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## Overview

### Useful For

Diagnosis of multiple sclerosis and other demyelinating conditions

Evaluation of patients presenting with a clinically isolated syndrome, which is a clinical episode where patient reports symptoms (headaches, optic neuritis, fatigue and many others, depending on the disease location) characteristic of inflammation and demyelination of the central nervous system

A testing recommendation in cases where the imaging findings are atypical, and in populations in which multiple sclerosis is less common (eg, children, older individuals, or non-white populations)

The test **is not useful** when a clear diagnosis is already known because a positive result does not correlate with severity of the disease or disease outcomes.

### Method Name

Nephelometry

### NY State Available

Yes

## Specimen

### Specimen Type

CSF

### Ordering Guidance

For evaluation of multiple sclerosis, Multiple Sclerosis (MS) Profile, Serum and Spinal Fluid, SFIN / Cerebrospinal Fluid (CSF) IgG Index, Serum and Spinal Fluid in conjunction with OLIG / Oligoclonal Banding, Serum and Spinal Fluid are still available as individually orderable tests.

In addition, a multiple sclerosis profile (MSP3 / Multiple Sclerosis (MS) Profile, Serum and Spinal Fluid) is available.

This profile starts with immunoglobulin kappa free light chain testing and when that is borderline or elevated, additional testing for oligoclonal banding will be performed and results interpreted accordingly.

**Specimen Required****Specimen Type:** Spinal fluid**Container/Tube:** Sterile vial**Specimen Volume:** 1 mL**Collection Instructions:** Label specimen as spinal fluid.**Forms**

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

**Reject Due To**

Gross hemolysis    Reject  
Gross icterus        OK

**Specimen Minimum Volume**

0.5 mL

**Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
CSF	Frozen (preferred)	28 days	
	Refrigerated		
	Ambient		

**Clinical & Interpretive****Clinical Information**

Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system (CNS). The clinical diagnosis of MS is centered on each individual patient, while applying diagnostic guidelines. Immunoglobulin free light chain (FLC) presence in cerebrospinal fluid (CSF) is an alternative for diagnosis of MS using nephelometry. Light chains are produced in excess during antibody formation and secreted from the plasma-cells or plasma-blasts. Quantitative FLC assays use antisera directed against epitopes that are exposed only when the light chains are free (unbound to heavy chain) in solution. FLC immunoassays can be used to specifically quantitate FLC even in the presence of large concentrations of polyclonal immunoglobulins.

Routine use of isoelectric focusing electrophoresis coupled with IgG-specific immunoblotting (IgG-IEF) identifies immunoglobulins specific to the CNS. This method is part of the diagnostic criteria used in cases of MS, ie, oligoclonal banding (OLIG / Oligoclonal Banding, Serum and Spinal Fluid). However, oligoclonal banding is a labor-intensive technique that includes subjective interpretation of IgG bands from paired CSF and serum. This test, when considered positive at a concentration greater than or equal to 0.1000 mg/dL as a medical decision point, has a sensitivity of 70.4% with a specificity of 86.8%. The differences between this test and the oligoclonal banding analysis are not statistically significant ( $p=0.20$ ) and the 2 tests show comparable performance. However, this test does not require a paired serum specimen, offers a shorter turnaround-time for results, and an objective quantitative result.

This testing is most useful in patients presenting with a clinically isolated syndrome, which is a clinical episode where patient reports symptoms (headaches, optic neuritis, fatigue and many others, depending on the disease location) characteristic of inflammation and demyelination of the central nervous system, and need to be checked by a neurologist. This is when the likelihood of a diagnosis of multiple sclerosis is greater or most likely but not yet known or confirmed. CSF laboratory testing is also strongly recommended in cases where the imaging findings are atypical, and in populations in which multiple sclerosis is less common (eg, children, older individuals, or non-white populations).

**Reference Values**

Medical Decision Point: 0.1000 mg/dL

**Interpretation**

When result is less than 0.1000 mg/dL, the kappa free light chain concentration measured in CSF is lower than the threshold associated with demyelinating disease. This is a negative result. Clinical correlation recommended.

When result is greater than or equal to 0.1000 mg/dL, the kappa free light chain concentration measured in CSF is at or greater than the threshold associated with demyelinating disease. This is a positive result. These findings, however, are not specific for multiple sclerosis (MS) because CSF-specific immunoglobulin synthesis may also be detected in patients with other neurologic diseases (infectious, inflammatory, cerebrovascular, autoimmune, and paraneoplastic). Clinical correlation recommended.

**Cautions**

No significant cautionary statements

**Supportive Data**

The revised 2017 McDonald criteria established detection of at least 2 CSF-specific oligoclonal bands as a substitute for dissemination in time.(1) Dissemination in time means the lesions observed of the central nervous system (CNS) in imaging studies have to grow over time and that new lesions are expected and confirm disease progression. Before the 2017 revision, patients would wait up to 6 months for a confirmed diagnosis to fulfill the definitive diagnostic criteria for multiple sclerosis (MS).

Based on a published Mayo Clinic study with 325 subjects, this test alone demonstrates comparable performance to OLIG / Oligoclonal Banding, Serum and Spinal Fluid along with increased sensitivity for demyelinating diseases.(2) Replacing an OLIG / Oligoclonal Banding, Serum and Spinal Fluid test with the kappa free light chain test would alleviate the need for serum and CSF IgG and albumin, and calculated conversions.

A second, larger cohort of over 1300 patient samples analyzed at Mayo Clinic, where 159 participants had demyelinating disease, was reviewed to validate the results of the first study with 325 subjects.

In this larger cohort, the Mayo Clinic OLIG / Oligoclonal Banding, Serum and Spinal Fluid test had a clinical sensitivity of 74% and clinical specificity of 88% when 2 unique CSF bands are used as a cutoff for positive. The kappa free light chain test, when considered positive at a concentration greater than or equal to 0.1000 mg/dL as a medical decision point, has a sensitivity of 70% with a specificity of 87%. The differences between the 2 tests are not statistically significant (p=0.20). The 2 tests show comparable performance without the need of a paired serum specimen, shorter turn-around-time for results, and an objective quantitative result.(3)

### **Clinical Reference**

1. Thompson AJ, Banwell BL, Barkhof F, et al: Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *The Lancet Neurology*. 2018 Feb;17(2):162-173
2. Gurtner KM, Shosha E, Bryant SC, et al: CSF free light chain identification of demyelinating disease: comparison with oligoclonal banding and other CSF indexes. *Clin Chem Lab Med*. 2018;56:1071-1080
3. Saadeh R, Pittock S, Bryant S, et al: CSF kappa Free Light Chains as a Potential Quantitative Alternative to Oligoclonal Bands in Multiple Sclerosis. American Academy of Neurology Annual Meeting. Philadelphia, PA 2019
5. Awad A, Hemmer B, Hartung HP, et al: Analyses of cerebrospinal fluid in the diagnosis and monitoring of multiple sclerosis. *J Neuroimmunol*. 2010;219:1-7
6. Hassan-Smith G, Durant L, Tsentemidou A, et al: High sensitivity and specificity of elevated cerebrospinal fluid kappa free light chains in suspected multiple sclerosis. *J Neuroimmunol*. 2014;276:175-179
7. Presslauer S, Milosavljevic D, Brucke T, et al: Elevated levels of kappa free light chains in CSF support the diagnosis of multiple sclerosis. *J Neurol*. 2008;255:1508-1514
8. Presslauer S, Milosavljevic D, Brucke T, et al: Validation of Kappa Free Light Chains as a Diagnostic Biomarker in Multiple Sclerosis and Clinically Isolated Syndrome: A multicenter study. *MSJ* 2016;22(4):502-510
9. Presslauer S, Milosavljevic D, Hubl W, et al: Kappa Free Light Chains: Diagnostic and Prognostic Relevance in MS and CIS. *PLoS ONE* 2014;9(2):e89945

10. Presslauer S, Milosavljevic D, Hubl W, et al: Kappa Free Light Chains: Diagnostic and Prognostic Relevance in MS and CIS. PLoS ONE 2014;9(2):e89945

11. Makshakov G, Nazarov V, Kochetova O, et al: Diagnostic and Prognostic Value of the Cerebrospinal Fluid Concentration of Immunoglobulin Free Light Chains in Clinically Isolated Syndrome with Conversion to Multiple Sclerosis. PLoS ONE 2015;10(11):e0143375

## Performance

### Method Description

In this nephelometric method, the light scattered onto the antigen-antibody complexes is measured. The intensity of the measured scattered light is proportional to the amount of antigen-antibody complexes in the sample under certain conditions.

Antigen-antibody complexes are formed when a sample containing antigen and the corresponding antiserum are put into a cuvette. A light beam is generated with a light emitting diode (LED), which is transmitted through the cuvette. The light is scattered onto the immuno-complexes that are present. An antigen-antibody complex is formed in the final measurement.

The result is calculated by subtracting the value of the final measurement from the initial measurement. The distribution of intensity of the scattered light depends on the ratio of the particle size of the antigen-antibody complexes to the radiated wavelength. (Instruction manual: Siemens Nephelometer II. Siemens, Inc; Version 2.3, 2008; Addendum to the Instruction Manual 2.3, 08/2017)

### PDF Report

No

### Specimen Retention Time

14 days

### Performing Laboratory Location

Rochester

## Fees & Codes

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**Test Classification**

This test has been modified from the manufacturer's instructions. Its performance characteristics were 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**

83521

**LOINC® Information**

Test ID	Test Order Name	Order LOINC Value
KCSF	Kappa Free Light Chain, CSF	48774-4

Result ID	Reporting Name	LOINC®
KCSF	Kappa Free Light Chain, CSF	48774-4