

# Fact Sheet

## Q&A on Relapsing vs Monophasic Rare Neuroimmune Disorders

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**Are diseases such as transverse myelitis (TM), acute flaccid myelitis (AFM), optic neuritis (ON), acute disseminated encephalomyelitis (ADEM), MOG antibody-associated disease (MOG-Ab disease), or neuromyelitis optica spectrum disorder (NMOSD) one-time or relapsing diseases?**

It depends. TM, ON, and syndromes resembling ADEM can occur in the setting of relapsing conditions, such as multiple sclerosis, neuromyelitis optica associated with aquaporin-4 antibodies (AQP-4), and some systemic/rheumatologic diseases. Once an individual has undergone sufficient workup for these conditions and they have been ruled out, the likelihood he or she has idiopathic transverse myelitis or monophasic ADEM increases, which are considered one-time disorders. In the past year, clinicians have also been able to test for a new antibody called MOG (myelin oligodendrocyte glycoprotein). Like AQP-4, MOG antibodies can be assessed with good accuracy through a blood sample. Although the MOG story is still unfolding, many physicians following patients who continue to test positive for MOG antibodies 6-12 months after the initial episode have reported relapsing disease in this population and are thought to have MOG antibody-associated disease.

**I had transverse myelitis (TM), optic neuritis (ON), or acute disseminated encephalomyelitis (ADEM) in the past and was told I don't have multiple sclerosis or neuromyelitis optica spectrum disorder (NMOSD). I am now experiencing new or worsening neurological symptoms? What should I do?**

It is very important for you and your provider to determine if the worsening symptoms are related to new inflammation (i.e., a relapse), or from some temporary disturbance in your body's normal state unmasking symptoms from a prior injury, without new inflammation (pseudo-relapse).

For symptoms that last over 24 hours and do not improve with rest, hydration, being in a comfortable temperature, and/or recovery from an acute illness (e.g., respiratory or urinary tract infection), contact your neurology provider. He or she may order blood or urine tests to make sure you are not experiencing any acute infections or metabolic disturbances. If ruled out, additional tests may include an MRI of suspected area of new inflammation (i.e., brain, spine, and/or optic nerves).

Evidence of new inflammation on MRI and/or symptoms related to a part of the nervous system that was not affected in the past suggests a new acute inflammatory episode. This should be treated with immunotherapy such as corticosteroids to stop ongoing inflammation, and trigger a discussion with your clinician about whether ongoing immunotherapy to prevent another attack is needed.

**If I am concerned I have a relapsing disorder, what should I do?**

Discuss this concern with your neurology provider, and ask if you would be an appropriate candidate to test for AQP-4 and MOG antibodies (available through Mayo Medical Laboratories as "CDS1" order).



**My doctors say they can still see TM or an area of damage on my MRI. Does this mean I have a relapsing disorder?**

During an inflammatory attack in the spinal cord, as occurs in TM, there may be evidence of inflammation on MRI (areas of contrast enhancement indicating compromise of the blood-brain-barrier) or an increase in inflammatory cells in cerebrospinal fluid. After this inflammation subsides, there may be evidence of where this attack occurred, or an area showing previous damage (T2/FLAIR abnormalities), but not ongoing inflammation (e.g., continued contrast enhancement). Gliosis, essentially a scar in the brain, can be seen for months or years and does not indicate ongoing inflammation or relapsing disease. An MRI that shows new inflammation suggests a new acute inflammatory episode.

**My doctor told me I am AQP-4 positive, now what?**

An episode consistent with neuromyelitis optica spectrum disorder and a single positive test for AQP-4 in blood or spinal fluid are typically adequate to establish a diagnosis of NMOSD. These individuals should be placed on immunosuppressive therapy, which we currently advise be continued indefinitely. This is because NMOSD attacks can be severe, cause lasting visual or motor impairment, and are very likely to recur unless treated.

**My doctor told me I am MOG positive, now what?**

This depends on when MOG antibodies were tested in relation to your demyelinating event. If MOG antibodies were detected at the time of the attack or in the first 6 months following attack, we recommend retesting for MOG antibodies 6-12 months after your event. If you become MOG negative, you are unlikely to have future relapses.

If MOG antibodies are positive again, you are considered to have MOG antibody-associated disease, and may be at risk for future demyelinating episodes. You should speak to your neurologist about whether you should be placed on a therapy to prevent the likelihood of a relapse.

For individuals who undergo MOG testing for the first time 12 months or greater after their demyelinating event, one positive MOG test would be sufficient to diagnosis persistent MOG antibodies and then you should have a discussion with your physician as above about chronic immunotherapy.

**I already have any existing diagnosis of multiple sclerosis or neuromyelitis optica spectrum disorder. Should I be tested for MOG?**

It depends on your clinical history and if you have tested positive for AQP-4. MOG testing is reasonable in people who've been told their presentation is atypical for multiple sclerosis and neuromyelitis optica spectrum disorder and previously have been negative on AQP-4 testing. AQP-4 positive patients with symptoms consistent with NMOSD do not need MOG testing, as being double positive (MOG and AQP-4 positive) is exceedingly rare. In addition, this information ultimately would not change management as recurrent MOG and AQP-4 associated NMOSD are currently managed very similarly.

People with presumptive multiple sclerosis who do not respond as well as expected to MS drugs should have a discussion with their doctor about MOG testing as MOG syndromes can be misdiagnosed as MS. A positive MOG test may change medical management as some MS therapies might be ineffective or perhaps even exacerbate MOG antibody-associated disease.

People with MRI and spinal fluid studies consistent with multiple sclerosis should not be routinely screened for MOG antibodies, but decided on a case-by-case basis after discussion with a neurologist.



## Glossary

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| <b>Central Nervous System</b>                           | Includes the brain, spinal cord, and optic nerve.   |
| <b>Monophasic rare neuroimmune disorder</b>             | A disorder that causes only one episode of inflammation in the central nervous system.  |
| <b>Recurrent or relapsing rare neuroimmune disorder</b> | A disorder that causes more than one episode of inflammation in the central nervous system.   |
| <b>Relapse</b>  | New inflammation in the central nervous system.   |
| <b>Pseudo-relapse</b>                                   | Temporary disturbance in the body's normal state unmasking or worsening symptoms from a prior injury, without new inflammation in the central nervous system.   |
| <b>Attack</b>   | An event of inflammation in the central nervous system.   |
| <b>Onset</b>  | The first symptoms of a rare neuroimmune disorder. Typically, the first attack.   |
| <b>Inflammation</b>                                     | Part of the body's immune system meant to eliminate noxious agents. In rare neuroimmune disorders, the immune system mistakenly attacks the brain, spinal cord, or optic nerve, causing inflammation in these areas |

## Author

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**Dr. Cynthia Wang** received her medical degree from University of Texas Southwestern Medical Center in Dallas, Texas and completed a pediatrics and pediatric neurology residency at Mott Children's Hospital, University of Michigan Health System in Ann Arbor, Michigan. Dr. Cynthia Wang completed her James T. Lubin Fellowship under the mentorship of Dr. Benjamin Greenberg at The University of Texas Southwestern and Children's Health. Her research study was a prospective, longitudinal study on acute disseminated encephalomyelitis (ADEM) to identify the clinical characteristics, treatment methods, and follow-up interventions that are associated with better and worse patient-centered outcomes.



| Disorder       | Areas of CNS Involvement   | Specific Diagnostic Tests  | Relapsing or Monophasic  | Ongoing Immunosuppression indicated? |
|----------------|--|--|--|--------------------------------------|
| ADEM           | Brain<br>Spinal Cord<br>Optic Nerve  | None if monophasic   | If MOG negative 6-12 months after onset, typically monophasic                  | No                                   |
|                |  | MOG Antibody   | If MOG positive 6-12 months after onset, might be recurrent (MOG-Ab disease)   | Yes                                  |
| AFM            | Spinal Cord (primarily grey matter)  | Enterovirus PCR in CSF (though virus is very difficult to isolate), positive enterovirus/ rhinovirus on respiratory specimen is supportive | Monophasic   | No                                   |
| Mog-Ab Disease | Brain<br>Spinal Cord<br>Optic Nerve  | MOG Antibody   | Uncertain, persistence of MOG antibodies are associated with relapsing disease | Yes, if relapses occur               |
| MS             | Brain<br>Spinal Cord<br>Optic Nerve  | None, though CSF oligoclonal bands are supportive  | Relapsing  | Yes                                  |
| NMOSD          | Brain<br>Spinal Cord (typically lesions more than 3 vertebral segments in length)<br>Optic Nerve | Aquaporin-4 antibody   | Relapsing  | Yes                                  |
| ON             | Optic Nerve  | None   | Depends if ON is a part of MS, NMOSD, or MOG-Ab disease                        | Typically yes if relapsing           |
| TM             | Spinal Cord (primarily white matter)   | None   | Monophasic   | No                                   |
|                |  |  | In very rare cases can be recurrent  | Case-by-case                         |

