TEST ID: CDS1
CNS Demyelinating Disease Evaluation, Serum

Useful for:
- Diagnosis of inflammatory demyelinating diseases (IDDs) 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

Testing Algorithm
When the results of this assay require further evaluation of myelin oligodendrocyte glycoprotein (MOG-IgG1), the MOG-IgG1 titer will be performed at an additional charge.
When the results of this assay require further evaluation of neuromyelitis optica (NMO)/Aquaporin-4-IgG, the neuromyelitis optica (NMO)/aquaporin-4-IgG titer will be performed at an additional charge.
See CNS Demyelinating Evaluation Algorithm-Serum in Special Instructions.

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. The disorder is now recognized as a spectrum of autoimmunity (termed NMO spectrum disorders: NMOSD). Brain lesions are observed in more than 60% of patients with NMOSD and approximately 10% will be MS-like. Children tend to have greater brain involvement than adults, and brain lesions are more symptomatic than is typical for adult patients. 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.

Reference Values
- MOG FACS, S
  - Negative
  - Reference values apply to all ages.
- NMO/AQP4 FACS, S
  - Negative
  - Reference values apply to all ages.

Analytic Time
7 days

Specimen Required
- Type: Serum
- Container/Tube: Preferred: Red top
  - Acceptable: Serum gel
- Specimen Volume: 3 mL

Content and Values Subject to Change. See the Mayo Medical Laboratories Test Catalog for Current Information.
Approximately 80% of patients with NMO are seropositive for aquaporin-4 (AQP4)-IgG. In the remaining 20% of patients, myelin oligodendrocyte glycoprotein (MOG)-IgG is detected in up to a third. 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 oligodendrogliopathy) and clinical outcome (worse vs better) is different. Detection of MOG-IgG also predicts relapse. More importantly, however, is that MOG-IgG seropositive IDDs are distinct from MS and treated differently. 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 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.

Using a similar assay to our MOG-IgG1 flow cytometry assay, Wingerchuk et al 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.

Testing of 1,109 consecutive sera sent for AQP4-IgG testing, 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 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. A recent longitudinal analysis with 2 year follow-up suggested that persistence of MOG-IgG is associated with relapses thus warranting relapse preventing. Detection of MOG-IgG1 allows distinction from MS and is generally indicative of a relapsing course, mandating initiation of immunosuppression, even after the first attack in some, thereby reducing attack frequency and disability in the future.

INTERPRETATION

A positive value for aquaporin-4 (AQP4)-IgG is consistent with an autoimmune astrocytopathy/neuromyelitis optica spectrum disorder (NMOSD) and justifies initiation of appropriate immunosuppressive therapy at the earliest possible time. This allows early initiation and maintenance of optimal therapy. Recommend follow-up in 3 to 6 months if NMOSD is suspected.

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 (ON) and transverse myelitis (TM) indicates an autoimmune oligodendrogliopathy with potential for relapsing course. Identification of MOG-IgG allows distinction from multiple sclerosis (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.

Detection of both antibodies is rare and unusual.

AQP4-IgG and MOG-IgG are not found in MS or healthy subjects.