Test Definition: MOGFS
Myelin Oligodendrocyte Glycoprotein (MOG-IgG) Fluorescence-Activated Cell Sorting (FACS) Assay, Serum

Overview

Useful For
Diagnosis of inflammatory demyelinating diseases (IDD) with similar phenotype to neuromyelitis optica spectrum disorder (NMOSD), including optic neuritis (single or bilateral) and transverse myelitis

Diagnosis of autoimmune myelin oligodendrocyte glycoprotein (MOG)-opathy

Diagnosis of neuromyelitis optica (NMO)

Distinguishing NMOSD, acute disseminated encephalomyelitis (ADEM), optic neuritis, and transverse myelitis from multiple sclerosis early in the course of disease

Diagnosis of ADEM

Prediction of a relapsing disease course

Reflex Tests

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Testing Algorithm
When the results of this assay require further evaluation, the reflex titer test will be performed at an additional charge.

Highlights
Myelin oligodendrocyte glycoprotein (MOG)-IgG with an NMO spectrum disorder like phenotype is now recognized as a sensitive and specific diagnostic antibody biomarker of inflammatory demyelinating disorders (IDDs).

Approximately 80% of patients fulfilling 2006 Wingerchuk criteria for neuromyelitis optica are seropositive for aquaporin-4 (AQP4)-IgG. Of the remaining 20%, one-third harbor MOG-IgG. Seropositivity predicts a relapsing phenotype and warrants immunosuppressive therapy. Patients only rarely harbor both antibodies.

There is currently no biomarker specific for MS (multiple sclerosis). Patients seropositive for MOG-IgG are commonly misdiagnosed as MS. Detection of MOG-IgG implies an inflammatory demyelinating disorder distinct from MS. MS therapies may worsen MOG-IgG associated IDDs, so correct diagnosis is important.

Seropositivity for MOG-IgG, in NMOSD like disorders, including optic neuritis (OT), transverse myelitis (TM), and acute disseminated encephalomyelitis (ADEM), predicts relapse and warrants consideration for maintenance immunosuppression.
Seropositivity for MOG-IgG in the setting of a severe relapse of central nervous system (CNS) demyelination warrants aggressive therapy with intravenous methylprednisolone or plasmapheresis.

Method Name
Flow Cytometry

NY State Available
Yes

Specimen

Specimen Type
Serum

Specimen Required

Patient Preparation: For optimal antibody detection, we recommend drawing the specimen before initiation of immunosuppressant medication.

Container/Tube:
Preferred: Red top
Acceptable: Serum gel

Specimen Volume: 2 mL

Forms
If not ordering electronically, complete, print, and send a Neurology Specialty Testing Client Test Request (T732) with the specimen.

Specimen Minimum Volume
1 mL

Reject Due To

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Specimen Stability Information

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Clinical & Interpretive

Clinical Information

Neuromyelitis optica (NMO), sometimes called Devic disease or opticospinal multiple sclerosis (MS) is a severe, relapsing, autoimmune, inflammatory and demyelinating central nervous system disease (IDD) that predominantly affects optic nerves and spinal cord. (1) The disorder is now recognized as a spectrum of autoimmunity (termed NMO spectrum disorders: NMOSD). (1-3) Brain lesions are observed in more than 60% of patients with NMOSD and approximately 10% will be MS-like. (4) Children tend to have greater brain involvement than adults, and brain lesions are more symptomatic than is typical for adult patients. (3) The clinical course is characterized by relapses of optic neuritis or transverse myelitis, or both. Some patients may present with acute disseminated encephalomyelitis (ADEM). Many patients with NMOSD are misdiagnosed as having MS. More effective treatments combined with earlier and more accurate diagnosis has led to improved outcomes.

Approximately 80% of patients with NMO are seropositive for aquaporin-4 (AQP4)-IgG. (5-7) In the remaining 20% of patients, myelin oligodendrocyte glycoprotein (MOG)-IgG is detected in up to a third. (8) The pathogenic target for the remaining patients remains unknown. Detection of MOG-IgG is diagnostic of central nervous system (CNS) inflammatory demyelination, where the clinical phenotype (NMOSD, optic neuritis, transverse myelitis, ADEM) may be similar, but the immunopathology (astrocytopathy vs oligodendrogyopathy) and clinical outcome (worse vs better) is different. (9) Detection of MOG-IgG also predicts relapse. (10) More importantly, however, is that MOG-IgG seropositive IDDs are distinct from MS and treated differently. (8, 9) Treatments for IDDs seropositive for MOG-IgG include corticosteroids and plasmapheresis for acute attacks and mycophenolate mofetil, azathioprine, and rituximab for relapse prevention. Disease modifying agents, treatments promoted for MS, have been reported to exacerbate MOG-IgG1 seropositive IDDS. Therefore, early diagnosis and initiation of appropriate immunosuppressant treatment is important to optimize the clinical outcome by preventing further attacks. In 2015, Waters and colleagues (11) from Oxford University established a novel cell based assay for the measurement of IgG1 MOG antibodies based on previous findings that MOG antibodies are almost exclusively of the IgG1 subclass. They showed that their MOG-IgG1 flow cytometry assay eliminated false positives without losing true positives with low titers. The detection of MOG-IgG1 allowed non MS demyelinating diseases (ADEM, AQP4-IgG negative neuromyelitis optica spectrum disorder: including ON, TM) to be distinguished from MS. (12)

Using a similar assay to our MOG-IgG1 flow cytometry assay, demonstrated high specificity of their MOG-IgG1 assay in which 49 patients with MS, 13 healthy control sera, and 37 AQP4-seropositive serum samples were all negative at a dilution of 1:20. Of 58 patients fulfilling 2006 Wingerchuk criteria for NMO, 21 (36%) tested negative for AQP4-IgG MOG-IgG1 was detected by cell based assay in 8 (38%) of these cases. (13)

Testing of 1,109 consecutive sera sent for AQP4-IgG testing. (12) revealed 40 AQP4-IgG and 65 MOG-IgG1 positive cases. None were positive for both. The clinical diagnoses obtained in 33 MOG-IgG1 positive patients included 4 NMO, 1 ADEM and 11 optic neuritis (n = 11). All 7 patients with probable MS were MOG-IgG1 negative. This study provides Class II evidence that the presence of serum MOG-IgG1 distinguishes non-MS central nervous system (CNS) demyelinating disorders from MS (sensitivity 24%, 95% confidence interval [CI] 9%-45%; specificity 100%, 95% CI 88%-100%).
The assay validated here, was developed using the MOG construct provided by Dr Waters(11) and the validation was based on a blinded comparison with the Oxford assay. Comparison was also made with the Euroimmun fixed cell based kit assay.(14)

A recent longitudinal analysis with 2 year follow-up suggested that persistence of MOG-IgG is associated with relapses thus warranting relapse preventing.(10) Detection of MOG-IgG1 allows distinction from MS and is generally indicative of a relapsing disease, mandating initiation of immunosuppression, even after the first attack in some, thereby reducing attack frequency and disability in the future.

Reference Values
Negative

Interpretation
A positive value for myelin oligodendrocyte glycoprotein (MOG)-IgG is consistent with an neuromyelitis optica (NMO)-like phenotype, and in the setting of acute disseminated encephalomyelitis (ADEM), optic neuritis and transverse myelitis indicates an autoimmune oligodendrogliopathy with potential for relapsing course. Identification of MOG-IgG allows distinction from MS and may justify initiation of appropriate immunosuppressive therapy (not MS disease-modifying agents) at the earliest possible time. This allows early initiation and maintenance of optimal therapy. Recommend follow-up in 3 to 6 months as persistence of MOG-IgG seropositivity predicts a relapsing course.

This autoantibody is not found in healthy subjects.

Cautions
Myelin oligodendrocyte glycoprotein (MOG)-IgG, specifically MOG-IgG1, may drop below detectable levels in setting of therapies for acute attack (IV methylprednisolone or plasmapheresis) or attack prevention (immunosuppressants).

Clinical Reference

**Performance**

**Method Description**
MOG-IgG1 Fluorescence-Activated Cell Sorting Assay (FACS)
Human embryonic kidney cells (HEK 293) are transfected transiently with a DNA plasmid that allows coexpression of both a reporter fluorescent protein (green fluorescent protein [AcGFP]) and full-length MOG. After 36 hours, a mixed population of cells (transfected expressing MOG on the surface and AcGFP in the cytoplasm and nontransfected lacking MOG and AcGFP) are lifted and resuspended in live cell-binding buffer. Cells are incubated with patient serum and an AlexaFluor 647-labeled secondary antibody is added. Two populations are gated on the basis of AcGFP expression: positive (high MOG expression) and negative (low or no MOG expression). Positivity is based on the ratio (Positive >2.5) of the median fluorescence intensity (MFI) of each cell population (MFI GFP positive:MFI GFP negative).(Unpublished Mayo method)

If MOG-IgG1 cell based flow cytometry (FACS) assay is positive at screening dilution, the MOG-IgG1 flow cytometry titer assay is performed at an additional charge.(Unpublished Mayo method)

**PDF Report**
No

**Day(s) Performed**
Monday, Tuesday, Thursday

**Report Available**
5 to 8 days

**Specimen Retention Time**
28 days

**Performing Laboratory Location**
Rochester
Test Definition: MOGFS
Myelin Oligodendrocyte Glycoprotein (MOG-IgG1) Fluorescence-Activated Cell Sorting (FACS) Assay, Serum

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
86363
86363-titer (if appropriate)

LOINC® Information

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