

# **History & Discovery**



# History & Discovery

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## 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.

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

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**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**

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

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### **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**

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**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

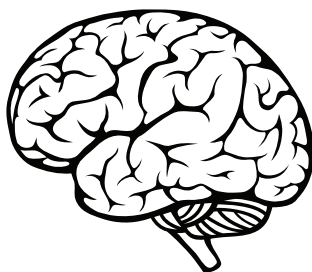
**For more information, visit:**  
**[guthyjacksonfoundation.org/ms-nmo](http://guthyjacksonfoundation.org/ms-nmo)**

- 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.

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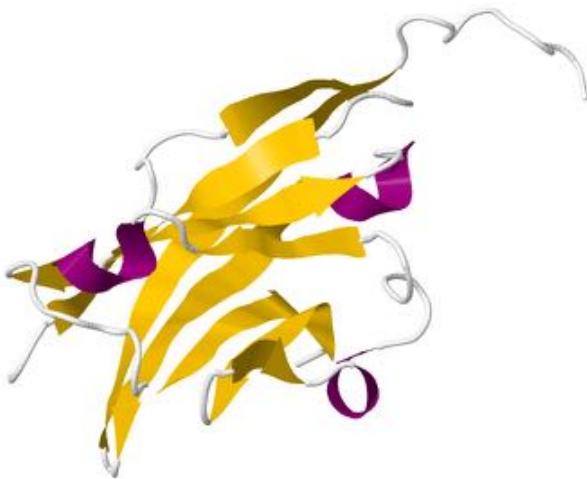
**Some MS medications do not help  
NMO patients and may actually  
worsen disease or cause more severe  
attacks and complications.**

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- 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 -  
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- 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?

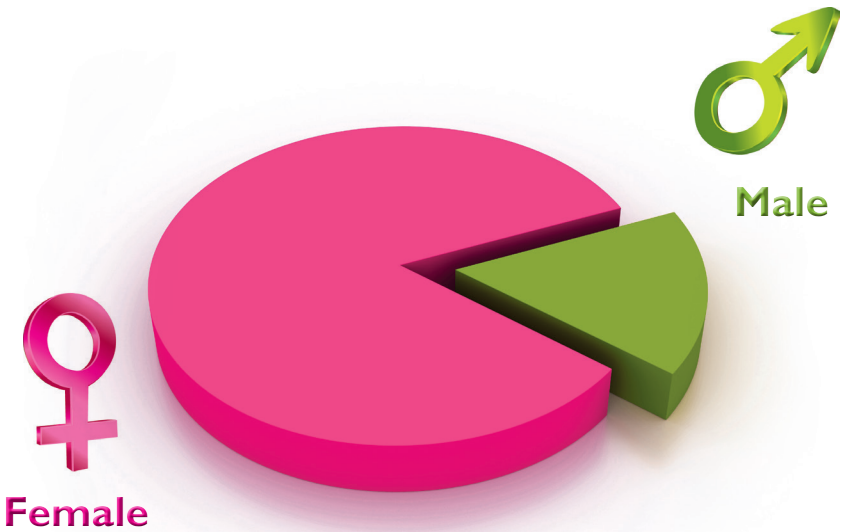
In the United States (U.S.), the National Institutes of Health (NIH) has historically considered NMO as a **rare orphan disease** (fewer than 200,000 people affected). While estimates may vary depending on several factors, currently in the United States NMO is estimated to affect approximately 4-10 per 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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Patients are increasingly being diagnosed earlier in the course of disease, and more accurately, aiding in longer and healthier lives.

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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](http://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?

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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](http://guthyjacksonfoundation.org/blood-bank)**