MAYO CLINIC LABORATORIES

Test Definition: MSP3

Multiple Sclerosis (MS) Profile, Serum and Spinal Fluid

Overview

Useful For

Diagnosing multiple sclerosis, especially helpful in patients with equivocal clinical or radiological findings

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
KCSFP	Kappa Free Light Chain, CSF	Yes, (KCSF)	Yes
XSRM	Additional sample for reflex OLIGS	No	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
OLIGS	Serum Bands	Yes, (Order OLIG, submit CSF and Serum)	No
OLIGC	CSF Bands	Yes, (Order OLIG, submit CSF and Serum)	No

Testing Algorithm

Kappa free light-chain testing will be performed by nephelometry on cerebral spinal fluid (CSF) samples. When kappa free light-chain testing indicates either borderline or positive results (> or =0.0600 mg/dL), the oligoclonal banding tests will be performed at an additional charge. If the time of testing exceeds the specimen stability for oligoclonal banding tests, only kappa free light-chain testing will be performed. Kappa free light-chain testing will only be performed up to specimen stability.

Special Instructions

- Central Nervous System Demyelinating Disease Diagnostic Algorithm

Method Name

KCSFP: Nephelometry
OLIGC, OLIGS: Isoelectric Focusing (IEF) with IgG Immunoblot Detection

NY State Available

Yes

Specimen

Specimen Type

CSF
Serum

Specimen Required

Both serum and spinal fluid are required. Spinal fluid must be obtained within 1 week of serum collection.

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

Specimen Type: Serum
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL
Collection Instructions:
1. Centrifuge and aliquot serum into a plastic vial within 2 hours of collection.
2. Label specimen as serum.

Forms

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

Specimen Minimum Volume

Serum, Spinal fluid: 0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
CSF	Frozen (preferred)	14 days	
	Refrigerated	72 hours	
	Ambient	24 hours	
Serum	Frozen (preferred)	14 days	
	Ambient	14 days	

	Refrigerated	14 days	

Clinical & Interpretive

Clinical Information

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease characterized by visual, motor, and sensory disturbances. The diagnosis of MS is dependent on clinical, radiological, and laboratory findings. The detection of increased intrathecal immunoglobulin synthesis is the basis for current diagnostic laboratory tests for MS. These tests include the kappa free light chain detection in cerebrospinal fluid (CSF) and CSF oligoclonal band detection.

Reference Values

KAPPA FREE LIGHT CHAIN
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

OLIGOCLONAL BANDS:
<2 bands

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. Testing for oligoclonal banding is not performed. 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). Clinical correlation is recommended. Automatic reflexing to oligoclonal bands will occur.

When result is 0.1000 mg/dL or more, 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). Clinical correlation is recommended. Automatic reflexing to oligoclonal bands will occur.

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% clinical sensitivity for the diagnosis of MS.(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 kappa value 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)

Given the difference in thresholds based on these studies and highest sensitivity at the threshold of 0.06 mg/dL, any CSF kappa free light-chain result greater than or equal to 0.06 mg/dL will reflex to oligoclonal banding when the multiple sclerosis profile test is ordered.

When the oligoclonal band assay detects 2 or more unique IgG bands in the CSF, the result is positive.

CSF is used in the diagnosis of MS by identifying increased intrathecal IgG synthesis qualitatively (oligoclonal bands). The presence of 2 or more unique CSF oligoclonal bands was reintroduced as one of the diagnostic criteria for MS in the 2017 revised McDonald criteria. These findings, however, are not specific for MS as CSF-specific IgG synthesis may also be found in patients with other neurologic diseases including infectious, inflammatory, cerebrovascular, and paraneoplastic disorders. Clinical correlation is recommended.

Cautions

Increased intrathecal immunoglobulin synthesis may occur in other inflammatory central nervous system diseases, and therefore, these assays are not specific for multiple sclerosis.

Supportive Data

In a cohort of 1307 patients, where 159 had demyelinating disease, the Mayo Clinic oligoclonal banding test had a clinical sensitivity of 74% and clinical specificity of 89%, area under the ROC curve of 0.813, when 2 or more unique cerebrospinal fluid (CSF) bands are used as a cutoff for positive. This 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 and the 2 tests show comparable performance with shorter turn-around-time for results and an objective quantitative result.

This panel combines the ease of use and interpretation of the quantitative measurement of kappa free light chains in CSF and allies it to the traditional interpretation of oligoclonal bands for optimized efficiency in laboratory testing for demyelinating diseases and improved test utilization.

Clinical Reference

1. McGinley MP, Goldschmidt CH, Rae-Grant AD: Diagnosis and treatment of multiple sclerosis: A review. JAMA. 2021;325(8):765-779. doi: 10.1001/jama.2020.26858
2. Hegen H, Walde J, Milosavljevic D, et al: Free light chains in the cerebrospinal fluid. Comparison of different methods to determine intrathecal synthesis. Clin Chem Lab Med. 2019;57(10):1574-1586. doi: 10.1515/cclm-2018-1300
3. Thompson AJ, Banwell BL, Barkhof F, et al: Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol. 2018;17(2):162-173
4. 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
5. 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
6. Hegen H, Zinganell A, Auer M, Deisenhammer F: The clinical significance of single or double bands in cerebrospinal fluid isoelectric focusing. A retrospective study and systematic review. PLoS One. 2019;14(4):e0215410. doi: 10.1371/journal.pone.0215410
7. Deisenhammer F, Zetterberg H, Fitzner B, Zettl UK: The Cerebrospinal fluid in multiple sclerosis. Front Immunol. 2019;10:726. doi: 10.3389/fimmu.2019.00726
8. Susse M, Hannich M, Petersmann A, et al: Kappa free light chains in cerebrospinal fluid to identify patients with

oligoclonal bands. Eur J Neurol. 2018;25(9):1134-1139. doi: 10.1111/ene.13667

Performance

Method Description

Kappa Free Light Chain:
Kappa free light chain is measured by nephelometric method in which 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 , 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)

Oligoclonal Banding:
The oligoclonal banding assay requires paired cerebrospinal fluid (CSF) and serum samples. Unconcentrated CSF and diluted serum are electrophoresed by isoelectric focusing. The separated IgG bands are visualized by an IgG immunoblot, and oligoclonal bands that are present in the CSF and not in the serum are reported. The assay uses reagents from Helena Laboratories.(Saadeh RS, Ramos PA, Algeciras-Schimnich A, Flanagan EP, Pittock SJ, Willrich MA. An Update on Laboratory-Based Diagnostic Biomarkers for Multiple Sclerosis and Beyond. Clin Chem. 2022;68(9):1134-1150. doi:10.1093/clinchem/hvac061)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

3 to 5 days

Specimen Retention Time

14 days

Performing Laboratory Location

Rochester

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
83916 x2 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MSP3	Multiple Sclerosis Profile	100757-4

Result ID	Test Result Name	Result LOINC® Value
KCSFP	Kappa Free Light Chain, CSF	48774-4
XSRM	Additional sample for Reflex OLIGS	No LOINC Needed