls can be affected, but as in adults, there is a propensity for females to be more commonly affected than males, at a ratio of 5:1 or higher.**



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Symptoms of Pediatric NMO

Children diagnosed having NMO usually present with acute, new neurological symptoms appearing within **a few hours or days**. These attacks can include symptoms of back, neck, or eye pain, blurred vision, or loss of vision in one eye or both eyes. Some children may experience other possible symptoms including:

- Weakness or numbness (tingling/itching) of the arms or legs
- Confusion or extreme lethargy at their attacks
- Stomach pain, nausea, vomiting, or hiccups
- Fever or seizures
- Muscle spasms / backaches
- Headaches

Some special features and effects of NMO in children may be considered:

- **Puberty may come early or be delayed** in pediatric NMO patients. Some girls with previously regular menstrual cycles will develop irregular periods. Even if NMO occurs during puberty, males with NMO can father children and females with NMO can become pregnant and have healthy babies with proper medical care.
- Some children may have **abnormal sodium levels** in their blood during an attack.
- The **effects of relapses** in pediatric NMO patients may be greater than those in MS patients, including impact on blood pressure, heart rate, and other bodily functions.
- **Some children with pediatric NMO may be shorter in stature** as they develop to teenagers and adults, because of prolonged steroid use or impact of NMO on pituitary activity such as growth hormone.

As in adult NMO, **keeping relapses to a minimum, and rapid diagnosis and therapeutic intervention** if they do occur, **are the keys to avoiding long-term disability, managing day-to-day symptoms and improving overall quality of life.**

Diagnosis of Pediatric NMO

Similar to adults, NMO diagnosis in children is usually made by a combination of **laboratory and clinical**

Diagnosis is usually made by a combination of clinical features, appearance of lesions or “spots” on the optic nerves, spinal cord or brain using MRI.

features, appearance of lesions or “spots” on the optic nerves, spinal cord or brain using MRI. Approximately **two-thirds of children** with NMO can also have **autoantibody to aquaporin-4** in their blood or spinal fluid. However, this **antibody may not be present at the onset of the disease**, and may only appear years later. Pediatric NMO often differs from childhood MS in the **distribution of MRI lesions**, as well as laboratory results such as oligoclonal bands (in MS) or the presence of the **aquaporin-4 autoantibody** (in NMO).

Treatment of Pediatric NMO

As in adult NMO, there are **no regulatory approved treatments** for children with NMO. Clinical specialists such as pediatric neurologists usually recommend **immunomodulatory treatment regimens** similar to those used in adults, except that the dosages and duration of therapy vary. For example, **corticosteroids**

such as prednisone and procedures such as **plasma exchange (PLEX)** are often used in pediatric NMO. Attacks or relapses are typically treated with a short course (usually up to a week) of IV corticosteroids, or IVIG or plasmapheresis. As in adults, it is important to prevent new attacks in children with NMO, and treatment with mycophenolate mofetil, azathioprine or rituximab is often considered for this reason.

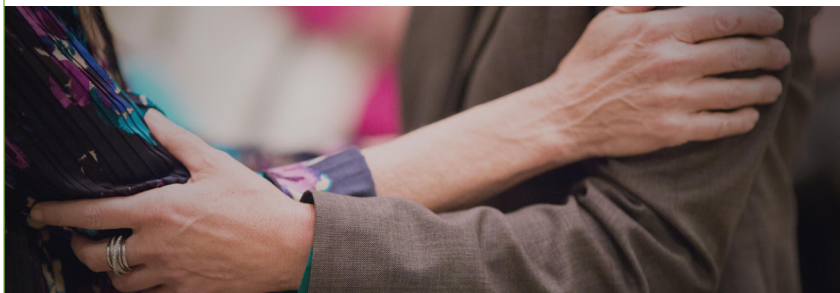


Research in Pediatric NMO

There is ongoing research to understand the causes of pediatric NMO including possible genetic predisposition, environmental associations, or dysfunctions in key

immune system checkpoints. As well, the 2015 IPND diagnostic criteria are helping to improve the speed and accuracy of NMO diagnosis. The effects of age, immune function and endocrine development are also being carefully studied in basic science and clinical research to better understand NMO. In addition, imaging methods are advancing to improve recognition of the effects of NMO on the CNS, and help refine prognosis. Importantly, **clinical trials are now ongoing to evaluate treatments for NMO in children when appropriate**, as well as adults.

You're invited to join...



- NMO Parental Support Group for parents with children who have NMO
- Pregnancy NMO Support Group for expecting NMO mothers
- Many more...

Find details on the NMO Resources app or on our website at:

guthyjacksonfoundation.org/support-groups

Advocates Specializing in Pediatric NMO

There are several centers across the U.S. and the world that have special experience in the diagnosis, treatment and management of NMO in children and adolescents. Care includes neurological expertise, family support, psychological therapists, social workers, occupational therapists and caregivers with special expertise in supportive and healthcare needs. Care is often co-managed by a specialist team as well as a patient's local neurologist or pediatrician.

3.5 Creating a Healthcare Team



QUICK READ

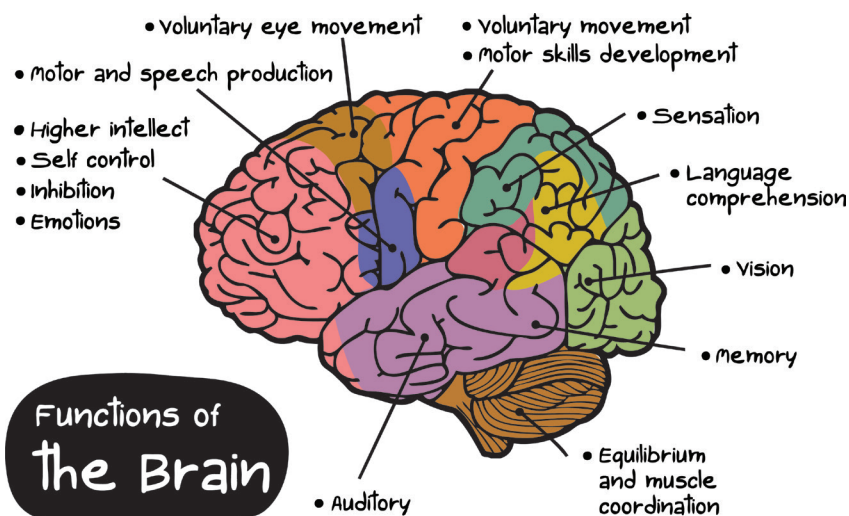
Healthcare professionals working together as a team may offer the most effective way to manage NMO. Start with the list below when considering a healthcare team:

- Primary Care Physician
- Neurologist (central nervous system specialist)
- NMO Neurology Expert
- Pediatric Neurologist
- NMO Nurse Specialist
- Ophthalmologist (eye doctor)
- Neuro-Ophthalmologist (NMO eye doctor)
- Neurology Fellow
- Physical Therapist
- Urologist (bladder and sexual functions)
- Gastroenterologist (bowel functions)
- Continence Advisor
- Occupational Therapist
- Clinical Psychologist
- Dietician / Nutritionist

NMO is a complex disease, and many patients benefit from a team of healthcare professionals having diverse expertise to help manage their health. This section describes some of these different roles.

Primary Care Physician (PCP)

The primary care physician (PCP) is responsible for providing routine health care to individuals seeking medical care. With his or her team, this doctor arranges day-to-day care, such as prescribing medications, arranging basic laboratory tests and monitoring results. When NMO is a potential diagnosis, a key role of the PCP is to rapidly engage the expertise of a neurologist with expertise and experience in NMO. The NMO neurologist works closely with the PCP and clinical care team to ensure that all aspects of diagnosis and treatment are implemented and monitored as necessary.



General Neurologist

A general neurologist focuses on diagnosing and treating diseases or medical conditions of the nervous system. This neurologist uses their expertise and knowledge to recognize and treat symptoms, and may refer a patient

to sub-specialists, such as an NMO neurologist, neuro-ophthalmologist, or other expert for further advice on diagnosis and management.

The general neurologist will be closely involved in the care of the patient alongside the team of providers. The neurologist may be seen for regular follow-ups or perhaps if needed, to admit the patient to a hospital at the time of a relapse.



NMO Neurologist

The NMO neurologist has special training, experience, and expertise in field of NMO and related neurological diseases. The NMO neurologist is responsible for ensuring the correct diagnosis is made as quickly as possible, and determines the most appropriate treatment for patients with a diagnosis or suspected diagnosis of NMO.

In addition, the NMO neurologist often leads the NMO clinical care team, and works closely with the specialist nurses and other members of the caregiver team to ensure the best possible care is delivered.



Pediatric Neurologist

Pediatric neurologists specialize in neurological care for patients 18 years old or younger. For children and adolescents with NMO, all care is managed by their pediatric neurologist, who works closely with the overall NMO clinical team. This doctor will ensure appropriate diagnosis, treatment, and continuity of care is in place for pediatric patients. It is important to have a pediatric neurologist closely involved in the daily management of all pediatric NMO cases since drug dosing and side effects can vary more so in children than adults.

NMO Nurse Specialist

Some, but not all medical neurology groups have an NMO nurse specialist, who can be a first point of contact for any day-to-day concerns of NMO patients. The NMO nurse specialist will take time to discuss the diagnosis, treatment plan, specific problems the patient may encounter and answer any basic questions the patient may have. The NMO nurse specialist may help provide:

- Information on the **condition, symptoms, medications** and other **therapies** available to increase educational understanding
- A rapid link to the NMO neurologist should there be concerns of **new or worsening symptoms** or indications of relapse
- **Support** with **relapse issues and care**
- **Facilitation** for working effectively with **healthcare professionals** such as neurologists, physicians and occupational therapists as well as nutritionists and other medical professionals
- **Education for other healthcare professionals** who might encounter NMO patients
- A link to transmit **clinical information** to the PCP, pediatric neurologist, and NMO clinical care team

Ophthalmologist

The ophthalmologist is an **expert in the assessment of visual problems** such as optic neuritis (ON). This doctor may also arrange scans and other tests to assess vision. He or she discusses findings with the NMO neurologist and connects patients with visual problems to appropriate local support services for visually impaired people.

Neuro-Ophthalmologist

A neuro-ophthalmologist is a specialist doctor trained in ophthalmology who specializes in eye diseases associated with neurological conditions. Thus, this physician has an **expertise in both neurology and ophthalmology** and generally practices and studies central nervous system (CNS) diseases that affect vision.

Some NMO patients see a neurologist who is also a neuro-ophthalmologist and who manages all aspects of patient care. In other cases, a neurologist may refer patients for consultation with a neuro-ophthalmologist for help with diagnosis, treatment, and clinical follow-up related to their vision.

NMO patients are encouraged to take an active role in their health care to help minimize the impact of disease, optimize treatment benefit, and enrich quality of life.



Neurology Fellow

A neurology Fellow is a **neurologist-in-training** who is early in their career and **gaining experience** in a specific area of interest. In addition, the neurology Fellow often conducts clinical research, and may assist patients in considering and enrolling in clinical trials. A patient may meet a neurology Fellow during a visit to the NMO clinic or while being admitted to the hospital for care.

Physical Therapist (PT)

As prescribed by neurologists or other physicians, physical therapists work to **enhance movement, coordination, and strength of the body**. A physical therapist will assess physical problems such as poor balance, limb weakness, stiffness and spasms. They will advise the neurologist on range of motion, level of activity and pain, and implement exercise or physical care programs, prevention, rehabilitation treatment plans.

NMO patients are encouraged to take an active role in their health care to help minimize the impact of disease, optimize treatment benefit, and enrich quality of life. Refer to local services for information or provision of aids such as walking sticks, hand supports, and wheelchairs.

Urologist

Patients may experience bladder and sexual dysfunction as a result of neurological damage due to NMO. The urologist is an **expert in urinary and sexual function**, and can perform bladder function tests. Specific medications are available and may be appropriate to manage urinary issues or sexual dysfunction in NMO patients.

Gastroenterologist

Similar to bladder issues, NMO may cause abnormal bowel function or control. Because the nervous system regulates normal bowel activity, **changes in neurologic function that lead to bowel dysfunction are not uncommon in NMO**. In addition, NMO may cause symptoms of prolonged nausea or hiccups. These issues are typically referred to a gastroenterologist for evaluation and management, including the use of specific medicines or dietary changes.

Continence Advisor

NMO patients may experience symptoms related to bowel and bladder function. Bladder and bowel problems can restrict daily activities and lead to embarrassment

and isolation, affecting both physical and mental health. Continence advisors **assess bladder and bowel problems, review medication regimens, suggest exercises to improve urinary and fecal incontinence, and provide advice regarding best practices for healthy living.**



Occupational Therapist (OT)

The role of the occupational therapist is to help patients **maintain independence in day-to-day activities.** This goal includes addressing activities related to personal care, domestic tasks, hobbies and employment that may be challenging due to fatigue or loss of functions such as vision, mobility or strength. Occupational therapists work to find different ways of doing routine tasks to help patients maintain their self-sufficiency and well-being.

Clinical Psychologist

Clinical psychologists **support patients and their families with the emotional adjustment of living with NMO**. By looking at emotional issues in context of NMO as a manageable aspect of one's life, psychologists can help individuals find solace and meaning on their NMO journey through coping strategies. They can also access cognitive problems (memory, thinking, focus) and make recommendations for beneficial exercises. Psychologists may also assist in behavioral modification, such as stopping smoking (which can worsen outcomes in NMO). **Psychologists are different from psychiatrists in that psychologists may not diagnose mental health diseases or prescribe medications.**

Dietitian / Nutritionist

The role of the dietitian or nutritionist is to **advise patients on nutrition, health, and dietary-related topics** to minimize impact of disease and enhance quality of life. For NMO patients, recommendations may be provided for weight management (weight gain or loss) or optimizing diets for nutrition, and for customizing special diets that may reduce bowel inflammation (e.g. acids, glutes, caffeine, alcohol), help manage weight issues and all nutritional concerns. Dietitians and nutritionists may also provide advice regarding supplements that may be helpful in NMO, such as vitamin D, calcium, or other nutrients if approved by the physician. For more information on diet and nutrition, refer to section 3.6.

Pain Management Team

The neurologic effects of NMO can cause pain in specific areas or more generally throughout the body. Beyond its discomfort, suffering from chronic pain can negatively affect daily living, create challenges in work, exercise or recreational activity, impair sleep, and have adverse impacts on meaningful relationships with others. Because the causes and effects of pain in NMO can be complex, pain management teams are often available to NMO patients. **The pain management team may consist of pain physicians, nurses, physiotherapists, occupational therapists, and psychologists, and function in a collective way.** This holistic approach ensures better pain management and coordination of care so that treatment goals are met.



3.6 Managing Diet and Nutrition



QUICK READ

Many medical caregivers and patients view dietary strategies as an important component of their treatment plans. Optimizing diet and nutrition may contribute to control or slow down NMO effects on the body, and help maintain overall good health.

To help people with NMO make informed decisions about diet and dietary supplements, the following text provides information about approaches that are not

absolutely proven, but are low risk and may benefit the underlying disease process in NMO.

Many people with NMO and related conditions may wish to use dietary approaches to help control the disease. The goal is to slow down the disease process in a safe and natural way. Paying close attention to diet and nutrition may provide a sense of control, hope and empowerment. **Medical caregivers generally agree that healthy diets are an important part of the overall care plan for their NMO patients.**



For those interested in using dietary strategies for NMO, it is extremely important to be well informed. High-quality information allows one to identify and use approaches that are low risk and potentially beneficial, and avoid those that are possibly harmful or ineffective. Due to the complexity of NMO and NMO medications, it may be difficult to obtain high-quality, unbiased NMO-specific dietary information. **Some dietary information may have financial incentives, biases, or limitations in evidence of benefit that lead to inaccurate and sometimes potentially dangerous information.**

When considering diet or nutrition changes, several key points should be kept in mind:

- Before trying specific dietary approaches (or any other unconventional therapies), the **risks and benefits** of these approaches should be discussed with your healthcare provider.



- **Unfortunately, no dietary approach has ever been systematically studied in NMO.** For those who are only interested in absolutely proven therapies, there is no dietary regimen that can be formally recommended as of yet.



Vitamin D

Recent studies have significantly changed our understanding of the role of vitamin D in health and disease. In the past, it was believed that most people have adequate vitamin D level from exposure to sunlight or intake of dairy products, and that the effects of vitamin D are restricted to regulating calcium absorption and maintaining bone health. However, much has been learned about production and function of vitamin D in recent years. **It is now recognized that vitamin D deficiency may exist among peoples of all countries.** In part, this phenomenon may be related to the beneficial effects of sunscreen in preventing

skin cancer. In addition to its effects on bones and calcium, **vitamin D exerts important actions on many other body systems, including the immune system.** Vitamin D has not been rigorously studied in NMO, but studies in other autoimmune conditions suggest **there may be some benefit to maintaining appropriate vitamin D levels consistently.**



Fatty Acids and Fats

Fatty acids are complex molecules that can have important actions on multiple body systems, including the immune system. There are two

types of fats that can render fatty acids in the process of digestion. **Saturated fats** are typically solid at room temperature, and are what we generally think of as “fat.”

White fat on or in red meat is an example of a saturated fat. The other major type of fat is **unsaturated fat**, which is typically liquid at room temperature, and is

commonly referred to as “oil.” Saturated and unsaturated fats may contain **monounsaturated fatty acids** (e.g. present in olive oil) or **polyunsaturated fatty acids**. The two main forms of polyunsaturated fatty acids are **omega-six fatty acids**, which are found in healthy oils such as sunflower and safflower seed oils, and **omega-three fatty acids**, which are enriched in fish oil.



Fatty acids can affect immune system function. **Immune system suppression, which could be beneficial for NMO, may result from omega-class fatty acids, and especially by omega-three fatty acids.**

This effect on the immune system may involve T cells, B cells, or other regulatory effectors of the immune system. Although omega-three and omega-six fatty acids have not been studied specifically in NMO, they have been studied in other immune diseases.



Sodium and Inflammation

Beyond its role in other conditions such as heart disease or kidney failure, too much salt in the diet may adversely affect NMO patients. Emerging clinical evidence suggests that **excess dietary sodium may promote inflammation and could worsen NMO.**

For example, the protein encoded by a gene called **SGK-1** governs sodium transport by sensing salt. Importantly, sodium causes this system to induce pro-inflammatory molecules such as **interleukin-17A (IL-17A)**, which is known to contribute to NMO disease.

Possible Harmful Dietary Supplements

Like medications, dietary supplements contain chemical compounds that may produce beneficial as well as harmful effects. **Certain supplements may actually activate the immune system and promote inflammation.** For this reason, NMO patients should

avoid dietary supplements that have potential harmful effects and lack any known beneficial effects for NMO. For NMO patients, there are three main types of possibly harmful supplements:

“Immune-Stimulants”

Some supplements, such as **Echinacea**, appear to activate various components of the immune system. Through this process, these supplements could actually **worsen NMO disease mechanisms, and/or counteract the therapeutic effects of NMO medications**. The potential risks of such supplements are based on scientific studies in the laboratory or as correlated with disease, and thus are theoretical. Nonetheless, immune-stimulating supplements should be approached with caution, and certainly should not be used in high doses, over extended periods of time, or without physician approval.

Do You Know...

Some supplements, such as Echinacea, appear to activate various components of the immune system and could be harmful in NMO.



Toxic Supplements

Many dietary supplements are well tolerated. However, some **may produce side effects that range in severity** from mild, such as sedation, to severe, such as liver or kidney toxicity, or death. Such toxic effects can be caused by the supplement material itself, or by contaminants contained in the supplement as a result of manufacturing. Unfortunately, the production of supplements is not typically monitored by regulatory agencies, and quality can vary widely from manufacturer to manufacturer.

Supplements that Affect Medications

Some dietary or nutritional supplements can have negative effects on medications used to manage or treat NMO or its attacks. For example, certain supplements may directly and negatively interact with medicines, including NMO medications (such as steroids and immune-modifying medications). Alternatively, certain supplements may stimulate the functions of the liver or other organs, and affect how NMO medicines are metabolized, distributed, or cleared from the body.

Diet & Nutrition on NMO TV

For information about diet and nutrition regarding autoimmunity and NMO, please visit our video library on our website at:

guthyjacksonfoundation.org/nmotv





A Three-Step Approach to Healthy Nutrition

STEP ONE: Eat a Well-Balanced Diet

To be certain that a diet has an adequate intake of a variety of nutrients, the following general guidelines should be followed:

- Consume a variety of nutrient-dense foods and beverages
- Limit the intake of saturated and trans-fats, cholesterol, added sugars, salt, and alcohol
- Consume adequate amounts of fruits and vegetables
- Eat a variety of vegetables and fruits each day
- Unless advised otherwise, consume three or more ounces of whole-grain products daily

- Consume less than 10 percent of calories from saturated fats
- Maintain total fat intake to between 20 and 35 percent of calories
- Consume fiber-rich foods
- Limit sodium intake

More specific information may be found at:
choosemyplate.gov



STEP TWO: Consider Diets and Supplements that May Balance the Immune System

NMO patients may want to consider strategies that aid in healthy immune system function and balance. Here are a few possible considerations toward that goal:

- Under the advice of your physician, take supplements of vitamin D if the blood level of vitamin D is low. Vitamin D levels may be determined with a simple blood test known as “25-hydroxyvitamin D.”
- Increase intake of omega-three fatty acids
 - Fatty fish (such as salmon)
 - Healthy oils (olive, safflower)
 - Specific supplements (fish oil, omega-class fatty acids)
 - Maintain or modestly increase intake of omega-six fatty acids
 - Decrease dietary sources of saturated fat
 - Supplement with vitamin E if omega-three or omega-six fatty acid intake is increased



STEP THREE: Avoid Adverse Supplements

NMO patients should avoid or use caution with supplements that may trigger immune system reactivity, cause significant side effects, or interact with medications. As with any dietary or nutritional supplement, consult your physician, dietician or nutritionist before beginning use of any supplements.

Expanding Perspective

There are many different types of unconventional therapies that may be used in NMO. The five main types of alternative and complementary therapy, along with representative examples, are:

- Organic based therapies: diets, dietary supplements
- Mind-body medicine: meditation, hypnosis, biofeedback
- Manipulative and body-based systems: massage, chiropractic medicine



- Alternative medical systems: traditional Chinese medicine, Ayurveda
- Energy therapies: magnets, therapeutic touch

Access the entire article free of charge on the GJCF website at:
guthyjacksonfoundation.org/diet-nmo

It is imperative that you talk with your doctor about dietary, nutritional, supplement or alternative medicine strategies if you are considering them as components of your treatment plan. Some clinics have an on-site nutritionist, while others have a recommended reading list for those interested in monitoring their nutrition as an attempt to control symptoms of NMO.

Do you know?

NMO clinical trials are essential to achieve regulatory approval for NMO therapy.

Read more about clinical trials in section 5.1 or on our website at:
guthyjacksonfoundation.org/clinical-trials

Living with NMO



Living with NMO

- 4.1 Fitness
- 4.2 Managing Fatigue
- 4.3 Coping with Loss of Vision
- 4.4 Managing Bowel and Bladder Problems
- 4.5 Occupational Therapy
- 4.6 Support with Daily Life
- 4.7 Daily Living Equipment
- 4.8 Modifying Your Home
- 4.9 Driving and Transportation
- 4.10 Social Security Disability Benefits in the U.S.
- 4.11 Support for Caregivers

4.1 Fitness

QUICK READ

Exercise routines and preferences may vary from person to person depending on overall health, degree of symptoms, limitations of mobility, and basic fitness levels. A healthy lifestyle promotes a balanced immune system, reducing the risks of inflammation while defending the body against infection. Regular exercise and enough sufficient rest are two of the keys to a healthy lifestyle. Seek advice from your doctor or physical therapist before beginning any exercise program.



The benefits of exercise may include:

- Improved muscle tone and flexibility
- Increased mobility and endurance
- Better bladder and bowel function
- Reduced fatigue and depression
- Improved attitude and social engagement

Additional aspects of an exercise program to be discussed with your health care team include:

- **Appropriate exercises** vs. those that should be avoided
- **Ideal levels of exercise** intensity, frequency, and recovery
- **Duration of workout** and any physical limitations

- **Referrals to other professionals**, such as a physical therapist, who can help create a personal exercise program that meets your needs
- **Managing body temperature** as NMO pain symptoms may be more pronounced if the body is overheated. You will find a number of personal cooling devices on the market today. Your doctor may have recommendations for cooling measures and devices to best meet your needs.

Yoga may be a good choice of exercise to help NMO patients.

Yoga may be a good choice of exercise to help NMO patients. Yoga emphasizes relaxation, breathing, stretching, and deliberate movements. Physical benefits can include flexibility, strength, muscle tone, pain reduction, and improved breathing. Improvements in mood and well-being, restful sleep, and increased energy have also been reported in patients who regularly perform Yoga exercises. Locating a yoga class close to home may help you to attend regularly. If a stretch or pose does not feel right to you, listen to your body. Talk with your instructor to learn proper technique and more options to meet your needs.



There are many different types and varieties of yoga programs. Although they may differ in their philosophy and techniques, all yoga styles have a number of potentially beneficial qualities, including:

- **Breathing techniques** to focus the mind and body
- Individualized, non-competitive, and **customizable programs**
- Emphasis on bodily **alignment**, which benefits posture and balance
- **Muscle strengthening**, stretching, and conditioning
- **Tension release** that may allow the body to feel more energized
- **Relaxation techniques** to reduce stress

Most NMO patients are able to exercise in many different ways. Because no two people experience

Although they may differ in their philosophy and techniques, all yoga styles have a number of potentially beneficial qualities.

NMO in the same way, exercise programs should account for individual capabilities and limitations. The advice of a physical therapist or exercise specialist can help to identify goals and target programs that are safe and have good muscle, bone, and respiratory benefits. If changes in mobility occur, ask your specialist to recommend modifications.

Keeping a regular exercise routine is an important lifestyle strategy for managing complications and maintaining physical and mental strength in living with NMO.

QUICK READ

To help manage fatigue, pace yourself as you perform daily activities. Meal planning, use of handheld or other electronic devices, and setting a daily schedule can help to accomplish your daily goals. Accepting help from family and friends can benefit everyone.

4.2 Managing Fatigue



Varying types or severity of symptoms can affect fatigue and are common among patients with neurological conditions. Some patients report no fatigue, while others report experiencing extreme fatigue.

What is fatigue?

Fatigue is generally defined as a feeling of lack of energy and motivation that can be physical, mental, or both. The sensation of fatigue is associated with feeling tired, weary, exhausted, and weak. Try not to be discouraged. Nearly everyone struggles with fatigue or overwork from time to time.

Fatigue in NMO

Some people with NMO experience overwhelming exhaustion by simply carrying out their everyday activities. Fatigue can set in without warning, and accomplishing routine tasks may become a real challenge. This degree of tiredness can be difficult to understand, and may lead to frustration and feelings of guilt or inadequacy.

What causes fatigue?

It is difficult to determine a specific reason for fatigue, which is commonly found in people with chronic or neurological illnesses. Possible causes include:

- **An initial attack or relapse** that requires the body to compensate during recovery for the changes that have occurred. Over time, fatigue may improve or disappear completely.
- **Getting used to a new way of life.** Living with NMO can be physically and psychologically tiring.
- **Sleep disturbances** that can be due to pain or incontinence. After a period of time, a patient may feel the effects of sleep deprivation and exhaustion.
- **Low mood, depression, frustration, and anger,** all feelings that can be associated with changes in life.
- **Medications** that can lead to feelings of tiredness and lethargy.

After a period of time, many people with NMO are able to determine which activities or events are likely to cause, increase or decrease the chances of fatigue. While some patients report that physical activity increases their level of fatigue, others report a benefit from being active. Sometimes fatigue is caused by setting unrealistic goals and trying to accomplish too much too soon.

Remember to pace yourself.

What is it like to live with fatigue?

Fatigue is subjective, hard to explain and difficult to measure. It can be difficult for others to appreciate and understand how debilitated a person may feel, even though they may appear fine. **Employers, friends and loved ones may all struggle to understand and empathize with fatigue, resulting in additional anxiety and stress for the patient living with NMO.** Clear and honest communication can help.

After a period of time, many people with NMO are able to determine which activities or events are likely to cause, increase, or decrease the chances of fatigue.

NMO patients realize that each daily task uses up energy. It can be helpful to prioritize the most important tasks of the day first, followed by optional tasks. In this way, energy can be focused on the most meaningful activities.



Ideas for managing fatigue

Here are suggestions that may help minimize the effects of fatigue:

- **Rest:** Don't be afraid to rest when your body says you should. One key to being able to accomplish critical daily activities is to rest before your energy level is depleted. If you can, take several rest breaks throughout the day.
- **Sleep:** Do your best to get a good night's sleep. If pain or incontinence issues interrupt sleep for more than one week, seek advice from your doctor. Keep caffeine intake at a healthy level and arrange for

One key to being able to accomplish critical daily activities is to rest before your energy level is depleted.

support in caring for children at night, if necessary. Try not to be hard on yourself if you have trouble sleeping. Meditation, music, and other tools may help improve sleep quality.

- **Daily Activities:** Plan your most important daily activities first and early in the day, and don't be afraid to explain your schedule. Talking with others about what you need may help you set realistic goals as you "talk them out." You never know, if you communicate more with others, help may come when you least expect it.
- **Cleaning:** Letting go of the responsibility of caring for your home can be difficult. In an effort to save energy, consider using lightweight equipment and carefully timing larger cleaning efforts. You may find a great benefit from accepting help with household chores or seek the help of a professional house cleaning service.
- **Laundry:** Try doing laundry one small load at a time throughout the week. This may help prevent doing multiple loads in one day, which can be exhausting.

- **Meal Preparation:** A well-balanced meal is a source of energy and health. Menu planning saves time, simplifies life, and makes meal time more enjoyable.

Plan ahead: Planning your daily, weekly, or even monthly routine can help you prioritize your goals and prevent all the “little things” from piling up. For example, a weekly meal plan can help to feel more organized and in control. Select easy recipes that don’t require a lot of prep work. Make weekly grocery lists from the meal plan to avoid multiple trips to the grocery store. Accept help from family or neighbors. A well-written grocery list can be easily followed by a caregiver.



Shopping: Consider shopping for food online and/or using home delivery services. Purchasing and storing pre-cut, washed vegetables, fruits, and frozen or canned foods may cost more but save steps in the end. Also, keep a good stock of “basics” which can be prepared as simple, nutritious meals.

Cooking: Pre-measure ingredients and arrange in the order they will be used to allow for interruptions. Use timers and reminder notes as needed. If practical, make more food than you need and save the extra for days when you don’t have the energy or interest to cook. When boiling vegetables or other foods, consider placing wire mesh baskets in your cooking pans. They can be easily lifted out for serving, removing the immediate need for heavy draining of pans full of hot liquid. Consider using a slow cooker to enable having hot meals ready at the end of the day when you are feeling most tired. Remember to pace yourself: divide food preparation throughout the day and/or week. Soak dishes and pans in the sink if possible to make cleanup easier when you have more energy.

- **Work:** In your workday, carefully consider your roles, responsibilities, and activities. Frequent breaks may prove helpful in your work schedule and aid in managing your energy reserves. Take into account the effect of your travel time to and from work. **You may want to share this NMO guide to help your employer and colleagues better understand the effects of NMO.**



- **Electric appliances:** Small, simple kitchen appliances can save time and energy. It may be best to choose appliances that are simple to dismantle and clean.
- **Mobility:** Each person's ability to walk and move around can vary. Some NMO patients will have little-to-no restrictions, while others will use walking aids or a wheelchair. It is important to remain as active and mobile as is healthful, and remember that mobility can change at different times during the course of NMO. Combining different forms of transportation, walking, and using a wheelchair can help to reserve energy.



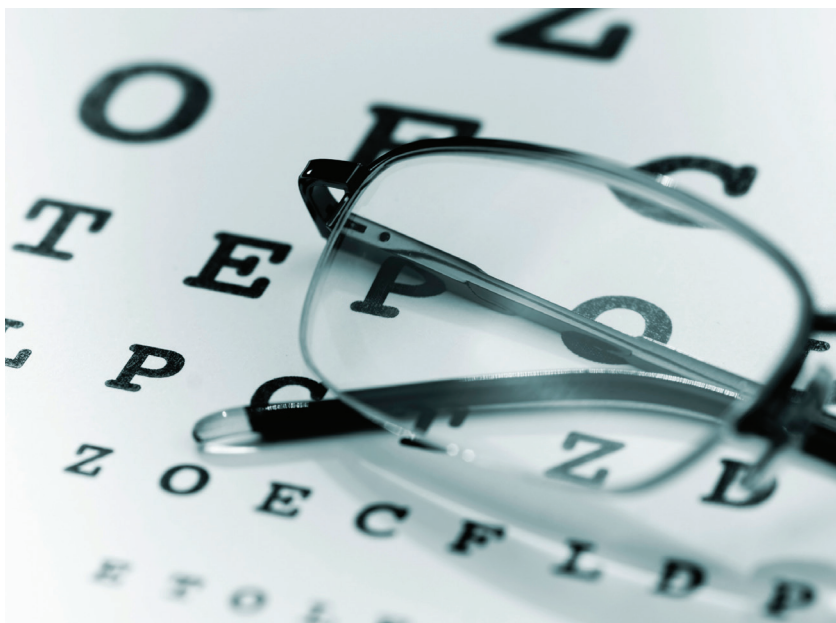
- **Leisure Activities:** It is widely recognized that a person's interests, hobbies, and leisure pursuits contribute to meaning, balance, and purpose in life. At the end of the day, you may find there is not enough energy left to try new activities or enjoy beloved pastimes. As stated above, prioritizing your interests, planning ahead, and managing energy may help you regain the ability to do the things you want to do.

Further sources of information on fatigue

The National Multiple Sclerosis Society (NMSS) website features comments and thoughts from people living with fatigue, anecdotes, and advice.

www.nationalmssociety.org

4.3 Coping with Loss of Vision



QUICK READ

The use of visual enhancements and technology can help NMO patients maintain more independence.

Vision problems can be common in NMO patients who have experienced inflammation of the optic nerve. The optic nerve transmits signals from the light-sensitive, inner layer at the back of the eye (called the **retina**) to the vision area of the brain.

Sight loss takes many forms. Visual impairment is a deeply personal experience and no two cases are exactly the same. Some patients can't see well in the

dark; others are affected by bright sunlight. Some have a restricted field of vision (**peripheral vision**) and others experience a loss of contrast or color. Everyone experiences some days where we may see better than other days.

How is visual impairment measured?

Partial sight can be hard to judge. If you cannot read normal newsprint while wearing glasses or contact lenses, then you could be considered partially sighted. Blindness and partial sight are formally defined terms which relate to the quality of vision, but **blindness does not necessarily mean the absence of light.**

Sources of support and services

Dealing with the emotional and practical impact of changes to your sight can be overwhelming, especially if there has been a sudden and unexpected deterioration as can be the case in NMO.

It is important to remember that you are not alone and that information, support and services are available to help you live your life as independently as possible.

Everyday equipment exists to make life easier.

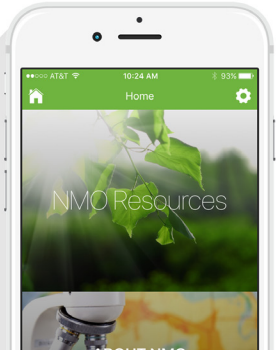
A wide range of tools and gadgets are available to help daily activities. A few examples include:

- Devices that alert you when a pot of liquid begins to boil.

- Tools that make a sound when a cup you are pouring water into is nearly full.
- Knives with an adjustable guide to help you cut even slices.
- Tactile watches and alarm clocks.

Accessible technology and telephones can aid communication. Computer products and telephone systems that can be useful include:

- Mobile phones with tactile, well-spaced buttons and the ability to read text messages aloud.
- Telephones with large, color-contrasting keypads.
- Computer screen readers.
- Magnification software.
- Voice-activated software and writing programs.



Learn More On NMO Resources.

*Download the app for free on
your Android or iOS device today!*




4.4 Managing Bowel and Bladder Problems



QUICK READ

Bowel issues are not uncommon. Evaluate your diet, research a bowel plan with your clinician, look into bowel-specific products, and carry back-up supplies when you travel.

In some patients, NMO can cause spinal cord lesions (known as **transverse myelitis**), which can cause disruption of bowel and bladder functions. This is termed **neurogenic bladder** or **neurogenic bowel**. If you experience neurogenic bladder or bowel issues that lead to loss of bladder and/or bowel control, **there are two important things to know:**

- **You are not alone.**
- **You have options.**

You Are Not Alone

According to the International Foundation for Functional Gastrointestinal Disorders, “bowel incontinence is very common. It occurs in **6 percent of women** younger than 40 and increases to **15 percent** of women aged 40 and older. **Between 6 percent and 10 percent of men** experience fecal incontinence, with a slight increase with age. Individuals with incontinence are often reluctant to report their symptoms; therefore, **the condition is believed to be widely under-diagnosed and hidden in our society.**”

Bowel and bladder accidents can happen, and it is not your fault.

The Urology Care Foundation states, “A quarter to a third of men and women in the U.S. suffer from urinary incontinence. **That means millions of Americans.**”

Incontinence can have a significant emotional and psychological impact on those who suffer from the symptoms. It can be embarrassing and distressing, and can have a negative impact on social and work situations, sexual intimacy, and relationships.

It is not unusual for NMO patients to have bowel or bladder issues. Sometimes the bowel or bladder is overactive, and some patients may have

issues with constipation or urine retention. **Bowel and bladder accidents can happen, and it is not your fault.** If you are having bladder issues, your physician might request a urodynamics study. There are also self-help measures that can be useful to some patients. It is important to maintain an honest dialogue with your doctor and caregivers.

You Have Options

Help is available to begin to regain control of your bladder and bowel. The first steps are to:

- Understand the functions of the bowel and bladder.
- Understand how NMO can disrupt bowel and bladder functions.
- Work with healthcare professionals to identify the types of challenges that are presented and explore possible rehabilitation and/or management options.



Avoiding caffeine and acidic foods can aid bladder control.

Sometimes diet can exacerbate bladder or bowel symptoms. Avoiding caffeine and acidic foods can aid bladder control. **Many patients keep a daily diary of fluid intake and output to accurately monitor their bladder habits.** Likewise, dietary fiber can stabilize bowel function, and keeping track of frequency of bowel movements can help plan activities best for time intervals of bowel or bladder functions.

Function of the Bladder and Bowel

The functions of the bowel and bladder are **to store waste and release it at appropriate times with intentional control.** Each has a muscular storage area: the bladder or the rectum. Each has an outlet, or a valve (called a sphincter) that operates under both voluntary and involuntary control. NMO may change the ability to control one or both sphincters.

How NMO can Disrupt Bowel and Bladder Functions

Spinal cord lesions that result from NMO can interrupt communication between the nerves in the spinal cord that regulate bladder and bowel functionality and

the brain. In this way, NMO can lead to incontinence, or the inability to control urine or stool expulsion.

Incontinence can occur in two ways:

- Involuntary release of urine or stool.
- Involuntary retention of urine or stool.

In addition, NMO lesions in the CNS can disrupt the sensation of having to urinate or have a bowel movement.

There are **two different types of incontinence mechanisms** that result from CNS lesions caused by NMO:

- **“Spastic” bladder or bowel** in which the sphincters or muscles of these organs that control release of urine or stool do not open normally, resulting in retention or constipation.
- **“Flaccid” bladder or bowel** in which the sphincters or muscles that control retention of urine or stool do not close normally, resulting in unexpected accidents.

**You can learn more about
NMO clinical trials on
our website at:**

guthyjacksonfoundation.org/clinical-trials

www.guthyjacksonfoundation.org

Cases in which bladder or bowel dysfunction are caused by neurologic issues are called **neurogenic bladder** or **neurogenic bowel**.

Communicating with your healthcare team about bladder or bowel dysfunction is the best way to regain control and confidence. Even if it may feel embarrassing at first, clearly and honestly expressing your experiences and concerns is the best way to find solutions.



Working with Healthcare Professionals

A **bladder and bowel plan** is a specific schedule, diet, exercise and in some cases, medical routine to best manage bladder and bowel dysfunction. These plans are customized by each person based on many factors, respecting daily activity and personal preference. Typically, bladder and bowel plans are developed under the guidance of a healthcare specialist.

One method for effective communication with your healthcare specialist is to first state your bladder or bowel concern, then introduce NMO as a potential cause. This approach allows healthcare professional the best chance of assessing all potential causes of the condition in your case. In turn, understanding the specific causes yields the best specific management plan or treatment. Healthcare providers with expertise in caring for patients with neurogenic bladder or bowel issues are knowledgeable and experienced in helping patients with these conditions.

Overview of Bladder and Bowel Management

Healthcare professionals target **three overall goals** to help patients manage their bladder and bowel:

- Prevention of incontinence and accidents
- Achieve consistent and predictable release periods
- Maintain general health and prevent complications such as impaction or constipation.

These goals can also help prevent:

- Developing a thick, inelastic spastic bladder.
- Frequent urinary tract infections.
- Kidney damage, which can result if the bladder is not well managed.

To help manage your bladder and bowel dysfunction, healthcare professionals encourage healthy lifestyle habits, such as being as active as possible, eating a well-balanced diet (refer to section 3.6), and drinking an appropriate amount of fluids. **Healthcare professionals offer these general guidelines to help optimize your bladder and bowel management:**

- Fluid intake should be spread out throughout an entire day, rather than consuming large amounts of fluid at one time.
- Fiber or a fiber supplement can be a good source to help achieve proper stool consistency.
- Exercise and/or an active lifestyle can help with **gastrointestinal (GI) motility.**
- Proper hygiene can help reduce the risk of infection.
- Establishing and following your bladder and bowel program.

The goal is to achieve independence, only relying on assistance when necessary. Being able to execute your own bladder and bowel routine without assistance helps you to regain confidence and helps to support your hygiene as well as the hygiene of your caregivers.

To help manage your bladder and bowel dysfunction, healthcare professionals encourage healthy lifestyle habits.

Bladder Management

People who suffer from **neurogenic bladder** might experience frequent and urgent urination or the inability to control urine retention. Options for management include:

■ Medications to relax the bladder

Many types of medications exist that might help an overactive bladder hold more urine. Consult your healthcare professional to determine which type of medication might be best for you.

■ Intermittent catheterization

A catheter is inserted into the bladder to empty urine and is removed when finished. Occurrence is approximately every 4 hours, generally 5 times per day.

People who have a **flaccid bladder** might experience constant leakage, or leakage during coughing, sneezing, or other activities. Medications have not been proven to be effective for flaccidity. However, options for effective management include:

■ Establishing and following a good periodization routine

Train the body to empty the bladder every 2 – 3 hours.

Attempt to use abdominal muscles to help empty the bladder.



■ Intermittent catheterization

If frequent urinary tract infections exist, intermittent catheterization might help continence maintenance.

QUICK READ

Tip: Drinking cranberry juice is believed to help prevent and/or treat urinary tract infections. If consuming large amounts of cranberry juice is not feasible, supplements in the form of cranberry powder or tablets may be helpful alternatives.

Want to know more about these options? Access the bowel and bladder videos on NMO TV, on our website at: **guthyjacksonfoundation.org/nmotv**

Maintaining Confidence and Independence

There are many products available that are used to avoid embarrassing bladder or bowel accidents. There are absorbent pads and adult pull-ups that cannot be seen under clothing. Many patients carry emergency supplies with them that include disposable moisturized wipes, spare undergarments, antibacterial soft soaps, and zip lock bags.

NMO patients are strongly encouraged to discuss incontinence with their doctors who can provide a viable program for better management and referral advice as needed. **With advice from physicians and diligent attention to bladder and bowel habits, most patients are able to carry out everyday routines without incontinence issues negatively impacting their lives.**

QUICK READ

Tip: There are many ways to get more **fiber** into your diet. Things like **chia** or **flax seeds** or **pharmaceutical products** are available. Consult your healthcare professional to discuss your options.

Want to know more about bladder and bowel management? Access more videos on NMO TV, on our website at:

guthyjacksonfoundation.org/nmotv

www.guthyjacksonfoundation.org



4.5 Occupational & Physical Therapy

Occupational and physical therapy are important options to help address physical effects of NMO. These approaches include **specific exercise programs, activities to enhance mobility, dexterity and balance, and maintaining physical fitness.** Together these programs often **greatly benefit NMO patients** in maintaining daily independence and capabilities, and **may aid in recovery from acute NMO episodes** (first attacks and/or relapses). Occupational and physical therapy are typically provided in specialized centers with specific expertise in these treatment strategies. **Your neurologist can help you find a center with the staff equipped to best address your specific therapeutic plan.**

Occupational and physical therapists are healthcare professionals who work with people who have temporary or long-term physical disabilities caused

by diseases such as NMO, or other medical conditions. These experts also help people who have communication or learning challenges. They help people who have difficulties with everyday tasks such as preparing a meal, taking a bath, lifting their legs into bed or using a computer keyboard. **The aim of occupational and physical therapy is to enable you to live as independently as possible at home, work, school and during leisure time.** These specialists can help you adapt to changes in your life and overcome practical problems by:

- Looking at ways an everyday task can be done differently to maintain your **independence** or **reduce** the effects of **pain** and **fatigue**
- **Offering advice on daily living equipment** that may help you to maintain your independence with a specific task or activity
- Recommending alterations or **changes to your home** to make it more accessible or safer for you
- Helping to address **education or work issues**



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Physical and occupational therapy often includes developing a maintenance routine consisting of **stretching, conditioning, and/or using adaptive equipment**. Centers will instruct patients on frequency and proper form in these activities over the course of a series of appointments. Once a patient achieves maximum benefit at the center, they **continue recommended activities on their own, in their own home or exercise venue**. Periodic reassessments might be scheduled if necessary.

4.6 Support with Daily Life

QUICK READ

Balancing the many roles each of us play in our lives and the lives of others can be complicated. NMO can make these roles more challenging. Identifying essential needs can help NMO patients determine what they can accomplish independently and when they may need help.

Coping with difficulty in carrying out your daily activities may present unique challenges. These difficulties can be experienced for a variety of reasons including fatigue, pain, and weakness due to the NMO itself, and/or the psychological impact it can produce.

Sometimes solutions to challenging tasks can have simple solutions by asking yourself, “Is there a way of doing this differently or more efficiently?”



Identify your most important roles and activities

It may be helpful for you to make a list of your activities in a 24-hour period. Begin with the moment you wake up in the morning until you go to sleep at night. Include any activities during the night if you awaken. Next to each activity record if you need help or note an “OK” if you can do it on your own.

It may be surprising just how complex our daily lives are in meeting basic needs from washing and dressing to household chores, shopping, cooking, employment, leisure activities, and socializing.

Why are roles important?

Our particular roles in life make us who we are; they contribute to our identity. These roles are many and varied including parent, child, caregiver, lover, friend,

homemaker, cook, shopper, cleaner, volunteer, employee, student, DIY expert or animal caretaker, among others. It is natural for NMO to impair performing one or more of these roles. **Remember, NMO is not your fault.** With the many recent advances in NMO medical care, in the majority of cases these **setbacks are temporary.** Is important to try to resume those things that have meaning in your life. Where possible, find ways around the difficulties so you can continue to play an important part in the role. Having family, friends, and caregivers participate in creative solutions can also promote positive experiences and **strong bonds that endure difficult times.**



Adapting to Change

Whether caused by NMO or not, everyone is affected by change. One key to making the most of change is to adapt to it as best you can. **Accentuate the positive.** From the list of daily activities recorded in the previous

section, you could prioritize those that are essential, most useful or desirable, and those that are not essential or have the least benefit or enjoyment in your daily routine.

This exercise can help to focus energies on what is most important.

Our daily schedules, roles and routines are very different. Some may live alone, while others live with and/or care for others. Our situations are unique and bring with them their own challenges and solutions. **Your list can help provide you with a clear picture of those roles and activities that are essential and desirable in your life.** It may also help to find ways to best fulfill these roles and goals in the most meaningful ways possible.

Finding New Solutions

Overcoming challenges and achieving goals may be found through many different approaches. For some, adapting to change may come in the form of changing the timing of an activity, or receiving support from a family member, friend, colleague, or caregiver. For example, a solution may require you to use your left hand for activities rather than your preferred right hand. For others, special equipment or routines may offer new ways to perform daily tasks. **Trial and error can be a valuable tool in finding solutions.** A wide range of products designed for people affected by neuromuscular illnesses are available as possible aids. Questions regarding performance of particular activities should be discussed with your doctor.



NMO Support Groups

More and more NMO support groups are being created to offer support for those affected by NMO. These groups are often led by NMO Advocate volunteers who may themselves be facing the challenges of NMO, and know what it can feel like. Other groups may be facilitated by relatives or caregivers of NMO patients who want to help the broader NMO community. Support groups exist in the forms of in-person groups, telephone conferences, and online groups. Types of support groups that have been created are:

- NMO Caregivers
- Pregnancy
- NMO Parents for pediatric cases
- Facebook groups (both private and public)
- Mens Group

- Local support groups
- more!

Join one of the many NMO support groups or create your own. Get NMOtion for NMO and visit our website at:

guthyjacksonfoundation.org/support-groups

Living with an “Invisible” Disability

In many cases of NMO, symptoms may not be visible to others. At times, NMO might not appear to affect an NMO patient physically, and therefore a patient might not appear to be disabled, or display signs of illness. In addition to NMO, many other types of medical conditions fall into this category. These conditions are sometimes referred to as **“invisible disabilities”** or **“invisible illnesses.”** Generally, people consider only those with outward signs of medical disabilities to “qualify” as being ill or impaired, and who need disability care and access. However, **awareness of invisible illnesses and disabilities is growing.** There are many online resources dedicated to these challenges, including “Invisible Illness Awareness Week.” Learn more online.

4.7 Daily Living Equipment

QUICK READ

Daily living equipment and technology can help NMO patients regain independence.



The effects of NMO can sometimes make previously simple, everyday tasks more difficult. **Equipment is available that can help to lessen these effects and regain greater independence.** This equipment is called **Daily Living Equipment**. Examples may include small gadgets such as electric can openers or self-leveling spoons to help at meal time. Likewise, voice-activated or virtual assistants can make computer use or internet access simpler. A stairlift is an example of a larger device that can help overcome difficulties in climbing stairs due to weakness or pain.

Daily living equipment and technologies such as these can also help with routine activities including bathing, dressing, doing laundry, cooking, getting out of bed, traveling, exercising and more. These activities all help patients to preserve or regain independence at home, work, and during leisure time.



Wheelchairs and Scooters

NMO patients can experience a decrease in mobility due to vision impairment, weakness, imbalance, or other reasons. Many people experience a reduction in their strength that may necessitate the use of a walking aid such as a cane or crutches. Others may experience a more extensive reduction in activity that results in inability or difficulty standing and walking.

In these cases, modern wheelchairs and personal scooters can be highly useful means for patients to remain mobile.

These can be light in weight, agile and portable, enabling mobility in the home and while traveling. For many, the use of a wheelchair can greatly aid in living life as normally as possible.

Many NMO patients improve over time with treatment and rehabilitation to such a degree that use of a these devices is no longer needed.

Types of Wheelchairs and Scooters

There are hundreds of styles of modern wheelchairs and personal scooters for differing needs and abilities. They fall into three main categories:

- **Self-Propelled:** these devices are propelled by the patient themselves.
- **Attendant-Propelled:** these devices are operated by someone who assists on behalf of a patient.
- **Electrical-Powered:** these devices run on batteries and enable the user to move easily and quickly with little or no physical effort. Batteries are re-charged overnight or when not in use.

Wheelchairs and scooters may be used in conjunction with an appropriate pressure cushion for greater comfort and support, and to avoid pressure points that can otherwise irritate skin and produce pressure sores.



Many home healthcare stores carry a variety of wheelchair and scooter styles, which are available in many different sizes and dimensions to provide best comfort and support. Some tilt to create different seating angles, and others can be raised or lowered in height to aid a user to reach something high up or communicate with others more easily at eye level. In many cases, modern wheelchairs and scooters are prescribed by a physician and **may be covered by medical insurance.**

Other Assistive Devices

Many types of devices are available that can assist individuals to regain independence for everyday living. Other examples of tools and devices that are available include:

- Assistive grip jar openers.
- Electric and/or V-shaped can openers.
- Easy-to-grip utensils.
- Automatic soap dispensers.

Do You Know...

You can learn more about NMO clinical trials on our website at:

guthyjacksonfoundation.org/clinical-trials

- Buttonhooks to help fasten clothes.
- Clothes with elastic waistbands or magnetic clasps.
- Velcro bras.
- Electric toothbrushes with wide handles for easier grip.
- Fanny pack to help carry supplies.
- Self-leveling spoons.
- Telephone headsets or headphones.

These are just a few examples of the many options that can help you keep or regain your independence.

4.8 Modifying Your Home

QUICK READ

Grab rails, shower chairs, and banisters installed in a residence can be relatively simple ways to help NMO patients have mobile independence.

Some of the effects of NMO such as reduced mobility, pain, or vision loss can result in difficulty getting around your home. The layout of your home may provide you with full independence and ease of access. Yet some newly-diagnosed NMO patients find that movement and access in their home are limited, especially in areas containing stairs or outdoor areas.



Solutions vary. They may come in the forms of a simple grab rail secured to the wall in your shower to help with stability, a second banister on the stairs to hold for balance, carefully positioned lighting to enhance vision, or additions such as a stairlift or permanent ramp to your front door. **A well-designed and accessible home can make a world of difference to your independence and ease of living.** There are hundreds of ideas and solutions available. It is most important to find solutions that are best suited for your specific needs.

Each person's home may have different options that allow for changes in lifestyle. If a home cannot accommodate the necessary changes, moving to a more suitable home may help some gain greater independence. **However, time is often needed to come to terms with such changes if they are needed.**

A well-designed and accessible home can make a world of difference to your independence and ease of living.

4.9 Driving and Transportation



QUICK READ

A careful assessment by an NMO patient and their healthcare team is key to determine the level of driving capability. Skills to assess include:

- Vision
- Physical ability
- Fatigue
- Cognitive changes

Along with the skills and capabilities of a patient, it is important to consider other factors that may affect driving safety. These include climate and road conditions, as well as vehicle maintenance.

Without question, driving is one of the most important means of independence for many people. It is a primary activity that enables connections to work and socializing outside of the home. Driving is often a necessity and a convenience, and represents personal freedom. In contrast, the prospect of losing one's ability to drive may trigger fears of becoming isolated, lonely, and dependent. When NMO affects driving skills, discussing the ability to drive can make a patient feel defensive and protective.

A careful assessment by each patient's healthcare team should be made to determine the level of ability to operate a moving vehicle. **Many NMO patients may continue driving as advised by their doctor.**

However, the demands of driving on the human body cannot be underestimated, and certain medications can impair decision making, energy, and stamina needed for safe driving. For these and related reasons, special care must be taken to ensure safety for those patients who continue to drive, and that of other drivers.

Vision: Unimpaired vision and peripheral vision are crucial to safe driving. Assessing **visual acuity** (clearness of vision) is important to determine any necessary adaptations such as vision correction that may be needed to fulfill driving regulations.

Physical/motor changes: For people with physical impairments, driving assessments include evaluation of motor involvement (muscle weakness), range-of-motion limitations, coordination, and sensory deficits in arms

and legs. Limitations in these areas can restrict the ability to operate a vehicle. **A wide range of adaptive controls may be considered for driving.** These controls generally require skilled professionals to assess, inform, and install.

Fatigue: Planning ahead is key to preventing fatigue from impacting driving. Knowing and anticipating signs of fatigue and scheduling outings accordingly can go a long way toward preventing or minimizing the effects of fatigue on driving.



Heat and Cold: Temperature extremes **may cause symptoms to worsen**, so plan ahead by scheduling outings during the part of the day that offers the most comfortable conditions. Park in areas that are protective from sun or wind if possible. Also, consider remote car ignitions to enable starting a car without getting inside. Heating or cooling a vehicle prior to driving can help reduce temperature-induced discomfort.

Cognitive Changes: Taking inventory of NMO symptoms as they relate to the ability to absorb, process, and apply important information to make quick decisions is crucial to safe driving.

Regular checkups with your doctor will help to diagnose any cognitive effects that may jeopardize driving safety. Together you can determine your ability to operate a motorized vehicle safely in the best interests of all concerned.

Public Transportation Services: Many cities have vehicles that have special equipment such as ramps, lifts, and designated seating that is specifically intended to assist persons with special needs. These services vary from city to city, but are often posted on community service websites and available from the city services department. It is important to become familiar with the public transportation services of your specific location to better plan your activities as needed.





4.10 Social Security Disability Benefits in the United States

NMO and its relapses can complicate day-to-day schedules and necessitate frequent medical visits. For these reasons, NMO can create challenges to routine employment and career choices. As a result, NMO patients may choose to seek financial assistance through government programs. For example, in certain cases, the **United States Social Security Disability (SSD)** program may offer benefits to help alleviate the financial costs of NMO by offering a monthly payment for medical care. **Understanding the Social Security Disability application process** is the first step toward determining if financial aid may be appropriate in your case.

The **Social Security Administration (SSA)** operates two disability programs including **Social Security Disability Insurance (SSDI)** and **Supplemental Security Income (SSI)**. To qualify for either program

Understanding the Social Security Disability application process is the first step toward determining if receiving the financial aid may be appropriate in your case.

you must meet the specific medical criteria, and the financial qualifications of the respective program to which you are applying.

Generally, to **qualify for SSDI benefits** you must have **earned enough work credits through previous employment**. The amount of earnings needed for credits may change slightly from year to year as average earnings levels change. The credits you earn remain on your Social Security record even if you change jobs or have no earnings for a period of time.

Unlike the SSDI program, the **SSI** program is not based on prior work activity. Instead, the SSI program is a **needs-based program**, where income and assets largely determine eligibility.



Considering the SSA Medical Criteria

When you apply for Social Security Disability benefits the SSA compares your condition to a listing of conditions in a reference known as the “Blue Book.” This publication contains all of the conditions that could potentially qualify an individual for SSDI or SSI benefits, along with the criteria that must be met for assistance in each condition. **While NMO is not included in the SSA Blue Book, you may still be approved for Social Security Disability benefits through a vocational medical allowance.** To achieve this specific aid, a patient must be able to prove to the SSA that their condition prevents them from working.

Preparing for the Social Security

While NMO is not included in the SSA “Blue Book,” you may still be approved for Social Security Disability.

Disability Application Process

As **NMO is not included in the SSA Blue Book**, patients may find that careful preparation for the application process offers the best chance for positive outcomes. **Key in this regard is documenting that your disability prevents you from performing work.** Obtaining documentation of the following information may be invaluable in this respect:

- Clinical histories
- Hospital records
- Lab results
- Treatment histories
- Written statements from treating physicians

By providing as much evidence as possible with your application, it will be easier for the SSA to understand how your condition qualifies you for benefits.

Applying for Social Security Disability Benefits

When you apply for disability benefits you will be asked to fill out a number of forms. Be sure to **fill out each form in its entirety and provide as much detail as possible in your answers.** Some individuals may choose to engage legal advocates to assist in form completion and submission. You will receive a decision regarding your claim approximately **two to four months** from the date



of your application. If you are awarded benefits, you will be notified as to what benefits you will receive, how much you will be receiving each month and when benefits will begin.

Appealing a Denial of Benefits

If you are denied benefits, you have **60 days** from the date of the notice to appeal the SSA decision. If you choose to appeal a denial of benefits, you may want to consider retaining the services of legal counsel. These professionals can help you determine why your initial claim was denied and assist you in gathering the evidence needed to strengthen and support your claim. A disability attorney can also represent you before the administrative law judge at your disability hearing.

Sources of Information

The United States Social Security Administration:

www.ssa.gov

Social Security Disability Help:

www.disability-benefits-help.org

4.11 Support for Caregivers



QUICK READ

Caregivers also need support to maintain healthy and balanced lives.

Caring for a relative, loved one or child with NMO can be a rewarding and fulfilling experience.

Caregivers include anyone who cares for an NMO patient on a day-to-day basis. Oftentimes, caregivers include parents, children, other relatives, or friends. It is important to remember the needs of caregivers. Many people who act as caregivers for NMO patients find it to be a rewarding and fulfilling experience. However, without the right support it may also be difficult at times. Some caregivers live with the person they are supporting, while others do not. Caregivers are people of all ages, even children who provide care for a parent. **Caregivers often have a need for information, financial and other support, and time away to connect with people who have similar needs.** It is perfectly normal to have complex feelings in a role as a caregiver. It may be challenging to cope with the life



Join or create an NMO Support Group.
Refer to section 6.5 for more.

changes that occur when the role is assumed, and a loved one is suffering from a chronic illness. **Support comes in many forms and may provide a tremendous help to a caregiver.**

Regular breaks from daily responsibilities, eating well and exercising regularly, and sufficient amounts of sleep are necessary to maintain good emotional and physical health.

It may be a good idea to accept help from a trusted friend or family member to allow time for a primary caregiver to run errands or visit friends.

A caring role is not a conventional job. There is no need for a caregiver to feel guilty about wanting a break or needing time off. In the long term, personal time can help avoid feeling isolated and depressed, and may improve coping with the demands of being a caregiver.



NMO Support Group Telecon

If you are an NMO caregiver, you are invited to join the NMO Support Group telecon. This group meets monthly by participants dialing a conference call line. If you would like to learn more or join this telephone support group, please visit our website for details: **guthyjacksonfoundation.org/support-groups**



Become an NMO Advocate

Anyone can be an NMO Advocate,
and signing up is easy! See Section 6.2
to find out how.

Hope for the Future



**ANSWERS
AHEAD**

Hope for the Future

- 5.1 NMO Clinical Trials – Get Informed
- 5.2 CIRCLES Biorepository for NMO Research
- 5.3 How can I become a CIRCLES participant?
- 5.4 What exciting discoveries have come from NMO research?
- 5.5 NMO International Clinical Consortium (ICC)
- 5.6 International Panel for NMO Diagnosis (IPND)

5.1 NMO Clinical Trials – Get Informed

QUICK READ

There is no regulatory-approved therapy for NMO. Clinical trials are designed to determine which medicines or procedures best benefit patients, and which may not. The **first-ever** NMO clinical trials in are in process, which offer hope for the future.

What is clinical research?

Clinical research is research that involves **patients**. Patients and other individuals can **volunteer** to participate in clinical research, carefully designed and conducted to **better understand disease**, and

find ways to prevent, diagnose, treat, and eventually cure it. These advances come with improved understanding of the causes and effects of the disease. **Clinical research** includes two basic types of investigation:

- 1. Clinical studies** typically aim to understand disease, its epidemiology or risk factors, and assess proof-of-concept of new ways to prevent or treat it.
- 2. Clinical trials** aim to test the safety and effectiveness of therapies to treat a disease with the goal of improving patient health and wellness.

All clinical research is required to adhere to careful protection of subjects and their information, and clinical trials in particular are regulated and monitored by the **U.S. Food and Drug Administration (FDA)** and the **National Institutes of Health (NIH)**.

For more information, please refer to the National Institutes of Health website:
www.nih.gov

Why do we need clinical trials?

Clinical trials are designed to determine which medicines or procedures **best benefit patients**, and which may not. These studies often involve expert teams from **academic, governmental, and pharmaceutical** sectors. In some cases, clinical trials seek to test the **efficacy of a new drug** for a disease which has no

Clinical trials are designed to determine which medicines or procedures best benefit patients, and which may not.

proven effective therapy. In other trials, one treatment is compared with another to examine which may be best in patients of differing disease stage or condition. Clinical trials are usually divided into different **phases**, each of which is designed to address a slightly different question:

- **Phase I:** usually designed to test the **safety** and to learn the best dosing regimen of a new drug to minimize side effects. Subjects are usually healthy volunteers, and the study is often **relatively short** in duration. **Subjects do not usually benefit from a Phase I study.**
- **Phase II:** usually designed to study the drug based on **results from Phase I**. Here, the drug, device, or procedure is evaluated in volunteer subjects who have the disease of interest. Phase II trials further refine safety, minimize adverse events, and begin to **explore** if and how the test agent may benefit the subject. **Some volunteer subjects may benefit from a Phase II study.**

- **Phase III:** usually **compares** the test candidate (drug, device, or procedure) to a commonly-used agent that has been proven to be at least somewhat effective in treating a condition, if one exists. This phase is designed to understand if the test agent is better than existing approaches, and where the agent might best fit in managing a particular disease.

For more information, please refer to the National Institutes of Health website: **www.nih.gov**



Why do people participate in clinical trials?

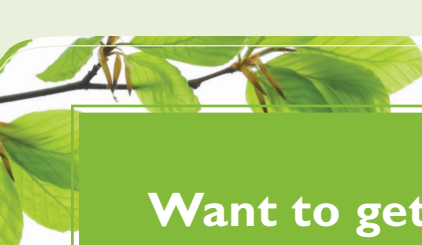
People participate in clinical trials for **many reasons**. Healthy individuals often say they participate to **help others** and to contribute to new or better ways to prevent or treat disease. **Volunteers who have**

a disease also participate to help others, but **may also receive new or improved experimental treatments**. In addition, subjects who are involved in clinical trials receive **additional care** and attention from the clinical trial staff. Sometimes, blood relatives of the patients with diseases participate in certain trials which evaluate the genetic components that may pose potential disease risks. *Information courtesy of nih.gov*

Who participates in clinical trials?

People from all walks of life participate in clinical trials. Some are healthy, while others may have illnesses. Sometimes, blood or genetic relatives of a person suffering from an illness can participate together in a clinical trial. Usually, each clinical trial or study specifies which subjects may participate. Factors that allow someone to participate in a clinical trial are **inclusion criteria**. Those that exclude or not allow participation are **exclusion criteria**. These criteria are based on factors such as age, gender, the type and stage of a disease, previous treatment history, and other medical

Subjects who are involved in clinical trials receive additional care and attention from the clinical trial staff.



Want to get **updates** about **NMO Clinical Trials?**

Get **NMOtion** by visiting our website at:
guthyjacksonfoundation.org/clinical-trials

conditions. Before joining a clinical trial, a participant must qualify for the study. Some research studies seek participants with illnesses or conditions to be studied in the clinical trial, others may need healthy volunteers, whereas some others require both. *Information courtesy of nih.gov*

The Guthy-Jackson Charitable Foundation Clinical Trial Position Statement

The Guthy-Jackson Charitable Foundation (GJCF) supports efforts directed at the prevention, diagnosis, treatment and cure of neuromyelitis optica (NMO) and NMO spectrum disorder (NMOSD). It facilitates scientific and clinical advances directed toward these goals.

The GJCF endorses clinical trials aimed at improving the health of NMO patients. **It neither sponsors nor conducts clinical trials, nor does it advocate for**

any specific therapeutic candidate or endorse any particular clinical trial design. The GJCF **plays no role** in the active enrollment of subjects in clinical trials, **nor does it participate** in interpreting clinical trial outcomes. The GJCF **functions neutrally** and **equitably** in all interactions with clinical trial sponsors, investigators and NMO stakeholders.

The GJCF facilitates access to educational resources in the public domain to provide individuals with the opportunity to learn about the latest scientific and clinical advances in NMO. By increasing awareness of these advances, including information about actively recruiting trials, the GJCF promotes informed decision-making by all members of the NMO community.

5.2 CIRCLES Biorepository for NMO Research

QUICK READ

Because NMO is rare, every blood sample, data point, and patient experience is an **invaluable piece** of the puzzle to solve it. Biospecimens and patient health data are precious resources that contain secrets to curing the disease. **Participating in CIRCLES is one of the most important actions you can take to be part of the cure for NMO.**

Biological samples (i.e. blood and other samples), and clinical health data from NMO patients and controls (qualified donors who do not have NMO) are vital for NMO research.

Many developments in NMO treatment come from doctors and researchers studying blood samples, other biological specimens, and clinical health data in a laboratory. Collecting biosamples and health data over years (called a **longitudinal study**) is critical to better understand NMO, including cause, epidemiology, relapse rates, best treatments, and similar factors – all key factors in finding a cure for a disease.

To advance NMO research, **GJCF built a biorepository that collects blood samples, other biospecimens and clinical health data (information)** of volunteer NMO patients and controls. The repository is called:

Collaborative
International
Research in
Clinical and
Longitudinal
Experience in NMO
Studies



What is CIRCLES?

CIRCLES is a **research study** that focuses on better understanding and enabling **cures for NMO**. It consists of two complementary programs:

- A network of academic sites and clinical laboratories with special expertise to enroll participants and collect data and biospecimens.
- Data and blood banks that ensure safe storage and ready access of clinical data and biospecimens for breakthrough research in NMO.

What is the CIRCLES Site Network?

The CIRCLES network consists of **multiple centers of excellence** with deep expertise in caring for and studying patients with NMO. CIRCLES sites are located at **leading medical centers** across North America.

The CIRCLES network features:

- CIRCLES sites in regions of the U.S. and Canada (also known as **Home Bases**) where participants can regularly contribute their clinical data and biospecimens.
- Biospecimen draw sites across the U.S. where CIRCLES participants can contribute biospecimens.
- A leading **principal investigator (PI)** in charge of each CIRCLES site.



- A clinical **research coordinator (CRC)** who explains the CIRCLES study, enrolls participants, schedules appointments, answers questions and coordinates clinical data and blood collection.

Regional CIRCLES sites include **leading universities** where neighboring NMO patients and qualified control participants can **donate blood and clinical data**. Regional sites allow participants who are unable to travel far distances to contribute to CIRCLES. These sites are considered **Home Bases** where NMO community members can participate, and join support group meetings, host events, and attend regional **NMO Patient Days**.

The CIRCLES Biorepository for NMO works in association with academic centers, reference laboratories, and commercial research organizations to **ensure best practices in data and biospecimen management**.

The **CIRCLES Biorepository** is a powerful resource to discover patterns in the course of a disease that are not obvious from any one individual.

What is the CIRCLES Biorepository?

The **CIRCLES** biorepository is a high-tech storage system for data and biospecimens collected through the **CIRCLES** network. The CIRCLES study collects data and biospecimens that need to be carefully prepared for best use in understanding and solving NMO. The CIRCLES biorepository combines a databank and bloodbank to serve this goal. Features of the CIRCLES biorepository include:

- A **centralized system** where samples and data are uniformly stored and secured to protect participant information and **biospecimen integrity**.
- The **largest collection** of clinical data and biospecimens in the world dedicated to **finding a cure for NMO**.
- An **efficient process** by which researchers can access data and biospecimens to accelerate **breakthrough advances** in NMO science and medicine.

How does the CIRCLES Biorepository help NMO research?

The CIRCLES Biorepository is a **powerful resource** that allows researchers to **discover** common features that many NMO patients share, and aspects of NMO that may be unique to each individual. Special ways in which **CIRCLES advances solutions** to NMO include:

- Enabling careful study of your NMO experience over an extended period of time.
- Understanding the epidemiology of NMO as compared to closely related diseases.
- Expanding the database of clinical features that can help speed best diagnosis and treatment.

Studying NMO in many individuals over a long period of time (called a **longitudinal study**) can reveal discoveries that are not possible otherwise.

Many developments in NMO
treatment come from doctors and
researchers studying blood samples
in the laboratory.



For example, researchers can examine factors that influence disease prognosis and quality of life, describe patient care patterns, assess effectiveness, safety, or toxicity of treatment, and study other outcomes measures. **In these ways the CIRCLES program supports quantum-leap breakthroughs and helps solve unanswered questions including:**

- What causes NMO?
- Is there a difference between AQP4 positive vs. MOG positive NMO?
- Is there a “typical” course of NMO, or does it vary in each individual?

Patients who participate in CIRCLES are critical in the effort to find a cure for NMO.

- How does geography or season relate to the disease course, if at all?
- Does a treatment lead to long-term benefits, such as fewer relapses?
- How is NMO severity or disability affected by new or existing therapies?
- What are the significant predictors of favorable vs. poor outcomes?
- How do NMO clinical practices vary, and what are best practices for managing NMO?
- Are there differences in the delivery and/or outcomes of care for NMO?

CIRCLES may also lead to assisting clinical trials to identify potential improvements in treatment.



NMO patients who participate in CIRCLES are critical in the effort to find a cure for NMO.

Biospecimens may ultimately serve to identify the best possible diagnosis and management of each NMO patient, and find new and more effective treatments.

Why is CIRCLES different from other biorepositories?

CIRCLES is the **largest biorepository in the world dedicated to solving NMO**. CIRCLES is uniquely designed to standardize how data and biospecimens are collected, archived and accessed. This allows **apple-to-apples comparison** of NMO in patients from diverse backgrounds and locations. Clinical data and samples are available to study by any qualified researcher. The foundation brings a synergistic team approach to enable this important goal. Its **Medical Advisory Board (MAB)** and **Biorepository Oversight Committee (BOC)** maintain the highest standards of NMO research. Members of the MAB and BOC are leaders in their complementary fields of study, and closely monitor the rapidly-growing medical and scientific



assets the CIRCLES program brings to NMO research. To accelerate breakthroughs that lead to tomorrow's cures, the foundation sponsors CIRCLES but allows institutions and companies to retain intellectual property. This fact incentivizes the process of turning molecules into medicines.

When you participate in CIRCLES, you are participating in the world's leading innovative research for NMO.

5.3 How Can I Become a CIRCLES Participant?

QUICK READ

CIRCLES is an interactive program where **participants help solve NMO** by providing invaluable data and biospecimens for research. In addition, CIRCLES participants are able to **meet one-on-one with leading NMO clinicians** at regular intervals. CIRCLES participants also benefit from opportunities to participate in support groups, meetings, and advocacy events, such as NMO Patient Days and other educational programs. Your regional CIRCLES site is your **Home Base** where you can **make a difference in solving NMO**.

Because NMO is a rare disease there is an urgent need for every patient to participate in the effort to solve this disease.

You Can Help Solve NMO

Thanks to dedicated patients, researchers and industry partners **there has never been a greater chance to solve NMO than there is today.** Because NMO is a rare disease every CIRCLES participant provides an invaluable piece to solving the NMO puzzle. **The more data and samples collected, the sooner answers can be found that will lead to new treatments and cures.** NMO patients and qualified controls can help meet this urgent need by participating in CIRCLES. If you or a family member have been diagnosed with NMO, please help by donating data and blood for NMO research.



NMO patients and
blood relatives can HELP!
**PARTICIPATE IN THE
CIRCLES BIOREPOSITORY**

Learn how on page 244

What does it mean to be a CIRCLES participant?

Becoming a CIRCLES participant is one of the most important actions you can take to be part of the cure to NMO. By participating, you are providing an invaluable contribution to solving NMO by:

- **Enrolling** in the CIRCLES study to establish baseline clinical data and biospecimen sets
- **Attending** regular follow-up visits at your regional CIRCLES Home Base to update your clinical data and biospecimens
- **Reporting** relapses or other clinical events to your CIRCLES site clinician principal investigator (PI) and clinical research coordinator (CRC)





How to Become a CIRCLES Participant

You can volunteer to become a CIRCLES participant by following these 4 simple steps:

1. Locate your regional CIRCLES site via:

- **GJCF website**
- **Smartphone App**
- Page 247 of this book

2. Contact the CRC at that site to schedule an appointment

3. Prepare to receive an enrollment package in the mail and complete it prior to your first visit. Your CRC can help you complete this information.

4. Schedule follow-up appointments with your CRC throughout the year; every year

Why is it important that I participate at my Regional CIRCLES site?

An important goal of the CIRCLES project is to collect data and biospecimens from participants consistently and at regular intervals. Each participant enrolls in CIRCLES through their regional CIRCLES site. **This site is your designated Home Base** for collection of clinical data and biospecimens. Collecting these materials at the same time as your clinical exam maximizes the quality of information you provide and enhances convenience for you. By actively participating in CIRCLES and related events at your regional Home Base CIRCLES site, you stay up to date in contributing to the cure through the CIRCLES program, **Regional NMO Patient Days**, and educational events.

What happens to my specimens and data?

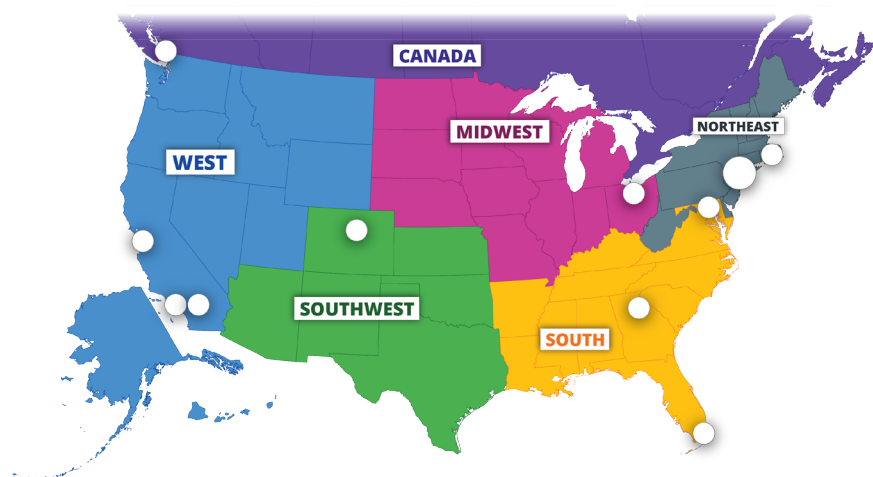
Blood samples are stored at the CIRCLES Biorepository, which is carefully controlled to ensure high-quality samples for NMO research. Qualified research staff enter data in a manner that protects participant information and coordinates data with biospecimens. Researchers

Blood samples are stored at a carefully controlled repository to ensure high sample quality.

request samples from the CIRCLES biorepository by submitting a written proposal describing their intended research. Proposals are reviewed by the BOC and GJCF to **ensure all samples distributed are used for cutting-edge research** that has the best chance for **quantum-leap advances** in understanding NMO, its causes, treatment, and cure.

Researchers who apply for and receive samples from the biorepository agree to **rapidly share results** from their research for inclusion in a database to **help other researchers make breakthroughs of their own**. This **success-drives-success model** accelerates turning discoveries in the test tube into treatments in the clinic.





Find your regional CIRCLES site home base to participate:

Western Region

Los Angeles, CA

Cedars-Sinai Medical Center

P.I. Nancy Sicotte, M.D.

University of Southern California

P.I. Lilyana Amezcua, M.D.

Stanford, CA

Stanford University

P.I. May Han, M.D.

Seattle, WA

Swedish Medical Center

P.I. Pavle Repovic, M.D.

Midwest Region

Cleveland, OH

Cleveland Clinic

P.I. Sarah Plachon Pope, Ph.D.

Northeast Region

Boston, MA

Harvard Medical School, Brigham & Women's Hospital, Partners MS Center

P.I. Tanuja Chitnis, M.D.

Massachusetts General Hospital, Multiple Sclerosis Clinic, Wang Ambulatory Care Center

P.I. Eric Klawiter, M.D.

New York, NY

Columbia University Medical Center

P.I. Claire Riley, M.D.

Judith Jaffe MS Center, Weill Cornell Medical College

P.I. Nancy Nealon, M.D.

**Research catalyzed by the foundation
has dramatically changed the landscape
of NMO science and medicine.**

Mount Sinai - Icahn School of Medicine

P.I. Ilana Katz Sand, M.D.

New York University Langone Medical Center

P.I. Ilya Kister, M.D.

Southern Region

Atlanta, GA

Shepherd Center

P.I. Ben Thrower, M.D.

Baltimore, MD

Johns Hopkins

P.I. Michael Levy, M.D., Ph.D

Miami, FL

University of Miami Miller School of Medicine

P.I. Leticia Tornes, M.D.

Canada

Vancouver, BC

University of British Columbia

P.I. Robert Carruthers, M.D.

Do You Know...

More and more CIRCLES sites are being created. Visit the foundation's website and/or smartphone app to find your regional CIRCLES site at:

guthyjacksonfoundation.org/draw-sites

5.4 What exciting discoveries have come from NMO research?

QUICK READ

The Guthy-Jackson Charitable Foundation is dedicated to advancing prevention, treatment, and an ultimate cure for NMO. Its research focus aims to better understand the causes and effects of NMO and NMOSD from the level of molecules and cells to the clinical impact of disease in patients.

Research catalyzed by the foundation has dramatically changed the landscape of NMO science and medicine. There are many ways through which these advances are evident, including:

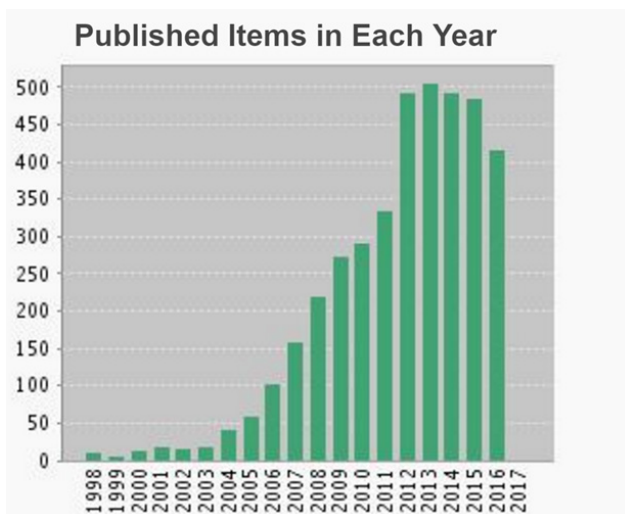
- NMO is now known to be more common than previously estimated or reported.
- Gender, race, geography and other factors are now known to contribute to NMO epidemiology.
- NMO pathogenesis involves a coordinated interaction among immune cells and molecules.
- Genes that potentially influence NMO risk have been analyzed and are being investigated.
- NMO diagnosis has been modernized for improved accuracy, specificity, and therapy.
- Biomarkers are emerging as signals of pathogenesis, relapse, and treatment effects.

The Guthy-Jackson Charitable Foundation is dedicated to advancing prevention, treatment, and an ultimate cure for NMO.

- NMO has been discovered to affect the brain and brainstem as well as the optic nerves and spinal cord.
- NMO is now clearly differentiated from MS in pathogenesis, diagnosis, and treatment.
- Existing treatments for NMO have been refined to best address each unique NMO case.
- Multiple clinical trials are now underway based on these exciting advances in NMO science.

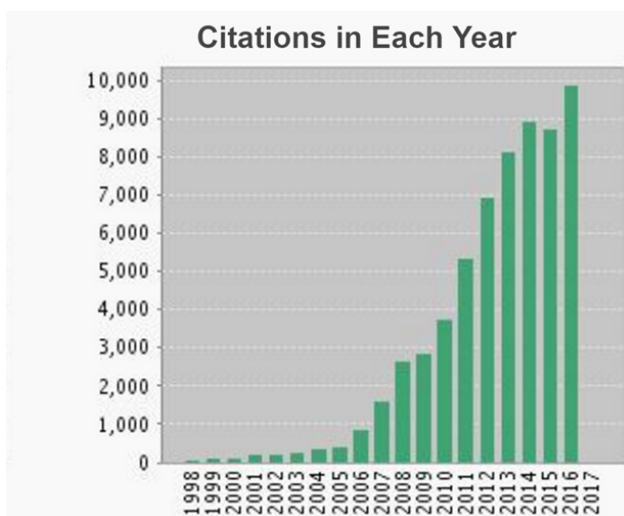
These promising advances are just the first steps on the path to solving NMO once and for all.





The Guthy-Jackson Charitable Foundation Funded Scientific and Clinical Research Sites

- Brigham and Women's Hospital, Harvard Medical School
- Charité Berlin
- Cleveland Clinic
- Duke University
- Johns Hopkins University
- Massachusetts General Hospital
- Mayo Clinic
- Mt. Sinai
- New York University
- Oxford University Medical Centre



- St. George's, University of London
- Stanford University
- The Scripps Research Institute
- The University of British Columbia
- University of California, Los Angeles
- University of California, San Francisco
- University of Colorado, Denver
- University of Texas Southwestern Medical Center
- University of Utah

For detailed descriptions of current and completed research projects, visit the GJCF website at:

guthyjacksonfoundation.org/research



Make a Financial Donation to NMO Research

You or someone you know can make an impact in the world of NMO by funding NMO science projects.

100 percent of all donations go directly to scientific research. All financial donations are directed to **The Guthy-Jackson Research Foundation, Inc.** This includes donations from public, private and government organizations, as well as donations from fundraising events, families, friends, and individuals like you.

If you or someone you know is interested in donating to NMO research, please visit:

guthyjacksonfoundation.org/donate to start the process, or contact us by phone at: 858-638-7638.

Want to learn more about donating to NMO research? Join the **NMO Advocacy Network**. Refer to chapter 6 to learn more.

5.5 NMO International Clinical Consortium (ICC)



The number of patients followed at any one site is generally too small to study all aspects of the disease. To meet this challenge, GJCf formed an **International Clinical Consortium (ICC)** comprised of clinicians and researchers from international centers. These worldwide centers work together in collaboration to apply uniform disease definitions, clinical assessment tools, and research advances. The goal of the ICC is to **create a multi-center collaboration for sharing clinical and biological data from NMO patients.** Members of the ICC have authored, co-authored and/or contributed to numerous NMO international collaborative consensus review articles. **These critical-**

path publications helped to advance NMO research and treatment. The ICC continues to be part of the cure for NMO. Visit the foundation's website for more information and access to review articles.

ICC SCIENTIFIC SNAPSHOT

NMO international collaborative consensus review articles published in collaboration with the GJCF ICC.

- **Treatment of NMO: Review and Recommendations**

Mult Scler Relat Disord.

2012 Oct;1 (4):180-187

PMID: 24555176

- **Challenges and Opportunities in Designing Clinical Trials for NMO**

Neurology.

2015 Apr 3. Epub

PMID: 25841026

- **Update on Biomarkers on NMO**

Neurol Neuroimmunol. Neuroinflamm.

2015 July 23;2(4). eCollection 2015.

PMID: 26236760

Find more ICC articles on the NMO Resources smartphone app and Spectrum, our digital NMO Library:
guthyjacksonfoundation.org/spectrum



5.6 International Panel for NMO Diagnosis (IPND)

Formed in 2011 and funded by The Guthy-Jackson Charitable Foundation, the International Panel for Neuromyelitis Optica Diagnosis (IPND) updated the 2006 diagnostic criteria for NMO. In its landmark paper published in 2015, this body of experts modernized the way NMO is diagnosed and differentiated from other diseases. This significant advancement also provided a global standard for NMOSD diagnosis. As a result, NMO patients — as well as patients who do not have NMO — receive more rapid and accurate diagnoses to speed the best therapy for their condition. The IPND 2015 criteria have already helped countless patients receive the best diagnosis and medical care.

The goal of the ICC is to create a multi-center collaboration for sharing clinical and biological data from NMO patients.

The IPND 2015 Diagnostic Criteria for NMOSD address the following key issues:

- Updated definitions and diagnostic criteria for NMO and NMOSD
- How related diseases such as MS may be differentiated from NMO
- NMO in relation to other autoimmune diseases
- Role of serological testing in diagnosis
- Role of radiology in diagnosis

Refer to section 2.5 for details about the IPND and the IPND 2015 NMO/NMOSD diagnostic criteria.



Do you know?

IT'S EASY TO FIND AN
NMO CLINICIAN ON
CONNECT THE DOCS

Visit guthyjacksonfoundation.org/doctors
to find your nearest NMO clinician.

Resources & Support



Resources & Support

- 6.1 Be Part of the NMO Movement
- 6.2 Get in **NMOtion**► for NMO
- 6.3 Join the LEAD Campaign for Cures
- 6.4 NMO Education Programs & Resources
- 6.5 Patient Stories
- 6.6 Support Groups & Advocacy Organizations
- 6.7 Suggested Reading
- 6.8 The Bookshelf
- 6.9 Spectrum: The Latest NMO Breakthroughs
- 6.10 NMO TV

6.1 Be Part of the NMO Movement

The mission to cure NMO is a living and breathing effort. Inspired by patients, it grows from family and friends to communities and countries. It is a hope and a plan to conquer NMO through dedication and determination to spread the word and find the answers. The NMO movement has many exciting parts always moving toward the goal of ending this rare disease once and for all. The following sections offer information and choices to participate as an NMO Advocate or Ambassador.

Get in motion with . . .

NMOtion

GET INVOLVED!

Visit guthyjacksonfoundation.org

6.2 Get in NMOtion► for NMO

QUICK READ

You are the cure. Everyone has a vital role to play in NMO research, education and awareness to find cures and save lives.

Every day, breakthrough advances in NMO research and medicine are being achieved. All over the world, clinicians, researchers, nurses, caregivers, families and friends are working with patients to learn more about NMO and find new answers. And, **there is much yet to be done to conquer NMO.**

Actively participating in the mission is the key to solve NMO. There are **many ways to participate** in this life-saving cause, and **everyone can do something.** Whether by joining a clinical trial or clinical research study such as the CIRCLES program (refer to Chapter 5), educating the community to raise NMO awareness or advocating on behalf of NMO patients, every hand and every voice counts.

There is a lot of work to be done. For example, **NMO can be unrecognized or initially diagnosed as MS or other disease, leading to inappropriate or delayed treatment.** Many doctors and even community neurologists have not yet heard of NMO or its new diagnostic criteria. Likewise, completing clinical trials relies on patients making informed decisions that can help themselves and other patients. All of these efforts and many others on the mission to cure NMO require education, awareness and advocacy. One of the most active programs toward these goals is **NMOtion►**.

What is “NMOtion”?

NMOtion (pronounced “in motion”) is the worldwide call to action dedicated to advancing research, education, awareness and advocacy for NMO. **NMOtion►** is a living and breathing network that brings together all



stakeholders with the same goal: **end NMO once and for all. NMOtion►** creates synergies that can help speed life-saving cures for NMO patients.

NMOtion► provides simple yet powerful options to take action in the mission for a cure. It is a gateway to clinical research, a platform for education and a podium to let your voice be heard. You can join programs to drive research, education, awareness, and advocacy and save lives, such as:

- Participate in the CIRCLES NMO Biobank
- Lead in the LEAD Campaign for Cures
- Promote the NMOpedia Education Platform
- Give voice to the NMO Ambassador Speakers' Bureau
- Become an NMO Advocate

What is the CIRCLES NMO Biobank?

Refer to Chapter 5 or visit:
guthyjacksonfoundation.org/blood-bank



6.3 Join the LEAD Campaign for Cures

LEAD Campaign for Cures

Everyone can be part of the mission to cure NMO. With so many exciting areas moving forward to cures, the foundation has created a bold new movement call the **LEAD Campaign for Cures**. **This program is about making choices and taking actions based on educating yourself of the latest NMO news.** From clinical trials seeking the first regulatory-approved treatments for NMO, to clinical studies testing new proof-of-concepts, being part of the cure is active not passive. **Each of us can decide how we can contribute to the cures through actions empowered by knowledge.**

The LEAD Campaign for Cures has **four basic steps to help**:

- **L**earn the facts about latest NMO research

NMO knowledge is growing at an incredibly fast pace based on breakthrough research and clinical trials focused on improving patient lives. Mastering the facts empowers you to take action.

- **E**ngage in the healthy NMO conversation

Being part of the mission to cure means more than just knowing about NMO. It means lending an open mind, a willing heart and a constructive voice to spread the word about NMO. From friends and families to community leaders, from physicians to philanthropists, everyone needs to know about NMO.

- **A**ssess your options to be part of the NMO cure

There are many ways you can take the next step to solving NMO. There have never been more opportunities to be part of the NMO success story. Every hand and every voice counts, and the time to act is now.

NMO patients and caregivers can best assess options regarding specific NMO treatment.

- **D**ecide how you will make an NMO difference

Turning hopes into realities takes action. Everyone can contribute to the cure in their own way. It is for each of us to decide how we can help change the world of NMO for the better.

Be an NMO LEADer.

- Fresh challenge activity for **NMOtion**►
- Main audiences: patients and doctors
- Integrate into GJCF educational assets
- Target for philanthropic development

For more information about the Lead Campaign, visit **guthyjacksonfoundation.org/lead**.



6.4 NMO Education Programs & Resources

NMOpedia Education Platform

NMOpedia is a digital education platform comprising of a series of informational PowerPoint presentations made available for the medical and scientific community by GJCF and its MAB. Each module offers a succinct exploration of the research surrounding NMO with

clearly-defined learning goals. NMO Advocates are invited to share NMOpedia with medical personnel who are not familiar with NMO. For more information, visit **guthyjacksonfoundation.org/nmopedia**.

NMO Webinars & Podcasts

Helping to inform the NMO community about research and clinical trials, GJCF hosts online educational webinars and podcasts. NMO clinicians, scientists and industry delegates discuss clinical trials, how they work and what they might mean for NMO, as well as relevant topics in NMO research and education. Access these NMO webinars and podcasts on our website at: **guthyjacksonfoundation.org/podcasts**.

NMO Ambassador Speakers' Bureau

Providing information and educational support to raise awareness of NMO on behalf of patients is key to the cure. NMO is a rare, autoimmune disease that is often mistaken for MS. Yet, NMO is quite distinct from MS in terms of causes, manifestations, diagnosis, treatment and natural history. There may be several reasons for underdiagnosis of NMO, including lack of information or awareness about NMO within the medical professional

LOCATE RECORDINGS OF
NMO Clinical Trial
webinars and podcasts
by visiting NMOtion at:
guthyjacksonfoundation.org/clinical-trials



community. There is also a general lack of awareness regarding NMO in the general community. For these reasons, a critical need exists to enhance basic education and recognition of NMO to help all patients receive the best diagnosis and most appropriate treatment as quickly as possible.

Overview & Goal

The NMO Ambassador Speakers' Bureau is an informal education and program that connects NMO awareness from patients to healthcare professionals, through shared information and experience. The goal of this approach to communication is to facilitate patients receiving the best quality and timely care, and families, friends and communities learning what they can do to help spread the word.

Method

The program recruits and trains committed members of the general public or medical community to give NMO presentations in person to interested audiences. Volunteers register to become NMO Ambassador

Speakers by contacting The Guthy-Jackson Charitable Foundation (GJCF). The foundation offers free training and presentation resources accessible online.

To learn more about becoming a volunteer member of the NMO Ambassador Speakers' Bureau, visit the foundation's website at: guthyjacksonfoundation.org

Become an NMO Advocate

An advocate is anyone who acts on behalf of NMO patients, families or other stakeholders to help find answers that improve and save lives. Advocates are patients, caregivers, friends, family, community organizations, research and medical professionals, and any member of the public who raises awareness or works to find a cure for NMO. The **only requirement** for becoming an advocate is **persistence** and the **desire to make a difference** in the lives of those living with NMO.

To get started, create a free account on the foundation's website at:

guthyjacksonfoundation.org/register

What is an advocate's role?

Advocates work individually or as a group with established organizations to build awareness in their local areas. Efforts can include anything from fundraisers, events and meetings to bake sales, car washes and more. An advocate may be asked to speak to a group of people who are interested in learning more about NMO.



Awareness and education come in many forms:

- Hosting educational presentations
- Hosting advocacy events
- Posting on social media
- Talking to friends and family

On **NMOtion**▶ you can sign up to receive information about NMO clinical trials, opportunities to advocate for NMO and how to participate in the GJCF NMO CIRCLES biorepository (refer to Chapter 5).

For additional advocacy ideas visit the **NMOtion**▶ website at: **guthyjacksonfoundation.org/nmotion**

NMO / MS...What You Need to Know Brochure

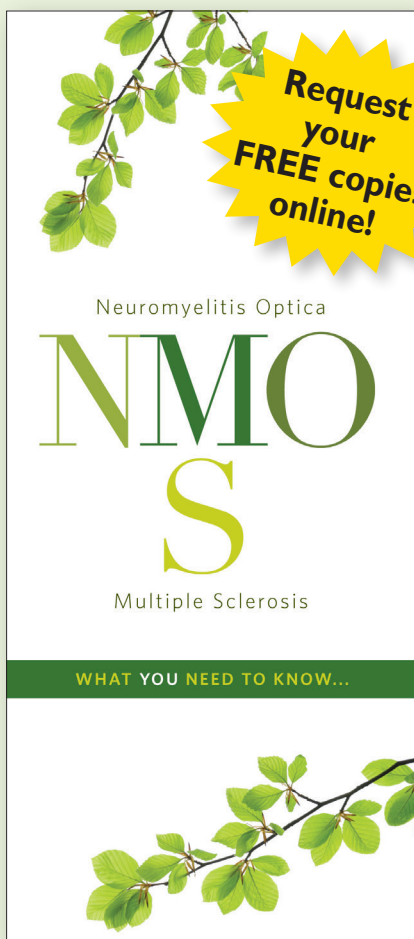
Help spread awareness about NMO!

The *NMO/MS What You Need to Know* brochure offers patients, advocates, and healthcare professionals additional resources to assist in considering NMO as a possible diagnosis.

Anyone can order these brochures. It's a great way to help educate:

- Clinicians
- Friends
- Nurses
- Event attendees
- Family
- Anyone else you can think of!

Request your free copies online at:
guthyjacksonfoundation.org/ms-nmo



How does GJCF support advocacy?

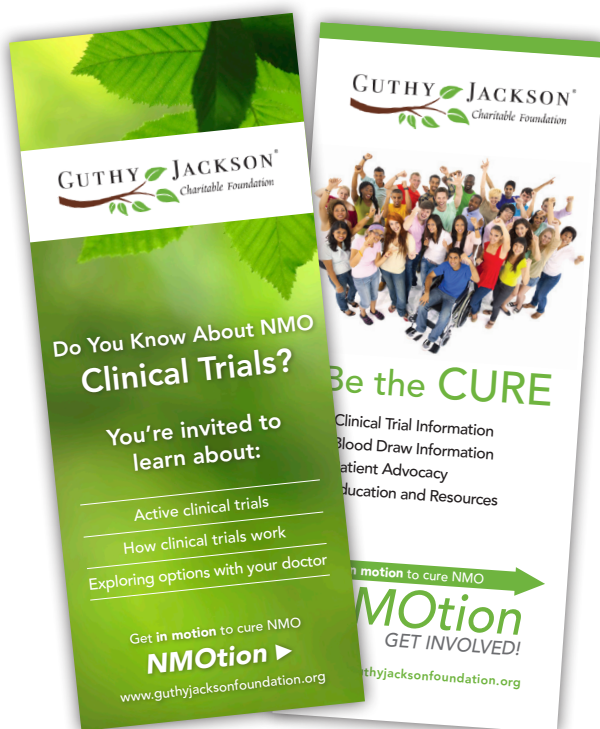
Advocates who are interested in hosting a community event may request an **NMO Share Package** that generally contain the following:

- Clinical Trials Information Card
- Items from the NMO Shop
- Brochures
- CD including:
 1. NMO Patient Resource Guide Card
 2. NMO Clinical Trial Information Card
 3. NMO fact sheet
 4. NMO CIRCLES biorepository fact sheet
 5. Rare disease fact sheet
 6. PowerPoint presentation about NMO and GJCF
 7. GJFC fact sheet
 8. GJRFI Giving Form for financial donations
- DVD with videos about NMO

All of these assets are also available for free download on the foundation's website. Visit **guthyjacksonfoundation.org/tools-for-download**.

NMO Helping Hands

NMO patients and families appreciate knowing that others care. Whether directly affected by NMO or not, everyone can help. NMO Helping Hands is a network of volunteers who are willing listeners who can offer support to NMO patients and families. Members of this network share their contact information on a purely voluntary basis. Typically, Helping Hands volunteers meet one another at NMO educational events or patient days, or maintain connectivity through social media or via phone. To learn more about becoming a volunteer member of NMO Helping Hands, visit the foundation's website at: **guthyjacksonfoundation.org**



NMO Clinical Trial Information Card

NMO Clinical Trial Information Card

Did you know that there are no current regulatory-approved therapeutics for NMO? For a therapeutic to be approved for NMO, formal clinical trial testing is required. There are a number of new NMO clinical trials underway seeking to establish specific treatments for NMO patients. To help raise awareness about NMO clinical trials, GJCF has produced an NMO Clinical Trial Information Card for the NMO community, which is shipped to NMO Advocates in the **NMO Share Package** free of cost. Visit [**guthyjacksonfoundation.org/advocate**](https://guthyjacksonfoundation.org/advocate) to become an Advocate and start raising awareness for NMO today.

Raise awareness on Social Media

Social media has become a powerful tool to help raise awareness about NMO. In addition to The Guthy-Jackson Charitable Foundation's Facebook, YouTube, and Twitter accounts, dozens of other NMO social media accounts and groups exist. Below are several hashtag keywords you can use when you post NMO education and awareness messaging on social media:

- #kNOwNMO
- #NMOTION
- #NMOclinicaltrials
- #NMOadvocacy
- #NMOawareness
- #NMOisnotMS





Donate to NMO Science

100% OF YOUR
FINANCIAL DONATION

goes directly to research for NMO as directed
by The Guthy-Jackson Research Foundation, Inc.

Visit: www.guthyjacksonfoundation.org/donate
to donate today!

6.5 Patient Stories

Oftentimes, nothing speaks louder than genuine, real-life accounts of people living with a rare disease. Personal narratives are an essential part of building upon communication, interpreting experiences and incorporating new information. On the **NMOtion**► site, the “Patient Stories” section offers reassurance and support from personal experiences shared by patients living with NMO.

Visit **guthyjacksonfoundation.org/stories** to share or read stories shared by our patient community.

6.6 Support Groups & Advocacy Organizations

The GJCF places a high value on its relationships with advocacy organizations in support of providing information, education and resources for those living with NMO. Joining a support group may be beneficial to NMO patients, caregivers, family and friends. New NMO support groups are being established all over the world. There are different types of NMO support groups ranging from in-person to telephone and online communities. You can access information about NMO support groups online at:

guthyjacksonfoundation.org/support-groups.

Advocacy Organizations

American Foundation for the Blind

New York, NY
212-502-7600
www.afb.org

Christine Ha The Blind Cook

theblindcook.com
christineha.com

CoachArt

Los Angeles, CA
www.coachart.org
213-736-2850

Craig Photography

craig-photography.blogspot.com

Myelin Repair Foundation

Saratoga, CA
408-871-2410
msfocus.org
Email: info@myelinrepair.org

National Eye Institute (NEI)

Bethesda, MD
301-496-5248
nei.nih.gov
Email: 2020@nei.nih.gov

National Institute of Neurological Disorders and Stroke (NINDS)

Bethesda, MD
800-352-9424
braininfo@ninds.nih.gov
Email: ninds.nih.gov

National Organization for Rare Disorders (NORD)

Danbury, CT
800-999-NORD (6673)
rarediseases.org
Email: orphan@rarediseases.org

NMO Diaries

www.nmodiaries.com

**NMO-UK Rare Illness Research Foundation
c/o Neuro support**

Liverpool, UK
nmo-ukresearchfoundation.org
Email: info@nmo-ukresearchfoundation.org

No More NMO – Riley's Story

nomorenmo.com

**Office of Rare Diseases
National Institutes of Health**

Bethesda, MD
301-402-4336
rarediseases.info.nih.gov
Email: ord@od.nih.gov

Oxford University NMO Clinic Department of Clinical Neurology

Oxford, UK
01865 234461
www.nmouk.nhs.uk
Email: annaliza.rye@orh.nhs.uk

The NMO Clinical and Research Program at UBC Hospital and Vancouver Coastal Health

Vancouver, BC
nmo.vchri.ca

Transverse Myelitis Association

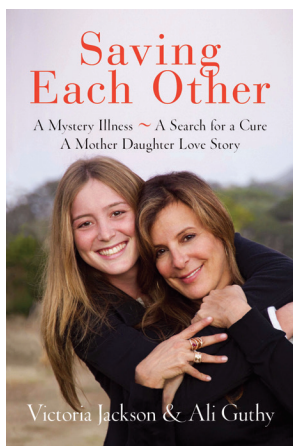
Powell, OH
myelitis.org

The Walton Centre NHS Foundation Trust

Liverpool, UK
www.nmouk.nhs.uk
Email: nmoAdvice@thwaltoncentre.nhs.uk

Visit the NMO Advocacy Network on **NMOtion►**:
guthyjacksonfoundation.org/advocacy for the
complete list of advocacy organizations.

6.7 Suggested Reading



Saving Each Other

Authors: Victoria Jackson
and Ali Guthy

In 2008, Victoria Jackson's daughter, Ali, began experiencing unusual symptoms of blurred vision and an ache in her eye. Her test results led to the diagnosis of a disease so rare, the chance that she had it was only 2%. Neuromyelitis optica (NMO) is a little understood, incurable, and often fatal autoimmune disease that can cause blindness, paralysis, and life-threatening seizures, and can afflict hundreds of thousands of people worldwide. At the age of 14, Ali was given a terrifying prognosis of between four to six years to live.

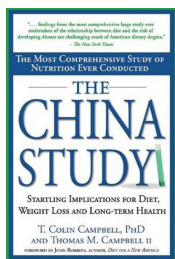
Saving Each Other: A Mother-Daughter Love Story begins just as Victoria and her husband Bill Guthy learn of Ali's disease, starting them on a powerful journey to save Ali, their only daughter, including bringing together a team of more than fifty of the world's leading experts in

**100% of all profits directly support
scientific and clinical research for
neuromyelitis optica through The
Guthy-Jackson Research Foundation, Inc.**

autoimmune and NMO-related diseases to create The Guthy-Jackson Charitable Foundation, which aims to find a cure for NMO.

6.8 The Bookshelf

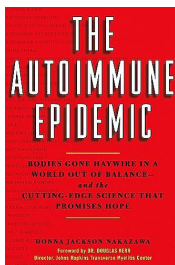
The GJCF welcomes diverse perspectives regarding autoimmune diseases. While it does not claim to agree with or refute their content, the following books may be of consideration for further reading:



The China Study

Author: T. Colin Campbell, Ph.D.

Referred to as the “Grand Prix of epidemiology” by The New York Times, the author examines more than 350 variables of health and nutrition with surveys from 6,500 adults in more than 2,500 counties across China and Taiwan, and suggests a connection between nutrition and heart disease, diabetes, and cancer.

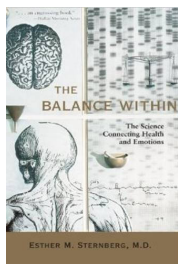


The Autoimmune Epidemic

Author: Donna Jackson Nakazawa

The author suggests how “autogens” — a term denoting chemical, lifestyle, and other triggers of autoimmune disease — may influence the human immune system.

Methods to protect the immune system while exploring possible causes and potential remedies for many autoimmune diseases and autoimmune-related diseases are considered.



The Balance Within

Author: Esther M. Sternberg

The author examines how stress may contribute to susceptibility to disease and its potential impact on the immune system. She explores whether understanding of these connections in scientific terms may help to answer questions such as “does stress make you sick?”, “is a positive outlook the key to better health?”, and “how do personal relationships, work, and other aspects of our lives affect health?”

AN EPIDEMIC OF ABSENCE

*A New Way of
Understanding
Allergies
and Autoimmune
Diseases*



MOISES VELASQUES-MANOFF

An Epidemic of Absence: A New Way of Understanding Allergies and Autoimmune Diseases

Author: Moises Velasques-Manoff

The author explores the dramatic rise of allergic and autoimmune diseases and the controversial, potentially groundbreaking therapies that scientists are developing to correct these disorders. The author’s exploration includes the “worm therapy,” probing the link between autism and a dysfunctional immune system, asking what will happen in developing countries regarding allergic disease and more.



Recipes from My Home Kitchen: Asian and American Comfort Food

Author: Christine Ha

Winner of Masterchef Season 3, in her kitchen, Christine Ha possesses a rare ingredient that most professionally-trained chefs never

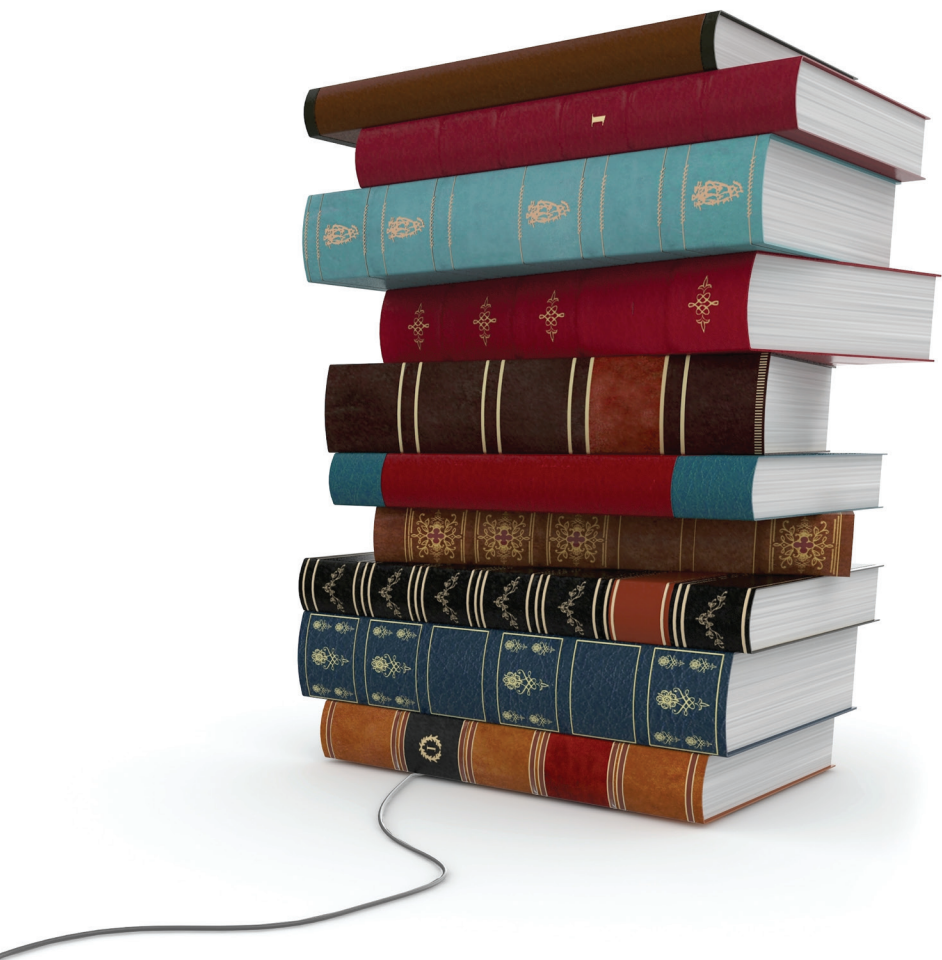
learn to use: the ability to cook by sense. After tragically losing her sight in her twenties, this remarkable home cook, who specializes in the mouthwatering, wildly popular Vietnamese comfort foods of her childhood, as well as beloved American standards that she came to love growing up in Texas, re-learned how to cook. Using her heightened senses, she turns out dishes that are remarkably delicious, accessible, luscious, and crave-worthy.

6.9 Spectrum: The Latest NMO Breakthroughs

Spectrum is The Guthy-Jackson Charitable Foundation's online NMO Library and is one of the largest collections of scientific and clinical NMO abstracts. **Every day, researchers are making more discoveries about NMO.** Learn about key topics like antibodies, aquaporins, astrocytes, therapies and much more. Inside the Spectrum NMO Library you will find also find a collection of topics ranging from diet and nutrition to autoimmunity in the forms of:

- **Scientific abstracts**
- **Videos**
- **Press articles**
- **Books**





The Guthy-Jackson Charitable Foundation's online NMO Library is one of the largest collections of scientific and clinical NMO abstracts.

Selections from the Spectrum NMO Library: Helpful NMO Publications for Clinicians, Scientists & Patients

Treatment of Neuromyelitis Optica: Review and Recommendations

Abstract

Neuromyelitis optica (NMO) is an autoimmune demyelinating disease preferentially targeting the optic nerves and spinal cord. Once regarded as a variant of multiple sclerosis (MS), NMO is now recognized to be a different disease with unique pathology and immunopathogenesis that does not respond to traditional MS immunomodulators such as interferons. Preventive therapy in NMO has focused on a range of immunosuppressive medications, none of which have been validated in a rigorous randomized trial.



However, multiple retrospective and a few recent prospective studies have provided evidence for the use of six medications for the prevention of NMO exacerbations: azathioprine, rituximab, mycophenolate mofetil, prednisone, methotrexate and mitoxantrone. This review provides a comprehensive analysis of each of these medications in NMO and concludes with a set of recommended consensus practices.

Integrative Continuum: Accelerating Therapeutic Advances in Rare Autoimmune Diseases

Abstract

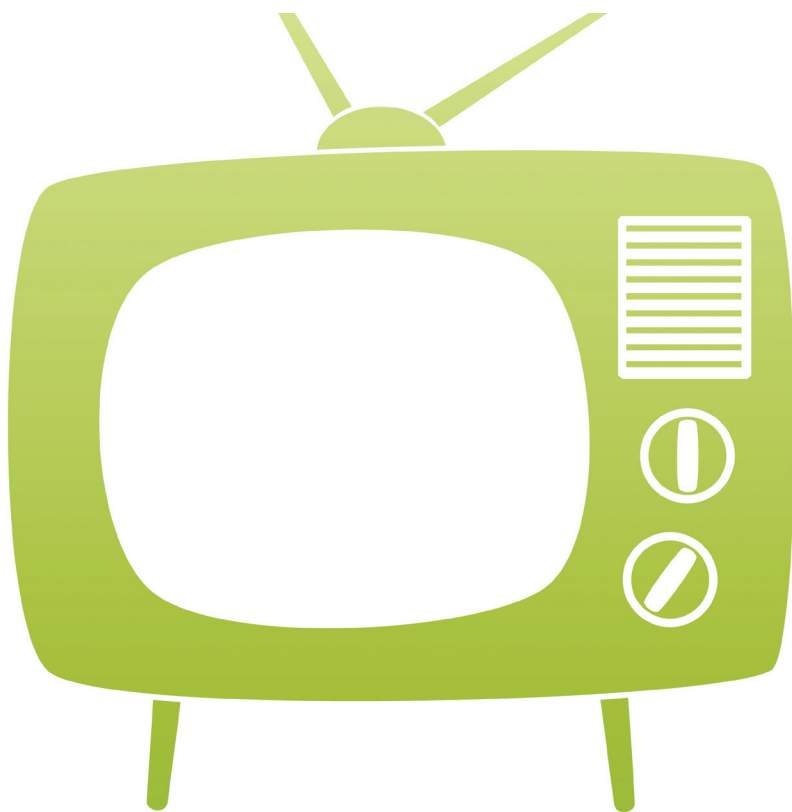
Autoimmune diseases are chronic, life threatening, and of burgeoning public health concern. They rank among the 10 most common causes of death in women, and some have incidence rates surpassing those of heart disease and cancer. Emerging information regarding molecular and cellular mechanisms affords opportunities for the discovery of novel therapeutic strategies or the repurposing of FDA-approved pharmacologic agents. Yet, obstacles to drug development amplify as an inverse function of the incidence of rare autoimmune disease;

**Help educate medical professionals
by downloading and sharing
NMO scientific papers and abstracts
from the NMO Library.**

challenges include heterogeneous clinical presentation, paucity of definitive biomarkers, and poorly validated measures of therapeutic response. An integrative continuum model to address these challenges is being applied to neuromyelitis optica (NMO)—a potentially devastating neurodegenerative process that has had limited therapeutic options. This model links target discovery with pharmacologic application to accelerate improved clinical efficacy. The application of such innovative strategies may help researchers overcome barriers to therapeutic advances in NMO and other rare autoimmune diseases.

Visit the NMO Library now to download papers and abstracts to share with clinicians, family and friends at:
guthyjacksonfoundation.org/spectrum





6.9 NMO TV

Aimed at helping the NMO community have the latest information at its disposal, **NMO TV** showcases the foundation's extensive video library, featuring **over 100 videos** about NMO. Informational videos about different aspects of living with NMO are easily viewed along with relevant topics suggested to help expand your understanding about topics like scientific research, managing stress and fatigue, NMO FAQs, and much more. Visit **guthyjacksonfoundation.org/nmotv** to view the collection of videos about NMO.

Directory of Clinicians

The Guthy-Jackson Charitable Foundation is “Connecting the Docs” by compiling a worldwide list of clinicians who treat NMO.



Directory of Clinicians “Connect the Docs”

With NMO being a rare orphan disease, simply finding a clinician who treats NMO can be difficult. To help patients find NMO clinicians, The Guthy-Jackson Charitable Foundation is “Connecting the Docs” by listing known clinicians who treat NMO. On the foundation’s website you will find a map with locations of NMO clinicians. Thus far, **over 200 clinicians** have been mapped all over the world and our list continues to grow.

The following pages contain an abbreviated list of “**Connect the Docs.**” If you receive treatment from or know of an NMO clinician(s) who you do not see in this list, please visit our website to find out if the clinician(s) is on our online map. If you would like to “connect a doc” by submitting information about a clinician who treats **NMO please visit our web page at:**
guthyjacksonfoundation.org/mapping-nmo/

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**Key Terms
& Facts**

**My NMO
Notes**

knowing [-ɪŋ] adj. An-
|| Instruit. || Malle. 8
délibéré, intentionné
chi, dénié, dénié,
knowingly [-ɪŋli]
ment, en connais-
Habilement, avec
knowledge ['nɒl-
it's common know-
not to my know-
science f.; con-
thorough know-
Carnal know-
known [nəʊn]
knuckle ['nʌ-
want, du do-



Key Terms & Facts

Acute – illnesses that appear quickly and have a short, sharp course.

Antibody – a protein produced by the body's immune system when it detects harmful substances called antigens.

Antigen – any substance that causes your immune system to produce antibodies against it.

Aquaporin-4 – a protein that allows water to leave and enter certain cells in the central nervous system.

Autoimmunity – relating to an immune response by the body against one of its own tissues, cells, or molecules.

Astrocyte – a supporting cell in the central nervous system, that appears to be targeted in NMO.

Axons – a long fiber of a nerve cell that acts somewhat like a fiber-optic cable carrying outgoing messages.

Blood-Brain Barrier (BBB) – junction between the blood supply and the central nervous system that regulates what comes in and out.

Brain stem – junction that connects the brain with the spinal cord.

Central nervous system (CNS) – the brain and spinal cord.

Complement – the group of proteins in normal blood serum and plasma that in combination with antibodies causes the destruction especially of particulate antigens (bacteria and foreign blood corpuscles).

Demyelination – the breakdown of the myelin sheath.

Fatigue – extreme tiredness.

Immune system – the various cells and organs that protect the body from viruses, bacteria and other illness.

Immunosuppressant – medication that purposefully weakens the immune system.

Inflammation – a protective attempt by the organism to remove the cause of damage and to initiate the healing process.

Longitudinally Extensive Transverse Myelitis (LETM) – an inflammatory and demyelinating attack on the spinal cord causing symptoms.

Monophasic – a disorder with a single phase or stage.

Myelin – a protective covering around a nerve, speeding up the transfer of electrical messages.

NMO-IgG – autoantibody marker that targets the water channel protein aquaporin-4 causing NMO.

Optic neuritis (ON) – an inflammatory and demyelinating attack on the optic nerve, causing visual symptoms.

Relapse – a new “attack” of NMO, which can affect optic nerves, spinal cord or brain/brainstem.

Repository – a location where de-identified samples such as blood and other biological specimens and clinical data from donors are confidentially stored.

Symptom – an impairment that is left after recovery from a relapse, for example pain or reduced vision.

Transverse myelitis (TM) – a neurological disorder caused by inflammation across both sides of one level, or segment, of the spinal cord.

White blood cells – the group of cells within the blood that regulate the immune system and mount the immune response to illness.

NMO Facts at a Glance

- **1804:** Dr. Antoine Portal publishes an **early case of disease** consistent with NMO.
- **1870: Sir Thomas Allbutt, M.D.**, initially describes a case of simultaneous optic neuritis and transverse myelitis that does not have obvious brain tissue involvement.
- **1894:** Eugène Devic, M.D., coins the term “neuromyéélite optique,” or **neuromyelitis optica**.
- **2006:** Vanda A. Lennon, M.D., Ph.D. and colleagues at the Mayo Clinic identify the NMOIgG antibody as being correlated specifically with NMO disease.
- Among patients with relapsing NMO, **roughly 50 percent** will have a relapse in the first year, **75 percent** by the third year and **90 percent** by the fifth year.
- People with **monophasic** (single attack) NMO, which is much less common than **relapsing NMO**, tend to have more severe attacks than those with the relapsing NMO; approximately 20 percent of patients have permanent vision loss, and 30 percent have permanent paralysis in one or both legs.
- Approximately **60 - 70 percent** of NMO patients have **detectable antibodies** (immune proteins) in their blood that target protein that channels water in and out of cells existing primarily in the brain and spinal cord called aquaporin 4 (AQP4).

- About **80 percent** of patients with NMO have distinct, **long lesions in the spinal cord** on MRI that are not typically present in patients with MS.
- An antibody, called **NMO-immunoglobulin G (NMO-IgG)**, is present in the blood of approximately 70 percent of NMO patients. Patients appropriately diagnosed with MS do not usually test positive for NMO-IgG (see section 1.6).
- **NMO is more common in women than men**, with a ratio of approximately **6:1**.
- The **median age of onset is between 32 and 40** years of age, based on reports from different regions of the world.
- Previous reports estimate up to **one-half million cases worldwide**.
- **Global statistics** on the prevalence of NMO has yet to be determined.
- Currently, NMO in the United States is estimated to affect approximately **1 in 25,000** people (estimates may vary depending on ethnic background).
- In the U.S., the National Institutes of Health (NIH) classifies NMO as a rare orphan disease (fewer than 200,000 people affected). **It is estimated that NMO affects at least 4,000 people in the U.S. alone. Worldwide, NMO is likely to affect tens of thousands of people based on prevalence rates in other countries.**

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Our goal is to provide insight to NMO, a rare and misunderstood disease. If this booklet provides new information and/or guidance, we will have fulfilled our objective.

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