

Overview

Useful For

Monitoring patients with monoclonal gammopathies

This test is **not recommended** to screen or establish a first-time diagnosis for a monoclonal gammopathy.

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
SPE	Protein Electrophoresis	No	Yes
TMAB	Therapeutic Antibody Administered?	No	Yes
TPE	Total Protein	Yes, (Order TP)	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
MPTS	M-protein Isotype MALDI-TOF MS, S	Yes, (Order MALD)	No
IFXED	Immunofixation Delta and Epsilon, S	Yes	No

Testing Algorithm

This test includes total protein and serum protein electrophoresis.

If a discrete electrophoresis band is not identified, the laboratory will evaluate the serum protein electrophoresis and, if necessary, perform M-protein isotype at an additional charge.

If a light chain is identified without a corresponding heavy chain during initial testing, immunofixation with IgD and IgE antisera will be performed at an additional charge.

If a history of an IgD or IgE has been previously established and no M-spike is seen on electrophoresis, immunofixation with IgD and IgE antisera will be performed at an additional charge.

Method Name

TPE: Colorimetric, Biuret

SPE: Agarose Gel Electrophoresis

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

Protein electrophoresis alone is not considered an adequate screen for monoclonal gammopathies. When screening a patient or establishing a first-time diagnosis for a monoclonal gammopathy, consider ordering DMOGA / Monoclonal Gammopathy, Diagnostic, Serum instead, which includes free light chain analysis.

Specimen Required

Protein electrophoresis alone is not considered an adequate screen for monoclonal gammopathies. When screening a patient or establishing a first-time diagnosis for a monoclonal gammopathy, consider ordering DMOGA / Monoclonal Gammopathy, Diagnostic, Serum instead, which includes free light chain analysis.

Specimen Required

Patient Preparation: Fasting (12 hour) preferred but not required

Collection Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Submission Container/Tube: Plastic vial

Specimen Volume: 1 mL

Collection Instructions: Centrifuge and aliquot serum into plastic vial.

Specimen Minimum Volume

0.5 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	14 days	
	Frozen	14 days	
	Ambient	7 days	

Clinical & Interpretive

Clinical Information

This profile includes both total protein and protein electrophoresis. The serum proteins can be grouped into 5 fractions by protein electrophoresis:

- Albumin, which represents almost two-thirds of the total serum protein
- Alpha-1, composed primarily of alpha-1-antitrypsin (A1AT), an alpha-1-acid glycoprotein
- Alpha-2, composed primarily of alpha-2-macroglobulin and haptoglobin
- Beta, composed primarily of transferrin and C3
- Gamma, composed primarily of immunoglobulins

The concentration of these fractions and the electrophoretic pattern may be characteristic of diseases such as monoclonal gammopathies, A1AT deficiency disease, nephrotic syndrome, and inflammatory processes associated with infection, liver disease, and autoimmune diseases.

Reference Values

TOTAL PROTEIN:

> or =1 year: 6.3-7.9 g/dL

Reference values have not been established for patients younger than 12 months of age.

PROTEIN ELECTROPHORESIS:

Albumin: 3.4-4.7 g/dL

Alpha 1-Globulin: 0.1-0.3 g/dL

Alpha 2-Globulin: 0.6-1.0 g/dL

Beta-Globulin: 0.7-1.2 g/dL

Gamma-Globulin: 0.6-1.6 g/dL

An interpretive comment is provided.

Reference values have not been established for patients younger than 16 years of age.

Interpretation

Monoclonal Gammopathies:

A characteristic monoclonal band (M-spike) is often found on serum protein electrophoresis (SPE) in the gamma globulin region and, more rarely, in the beta or alpha-2 regions. The finding of an M-spike, restricted migration, or hypogammaglobulinemic SPE pattern is suggestive of a possible monoclonal protein. Immunoaffinity purification followed by matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS) is performed to identify any immunoglobulin heavy and light chains present.

-A monoclonal IgG or IgA of greater than 3 g/dL is consistent with multiple myeloma (MM).

-A monoclonal IgG or IgA of less than 3 g/dL may be consistent with monoclonal gammopathy of undetermined significance, primary systemic amyloidosis, early or treated myeloma, as well as a number of other monoclonal gammopathies.

-A monoclonal IgM of greater than 3 g/dL is consistent with macroglobulinemia.

-The initial identification of a serum M-spike greater than 1.5 g/dL on SPE should be followed by MPSU / Monoclonal Protein Study, 24 Hour, Urine.

-The initial identification of an IgM, IgA, or IgG M-spike greater than 4 g/dL, greater than 5 g/dL, and greater than 6 g/dL, respectively, should be followed by SVISC / Viscosity, Serum.

After the initial identification of an M-spike, quantitation of the M-spike on follow-up SPE can be used to monitor the monoclonal gammopathy. However, if the monoclonal protein falls within the beta region (most commonly an IgA or an

IgM), quantitative immunoglobulin levels may be a more useful tool to follow the monoclonal protein level than SPE. A decrease or increase of the M-spike that is greater than 0.5 g/dL is considered a significant change.

Patients suspected of having a monoclonal gammopathy may have normal SPE patterns. Approximately 11% of patients with MM have a completely normal SPE, with the monoclonal protein only identified by MALDI-TOF MS. Approximately 8% of MM patients have hypogammaglobulinemia without a quantifiable M-spike on SPE, but identified by MALDI-TOF MS. Accordingly, a normal serum SPE does not rule out the disease and should not be used to screen for the disorder. DMOGA / Monoclonal Gammopathy, Diagnostic, Serum, which includes MALDI-TOF MS and serum free light chains, conforms to the International Myeloma Working Group guidelines for screening and should be performed if there is clinical suspicion.

Other Abnormal SPE Findings:

- A qualitatively normal but elevated gamma fraction (polyclonal hypergammaglobulinemia) is consistent with infection, liver disease, or autoimmune disease.
- A depressed gamma fraction (hypogammaglobulinemia) is consistent with immune deficiency and can also be associated with primary amyloidosis or nephrotic syndrome.
- A decreased albumin (<2 g/dL), increased alpha-2 fraction (>1.1 g/dL), and decreased gamma fraction (<1 g/dL) is consistent with nephritic syndrome and, when seen in an adult older than 40 years, should be followed by MPSU / Monoclonal Protein Study, 24 Hour, Urine.
- In the hereditary deficiency of a protein (eg, agammaglobulinemia, alpha-1-antitrypsin [A1AT] deficiency, hypoalbuminemia), the affected fraction is faint or absent.
- An absent alpha-1 fraction is consistent with A1AT deficiency disease and should be followed by a quantitative A1AT assay (AAT / Alpha-1-Antitrypsin, Serum).

Cautions

Very large IgG M-spikes (>4 g/dL) may saturate the protein stain. In these situations, quantitative IgG assays (IGG / Immunoglobulin G, [IgG], Serum) should be performed to accurately determine M-spike concentrations to monitor disease progression or response to therapy.

Fibrinogen will migrate as a distinct band in the beta-gamma-fraction. Serum samples from new patients with a beta-gamma band are to be treated with thrombin to ensure complete conversion of fibrinogen.

Hemolysis may augment the beta fraction.

Penicillin may split the albumin band.

Radiographic agents may produce an uninterpretable pattern.

Clinical Reference

1. Mills JR, Kohlhagen MC, Dasari S, et al: Comprehensive assessment of M-Proteins using nanobody enrichment coupled to MALDI-TOF mass spectrometry. Clin Chem. 2016 Oct;62(10):1334-1344
2. Milani P, Murray DL, Barnidge DR, et al: The utility of MASS-FIX to detect and monitor monoclonal proteins in the clinic. Am J Hematol. 2017 Aug;92(8):772-779

Performance

Method Description

Electrophoresis:

Serum proteins are separated in an electric field according to their size, shape, and electric charge. The separation is performed on agarose gels. The proteins are visualized by staining with acid blue, and the intensity of staining is quantitated by densitometry. Multiplying by the serum total protein (Coomassie blue) converts the percentage of protein in each fraction into serum concentration. (Instruction manual: Helena SPIFE Touch. Helena Laboratories, Corporation; 11/2016; package insert: Helena SPIFE Touch SPE Pro 277. Helena Laboratories, Corporation; 06/2018)

Immunofixation:

Immunofixation is performed with Sebia reagent sets specific for delta and epsilon immunoglobulin heavy chains and kappa and lambda light chains. Immunofixation electrophoresis is performed in 4 stages: 1) separation of proteins by electrophoresis on an agarose gel; 2) immunofixation (immunoprecipitation) and fixation of the electrophoresed proteins; 3) removal of unprecipitated soluble proteins by blotting and washing; and 4) staining of the precipitated proteins for visualization. (Package insert: Sebia HYDRAGEL 1, 2, 4, and 9 IF kit. Sebia Inc; 07/2020)

M-protein Isotype:

M-protein isotype by matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS) is performed with immunoaffinity purification followed by MALDI-TOF MS analysis. For the immunoaffinity purification, patient serum is applied to 5 separate immunoaffinity resins (CaptureSelect, Life Sciences) specific to immunoglobulin G, A, M, K, and L. Unbound protein is washed away and the isolated immunoglobulins are broken down in to their reduced to separate the heavy and light chains subunits to be analyzed via MALDI-TOF mass spectrometry. The 5 separate spectra from each patient immunopurification are overlaid and investigated for an overabundance of immunoglobulin and immunoglobulin light chain. (Kohlhagen M, Dasari S, Willrich M, et al: Automation and validation of a MALDI-TOF MS (Mass-Fix) replacement of immunofixation electrophoresis in the clinical lab. Clin Chem Lab Med. 2020 Aug 3;59(1):155-163. doi: 10.1515/cclm-2020-0581)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

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

CPT Code Information

84155
84165
0077U (if appropriate)
86334 (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
TMOGA	Monoclonal Gammopathy Monitor, S	90991-1

Result ID	Test Result Name	Result LOINC® Value
TPE	Total Protein	2885-2
602837	Albumin	2862-1
602838	Alpha-1 Globulin	2865-4
602839	Alpha-2 Globulin	2868-8
602840	Beta-Globulin	2871-2
602841	Gamma-Globulin	2874-6
602842	A/G Ratio	44429-9
602843	M spike	51435-6
602844	M spike	35559-4
602836	Impression	49296-7
TMAB	Therapeutic Antibody Administered?	98855-0