Test Definition: KCSF

Immunoglobulin Kappa Free Light Chain, Spinal Fluid

Overview

Useful For

Diagnosing multiple sclerosis and other demyelinating conditions

Evaluating patients who present with a clinically isolated syndrome in which the 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

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)

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, SFIG / Cerebrospinal Fluid IgG Index Profile, Serum and Spinal Fluid and OLIG / Oligoclonal Banding, Serum and Spinal Fluid are available as individually orderable tests.

In addition, a multiple sclerosis cascade (MSP3 / Multiple Sclerosis [MS] Cascade, Serum and Spinal Fluid) is available. This profile starts with immunoglobulin kappa free light chain testing. If the result is borderline or elevated, additional testing for oligoclonal banding will be performed and results interpreted accordingly.

Specimen Required

Specimen Type: Spinal fluid (CSF)
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.

Specimen Minimum Volume

0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
CSF	Frozen (preferred)	28 days	
	Ambient	24 hours	
	Refrigerated	72 hours	

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 patient while applying diagnostic guidelines. Immunoglobulin free light chain (FLC) presence in cerebrospinal fluid (CSF) is an alternative for diagnosing MS using nephelometry. Light chains are produced in excess during antibody formation and secreted from plasma cells or plasmablasts. 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 identifies immunoglobulins specific to the CNS. This method is part of the diagnostic criteria used for 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 CNS, and needs to be checked by a neurologist. This is when the likelihood of a diagnosis of MS 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 MS is less common (eg, children, older individuals, or non-White populations).

Reference Values

Medical Decision Point: 0.1000 mg/dL
Positive: > or =0.1000 mg/dL
Borderline: 0.0600 mg/dL-0.0999 mg/dL
Negative <0.0600 mg/dL

Interpretation

When result is less than 0.0600 mg/dL, the kappa free light-chain concentration measured in cerebrospinal fluid (CSF) is lower than the threshold associated with demyelinating disease. This is a negative result. Clinical correlation is recommended.

When result is between 0.0600 and 0.0999 mg/dL, this is a borderline result. These findings 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). If clinically indicated, consider additional CSF testing such as oligoclonal banding by isoelectric focusing and CSF IgG index.

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 MS because CSF-specific immunoglobulin synthesis may also be detected in patients with other neurologic diseases (infectious, inflammatory, cerebrovascular, autoimmune, and paraneoplastic). If clinically indicated, consider additional CSF testing such as oligoclonal banding by isoelectric focusing and CSF IgG index.

A Mayo Clinic study published in 2018 with 325 patients suggested that a kappa free light-chain concentration in CSF greater than or equal to 0.06 mg/dL has 92.5% clinical sensitivity in the diagnosis of multiple sclerosis.(1)

A second, larger Mayo Clinic study with 1355 patients published in 2021 showed that a kappa CSF concentration greater than or equal to 0.06 mg/dL had approximately 89% sensitivity. When the kappa level was greater than or equal to 0.1 mg/dL, it had similar sensitivity (87%) to the finding of two unique CSF oligoclonal bands (89%).(2)

The 2024 revisions to the McDonald criteria for diagnosing multiple sclerosis (MS) added the kappa free light chain (kFLC) index as an appropriate paraclinical test.(3) The kFLC index is considered interchangeable with oligoclonal band (OBC) testing and may be used as evidence of a positive cerebrospinal fluid (CSF) result. This calculation requires kFLC measurements using CSF (KCSF / Immunoglobulin Kappa Free Light Chain, Spinal Fluid) and serum (FLCS / Immunoglobulin Free Light Chains, Serum) specimens as well as albumin measurements using CSF (ALBSF / Albumin, Spinal Fluid) and serum (ALB / Albumin, Serum) specimens. Mayo Clinic Laboratories has created a Kappa Index Calculator to assist in determining the multiple sclerosis diagnosis.

The weighted average sensitivity and specificity were 88% (range, 52%-100%) and 89% (range, 69%-100%), respectively,

for the kFLC index and 85% (range, 37%-100%) and 92% (range, 74%-100%), respectively, for OCB testing.(4) Studies comparing nephelometry and turbidimetry found no significant differences in kFLC index sensitivity relative to OCB testing, suggesting that the analytical platform does not affect the calculation.(4)

Cautions

No significant cautionary statements

Supportive Data

The revised 2017 McDonald criteria established detection of at least 2 cerebrospinal fluid (CSF)-specific oligoclonal bands as a substitute for dissemination in time.(3) Dissemination in time means the lesions observed of the central nervous system 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.

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.(1)

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.(2)

Clinical Reference

1. 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(7):1071-1080
2. Saadeh RS, Bryant SC, McKeon A, et al. CSF kappa free light chains: Cutoff validation for diagnosing multiple sclerosis. Mayo Clin Proc. 2022;97(4):738-751. doi:10.1016/j.mayocp.2021.09.014
3. Montalban X, Lebrun-Frenay C, Oh J, et al. Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria. Lancet Neurol. 2025;24(10):850-865. doi:10.1016/S1474-4422(25)00270-4
4. Hegen H, Walde J, Berek K, et al. Cerebrospinal fluid kappa free light chains for the diagnosis of multiple sclerosis: A systematic review and meta-analysis. Mult Scler. 2023;29(2):169-181. doi:10.1177/13524585221134213
5. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. The Lancet Neurology. 2018;17(2):162-173
6. 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
7. Awad A, Hemmer B, Hartung HP, Kieseier B, Bennett JL, Stuve O. Analyses of cerebrospinal fluid in the diagnosis and monitoring of multiple sclerosis. J Neuroimmunol. 2010;219(1-2):1-7
8. Hassan-Smith G, Durant L, Tsentemeidou A, et al. High sensitivity and specificity of elevated cerebrospinal fluid kappa free light chains in suspected multiple sclerosis. J Neuroimmunol. 2014;276(1-2):175-179
9. 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(10):1508-1514
10. 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. Mult Scler. 2016;22(4):502-10
11. Presslauer S, Milosavljevic D, Hubl W, Parigger S, Schneider-Koch G, Bruecke T. Kappa free light chains: Diagnostic and prognostic relevance in MS and CIS. PLoS One. 2014;9(2):e89945
12. Makshakov G, Nazarov V, Kochetova O, Surkova E, Lapin S, Evdoshenko E. 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 by the antigen-antibody complexes are 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, which is transmitted through the cuvette. The light is scattered by 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, 07/2019)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

1 to 3 days

Specimen Retention Time

14 days

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

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 account representative. For assistance, contact Customer Service.

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	Test Result Name	Result LOINC® Value
KCSF	Kappa Free Light Chain, CSF	48774-4