CNS DEMYELINATING DISEASES (AQP4 AND MOG)

TESTING TO DISTINGUISH A SPECTRUM OF DEMYELINATING DISEASES FROM MS
DISTINGUISHING A SPECTRUM OF AUTOIMMUNE DEMYELINATING DISEASES FROM MS

NEUROMYELITIS OPTICA SPECTRUM DISORDERS
Neuromyelitis optica (NMO) is an inflammatory, demyelinating disease of the central nervous system. NMO is characterized by severe relapsing attacks of optic neuritis and transverse myelitis. Unlike the attacks associated with multiple sclerosis (MS), NMO attacks commonly spare the brain in the early stages.

The spectrum of NMO was traditionally restricted to the optic nerves and the spinal cord. However, Mayo Clinic physician/scientist Vanda Lennon, M.D., Ph.D., discovered an antibody that targets aquaporin-4, the water channel on astrocytes, and it is a sensitive and specific biomarker for NMO. Since that discovery, a much broader category called “NMO spectrum disorders” (NMOSD) has evolved.

OVERLAP OF PHENOTYPES

<table>
<thead>
<tr>
<th>Neurological Manifestation</th>
<th>Frequency of AQP4</th>
<th>Frequency of MOG</th>
</tr>
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<tbody>
<tr>
<td>NMO</td>
<td>80%</td>
<td>7%</td>
</tr>
<tr>
<td>Recurrent Longitudinally Extensive Transverse Myelitis (LETM)</td>
<td>60–80%</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Single Occurrence of LETM</td>
<td>40%</td>
<td>20%</td>
</tr>
<tr>
<td>Recurrent Optic Neuritis</td>
<td>15%</td>
<td>25%</td>
</tr>
<tr>
<td>Chronic relapsing inflammatory optic neuropathy (CRION)</td>
<td>&lt;5%</td>
<td>25%</td>
</tr>
<tr>
<td>Single Occurrence of Optic Neuritis</td>
<td>&lt;5%</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Intractable Vomiting/ Area Postrema Syndrome</td>
<td>&lt;5%</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Acute Disseminated Encephalomyelitis (ADEM), Posterior Reversible Encephalopathy Syndrome (PRES)</td>
<td>&lt;5%</td>
<td>40%</td>
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</tbody>
</table>

MYELIN OLIGODENDROCYTE GLYCOPROTEIN (MOG)-OPATHY
Detection of MOG-IgG1 is diagnostic of central nervous system (CNS) inflammatory demyelination, where the clinical phenotype (NMO, optic neuritis, transverse myelitis, acute disseminated encephalomyelitis [ADEM]) may be similar, but the immunopathology (astrocytopathy vs. oligodendrogliopathy) and clinical outcome (worse vs. better) are different. Detection of MOG-IgG1 also predicts disease relapse.

More importantly, MOG-IgG1 seropositive inflammatory demyelinating diseases (IDDs) are distinct from MS and are treated differently, and these MS treatments have been reported to worsen MOG-IgG1 seropositive IDDs.

WHY TEST FOR AQP4 AND MOG?

TO DISTINGUISH NMOSD AND MOG-OPATHIES FROM MS
Although NMOSD and MOG-opathies can have very similar clinical and radiologic characteristics to MS, the diseases are treated very differently:

- A majority of NMO patients, typically women, are initially misdiagnosed with MS.
- While NMO and MOG-opathies are treated by immunosuppressant therapy, MS is treated by immunomodulation therapy, which may worsen NMO.

EARLY DIAGNOSIS AND TREATMENT MAY PREVENT FURTHER ATTACKS IN NMOSD
Unlike MS, the neurological disability caused by NMO spectrum disorders and MOG-opathies is based on the number of attacks rather than a progressive phase of the illness:

- Initiating therapy early in the course to eliminate recurrence of attacks will minimize patient disability.
- If not treated appropriately, within five years, 50% of NMO patients lose functional vision in at least one eye or are unable to walk. Recent data suggests that patients with MOG-opathy may have less disability.
WHICH TESTS SHOULD I ORDER?

- CNS Demyelinating Disease Evaluation, Serum (Mayo ID: CDS1) TAT: 7 Days
- Neuromyelitis Optica (NMO)/Aquaporin-4-IgG Fluorescence-Activated Cell Sorting (FACS) Assay, Serum (Mayo ID: NMOFS) TAT: 5 Days
- Myelin Oligodendrocyte Glycoprotein (MOG-IgG1) Fluorescence-Activated Cell Sorting (FACS) Assay, Serum (Mayo ID: MOGFS) TAT: 5 Days

WHEN SHOULD I ORDER THE CNS DEMYELINATING DISEASE EVALUATION?

NERVE OR SPINAL CORD INVOLVEMENT

- DEFINITELY ORDER
  - LONG SPINAL CORD LESION
  - MULTIPLE EPISODES OF OPTIC NEURITIS
- CONSIDER ORDERING
  - SHORT SPINAL CORD LESION

SYMPTOMS OUTSIDE OPTIC NERVE OR SPINAL CORD

- DEFINITELY ORDER
  - When any of the symptoms below are present in combination with either a single episode of optic neuritis or short spinal cord lesions.
  - When ADEM is suspected.
- CONSIDER ORDERING
  - Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting.
  - Acute brainstem syndrome.
  - Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions.
  - Symptomatic cerebral syndrome with NMOSD-typical brain lesions.

FACS: A SUPERIOR METHOD OF TESTING

Mayo Clinic has developed the only fluorescence-activated cell sorting (FACS) live cell-binding assay that is currently available in the U.S. for antibody detection of AQP4 and MOG. FACS is recommended by international leaders in neuroimmunology for its increased sensitivity and specificity.

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>FACS Live Cell-Binding Assay</td>
<td>&gt;80%</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>ELISA</td>
<td>60–65%</td>
<td>99%</td>
</tr>
<tr>
<td>Indirect Immunofluorescence</td>
<td>50–55%</td>
<td>&gt;99%</td>
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</table>

The likelihood of having a false-positive result with ELISA methodology is at least 5x greater when compared with the Mayo Clinic cell-binding assay.²

CUSTOMER SERVICE FOR CLINICAL SPECIALISTS / 855-516-8404 OR +1-855-379-3115 (INT’L)
MAYO CLINIC DISCOVERY AND ASSAY PERFORMANCE
PUBLICATIONS FOR NMO

DISCOVERY OF ANTIBODY MARKER FOR NMO

IDENTIFICATION OF AQUAPORIN-4 AS ANTIBODY TARGET

AQP4-IGG FACS ASSAY SUPERIOR PERFORMANCE

CITATIONS

A HISTORY OF INNOVATION AND DISCOVERY

Recognized as a world leader in the diagnosis and treatment of autoimmune neurologic disorders and demyelinating diseases, Mayo Clinic mounts unmatched resources for uncovering novel syndromes, developing new diagnostic biomarkers and unique laboratory tests.

COLLEGIATE ACCESS TO MAYO CLINIC NEUROLOGISTS

Neurologists are available for consultation and assistance in the interpretation of autoantibody evaluations. These conversations enable the best diagnosis and treatment approach, as they provide our neurologists the opportunity to ask additional clinical information, as well as address the questions of the ordering neurologist.


FOR MORE INFORMATION ABOUT AUTOIMMUNE NEUROLOGY TESTING, VISIT US AT:

mayomedicallaboratories.com/nmo

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