MAYO CLINIC LABORATORIES

Test Definition: MPEP

Monoclonal Protein Study, Expanded Panel, Serum

Overview

Useful For

Diagnosis of monoclonal gammopathies

Eliminating the need for urine monoclonal studies as a part of initial diagnostic studies (ie, rule-out monoclonal gammopathy)

Assessing risk of progression from monoclonal gammopathy of undetermined significance to multiple myeloma

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
TPE	Total Protein	Yes, (order TP)	Yes
ELP	Protein Electrophoresis	Yes, (order PEL)	Yes
IMFX	Immunofixation	Yes, Order IMFXO)	Yes
KFLCS	Kappa Free Light Chain, S	Yes, (order FLCS)	Yes
LFLCS	Lambda Free Light Chain, S	Yes, (order FLCS)	Yes
KLRS	Kappa/Lambda FLC Ratio	Yes, (order FLCS)	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
IFXED	Immunofixation Delta and Epsilon, S	Yes	No

Testing Algorithm

Includes total protein, serum protein electrophoresis, and heavy-chain and light-chain typing (kappa and lambda). If a monoclonal light chain is detected in the absence of an associated monoclonal heavy chain, an immunofixation electrophoresis specific for delta and epsilon chains is performed.

Method Name

TPE: Biuret
ELP: Agarose Gel Electrophoresis
IMFX, IFXED: Immunofixation
KFLCS, LFLCS: Turbidimetry
KLRS: Calculation

NY State Available

No

Specimen

Specimen Type
Serum

Specimen Required
Patient Preparation:
Fasting: 8 hours, preferred but not required
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 2 mL serum
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Specimen Minimum Volume
1.5 mL

Reject Due To

Gross lipemia	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information
Monoclonal proteins are markers of plasma cell proliferative disorders. It is recommended that serum and urine protein electrophoresis (PEL) and immunofixation electrophoresis (IFE) be performed as part of the diagnostic algorithm (eg, MPSS / Monoclonal Protein Study, Serum and MPSU / Monoclonal Protein Study, 24 Hour, Urine). A monoclonal band (M-spike) on serum and/or urine PEL identifies a monoclonal process and quantitates the abnormality. IFE characterizes the type of monoclonal protein (gamma, alpha, mu, delta, or epsilon heavy chain; kappa [K] or lambda [L] light chain). IFE is also more sensitive than PEL for detecting small abnormalities that may be present in diseases such as light chain multiple myeloma, oligosecretory myeloma, and plasmacytomas.

With the addition of the serum free light-chain (FLC) assay, the expanded monoclonal protein study provides even more

diagnostic sensitivity for the monoclonal light-chain diseases such as primary amyloid and light-chain deposition disease; disorders that often do not have serum monoclonal proteins in high enough concentration to be detected and quantitated by PEL. The FLC assay is specific for free kappa and lambda light chains and does not recognize light chains bound to intact immunoglobulin. Importantly, the addition of the serum FLC assay to serum PEL and IFE makes the serum diagnostic studies sufficiently sensitive so that urine specimens are no longer required as part of initial diagnostic studies.

Monoclonal gammopathies may be present in a wide spectrum of diseases that include malignancies of plasma cells or B lymphocytes (multiple myeloma [MM], macroglobulinemia, plasmacytoma, B-cell lymphoma), disorders of monoclonal protein structure (primary amyloid, light-chain deposition disease, cryoglobulinemia), and apparently benign, premalignant conditions (monoclonal gammopathy of undetermined significance [MGUS], smoldering MM). While the identification of the monoclonal gammopathy is a laboratory diagnosis, the specific clinical diagnosis is dependent on a number of other laboratory and clinical assessments.

If a monoclonal protein pattern is detected by IFE or FLC, a diagnosis of a monoclonal gammopathy is established. Once a monoclonal gammopathy has been diagnosed, the size of the clonal abnormality can be monitored by PEL or FLC and, in some instances, by quantitative immunoglobulins. In addition, if the patient is asymptomatic and has a diagnosis of MGUS, the expanded monoclonal protein study panel provides the information (size of M-spike, monoclonal protein isotype, FLC K/L ratio) needed for a MGUS progression risk assessment (see Interpretation).

Reference Values

PROTEIN, TOTAL
> or =1 year: 6.3-7.9 g/dL
Reference values have not been established for patients that are 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
M-spike: 0.0 g/dL
An interpretive comment is provided with the report.
Reference values have not been established for patients that are younger than 16 years of age

IMMUNOFIXATION
Immunofixation: No monoclonal protein detected
Flag, Immunofixation: Negative

KAPPA-FREE LIGHT CHAIN
0.33-1.94 mg/dL

LAMBDA-FREE LIGHT CHAIN
0.57-2.63 mg/dL

KAPPA/LAMBDA-FREE LIGHT-CHAIN RATIO
0.26-1.65

Interpretation

Monoclonal Gammopathies:
-A characteristic monoclonal band (M-spike) is often found on protein electrophoresis (PEL) 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 PEL pattern is suggestive of a possible monoclonal protein. Immunofixation electrophoresis (IFE) is performed to identify the immunoglobulin heavy chain and/or light chain.
-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 (MGUS), 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.
-An abnormal serum free light chain (FLC) kappa/lambda (K/L) ratio in the presence of a normal IFE suggests a monoclonal light-chain process and should be followed by MPSU / Monoclonal Protein Study, 24 Hour, Urine.
-The initial identification of a serum M-spike greater than 1.5 g/dL on PEL 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 VISCS / Viscosity, Serum.
-After the initial identification of a monoclonal band, quantitation of the M-spike on follow-up PEL 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 more a useful tool to follow the monoclonal protein level than PEL. A decrease or increase of the M-spike that is greater than 0.5 g/dL is considered a significant change.
-Patients with monoclonal light chain diseases who have no serum or urine M-spike may be monitored with the serum FLC value.
-Patients suspected of having a monoclonal gammopathy may have normal serum PEL patterns. Approximately 11% of patients with MM have a completely normal serum PEL, with the monoclonal protein only identified by IFE. Approximately 8% of MM patients have hypogammaglobulinemia without a quantifiable M-spike on PEL but identified by IFE and/or FLC. Accordingly, a normal serum PEL does not rule out the disease and PEL alone should not be used to screen for the disorder if the clinical suspicion is high.

MGUS Prognosis:
-Low-risk MGUS patients are defined as having an M-spike of less than 1.5 g/dL, IgG monoclonal protein, and a normal FLC K/L ratio (0.25-1.65), and these patients have a lifetime risk of progression to MM of less than 5%.
-High-risk MGUS patients (M-spike >1.5, IgA or IgM, abnormal FLC ratio) have a lifetime risk of progression to MM of 60%.

Other Abnormal PEL 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 (>1.2 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

Protein electrophoresis (PEL) alone is not considered an adequate screen for monoclonal gammopathies.

Very large IgG M-spikes (>4 g/dL) may saturate the protein stain. In these situations, quantitative IgG assays more accurately determine M-spike concentrations for monitoring disease progression or response to therapy.

Although the PEL M-spike is the recommended method of monitoring monoclonal gammopathies, IgA and IgM proteins that are contained in the beta fraction may be more accurately monitored by quantitative immunoglobulins.

Fibrinogen will migrate as a distinct band in the beta-gamma fraction but will be negative on immunofixation electrophoresis.

Hemolysis may augment the beta fraction.

Penicillin may split the albumin band.

Radiographic agents may produce an uninterpretable pattern.

Clinical Reference

1. Keren DF, Humphrey RL: Clinical indications and applications of serum and urine protein electrophoresis. In: Detrick BD, Hamilton RG, Schmitz JL, eds. Manual of Molecular and Clinical Laboratory Immunology. 8th ed. 2016:chap 8
2. Rajkumar SV, Kyle RA, Therneau TM, et al: Serum free light chain ratio is an independent risk factor for progression in monoclonal gammopathy of undetermined significance. Blood. 2005;106:812-817
3. Katzmann JA, Dispenzieri A, Kyle RA, et al: Elimination of the need for urine studies in the screening algorithm for monoclonal gammopathies by using serum immunofixation and free light chain assays. Mayo Clin Proc. 2006;81(12):1575-1578
4. Katzmann JA, Keren DF. Strategy for detecting and following monoclonal gammopathies. In: Detrick BD, Hamilton RG, Schmitz JL, eds. Manual of Molecular and Clinical Laboratory Immunology. 8th ed. ASM Press; 2016:112-124

Performance

Method Description

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 amido black and the intensity of staining is

quantitated by densitometry (Sebia HYDRASYS 2 Scan). Multiplying by the serum total protein converts the percentage of protein in each fraction into serum concentration.(Package insert: Hydragel 30 Protein [E]. Sebia, Inc; 12/2017)

Immunofixation:
Immunofixation is performed with Sebia reagent sets and are specific for gamma, alpha, mu, kappa, and lambda immunoglobulin heavy and light chains.(Package insert: Sebia Hydrasys Hydragel 1, 2, 4, 9IF, Sebia Inc; 09/2015)

Free Light Chains:
The quantitation of free light chain (FLC) by turbidimetry uses FLC antisera. Undetected antigen excess is a rare event but cannot be excluded. If the free light chain results do not agree with other clinical or laboratory findings, or if the sample is from a patient that has previously demonstrated antigen excess, the result must be checked by retesting at a higher sample dilution. Results should always be interpreted in conjunction with other laboratory tests and clinical evidence; any anomalies should be discussed with the testing laboratory.(Package inserts: Optilite Freelite Kappa Free Kit. The Binding Site Group, Ltd; 06/2015; Optilite Freelite Lambda Free Kit. The Binding Site Group, Ltd; 06/2015)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
Same day/1 to 2 days

Specimen Retention Time
7 days

Performing Laboratory Location
Mayo Clinic Jacksonville Clinical Lab

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 cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

83521 x 2
84155
84165
86334
86334-Immunofixation Delta and Epsilon (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MPEP	Monoclonal Protein Expanded Panel,S	In Process

Result ID	Test Result Name	Result LOINC® Value
81653	Immunofixation	74665-1
606977	Flag, Immunofixation	No LOINC Needed
TPE	Total Protein	2885-2
2769	Albumin	2862-1
2770	Alpha-1 Globulin	2865-4
2771	Alpha-2 Globulin	2868-8
2773	Beta-Globulin	2871-2
2774	Gamma-Globulin	2874-6
2785	A/G Ratio	44429-9
22308	M spike	33358-3
22309	M spike	33358-3
15254	Impression	49296-7
LFLCS	Lambda Free Light Chain, S	33944-0
KLRS	Kappa/Lambda FLC Ratio	104546-7
KFLCS	Kappa Free Light Chain, S	104544-2