Overview

Useful For
Screening patients with suspected monoclonal gammopathies

Diagnosis of monoclonal gammopathies, when used in conjunction with matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS) and free light chains

Profile Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>TPE</td>
<td>Total Protein</td>
<td>Yes, (Order TP)</td>
<td>Yes</td>
</tr>
<tr>
<td>SPE</td>
<td>Protein Electrophoresis</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Reflex Tests

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMFX</td>
<td>Immunofixation</td>
<td>Yes, (Order IMFXO)</td>
<td>No</td>
</tr>
<tr>
<td>MPTS</td>
<td>M-protein Isotype MALDI-TOF MS, S</td>
<td>Yes, (Order MALDO)</td>
<td>No</td>
</tr>
</tbody>
</table>

Testing Algorithm

This test includes total protein and serum protein electrophoresis.

If a discrete electrophoresis band is 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.

The following algorithms are available in Special Instructions:

- Laboratory Approach to the Diagnosis of Amyloidosis
- Laboratory Screening Tests for Suspected Multiple Myeloma

Special Instructions

- Laboratory Approach to the Diagnosis of Amyloidosis
- Laboratory Screening Tests for Suspected Multiple Myeloma

Method Name

TPE: Biuret

SPE: Agarose Gel Electrophoresis
NY State Available
Yes

Specimen

Specimen Type
Serum

Advisory Information
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 SMOGA / Monoclonal Gammopathy Screen, Serum instead, which includes free light chain analysis.

If free light chain testing has already been performed locally, SPISO / Protein Electrophoresis and Isotype, Serum may be ordered instead of SMOGA / Monoclonal Gammopathy Screen, Serum for a first-time diagnosis.

For monitoring patients with a diagnosis of monoclonal gammopathy, order MMOGA / Monoclonal Gammopathy Monitoring, Serum.

Necessary Information
Indicate if multiple myeloma is suspected.

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

Container/Tube:

Preferred: Serum gel
Acceptable: Red top

Specimen Volume: 1 mL

Specimen Minimum Volume
0.5 mL

Reject Due To

<table>
<thead>
<tr>
<th>Gross hemolysis</th>
<th>OK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross lipemia</td>
<td>OK</td>
</tr>
<tr>
<td>Gross icterus</td>
<td>OK</td>
</tr>
</tbody>
</table>

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Refrigerated (preferred)</td>
<td>14 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td>14 days</td>
<td></td>
</tr>
</tbody>
</table>
Clinical and 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 that are <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 with the report.

Reference values have not been established for patients that are <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 a M-spike, restricted migration, or hypogammaglobulinemic SPE pattern is suggestive of a possible monoclonal protein and should be confirmed by immunoaffinity-purification matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS) to identify any immunoglobulin heavy or light chains. A MPSU / Monoclonal Protein Study, Urine is suggested for first-time M-spike patients to assess for renal disease that can be associated with an M-spike.

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

-A monoclonal IgG or IgA 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 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 VISCS / 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 more a 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 serum SPE patterns. Approximately 11% of patients with MM have a completely normal serum 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. The SMOGA / Monoclonal Gammopathy Screen, Serum, which includes MALDI-TOF MS, and serum free light chains, conforms to the International Myeloma Working Group (IMWG) 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 nephrotic 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 specimens 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


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 (Helen Quick Scan 2000). Multiplying by the serum total protein (Coomasie blue) converts the percentage of protein in each fraction into serum concentration.(Helena SPIFE 3000 Instruction Manual and Helen SPIFE SPE Vis Gel package insert 2001; Kyle RA, Katzmann JA, Lust JA, Dispenzieri, A: Clinical indications and applications of electrophoresis and immunofixation. In Manual of Clinical Laboratory Immunology. Sixth Edition. Edited by NR Rose, et al. Washington DC. ASM Press, 2002 p 71-91)

M-protein Isotype matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS):

M-protein isotype by 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 into 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.(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, 92(8):772-779 doi: 10.1002/ajh.24772)
Test Definition: SPEP
Electrophoresis, Protein, S

No

Day(s) and Time(s) Test Performed
TPE, SPE, IMFX:
Monday through Saturday; 1 p.m.

MPTS:
Monday through Friday; 8 a.m.

Analytic Time
Same day/1 day

Maximum Laboratory Time
3 days

Specimen Retention Time
14 days

Performing Laboratory Location
Rochester

Fees and 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 Regional Manager. For assistance, contact Customer Service.

Test Classification
See Individual Test IDs

CPT Code Information
84155

84165

0077U (if appropriate)

86334 (if appropriate)

LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPEP</td>
<td>Electrophoresis, Protein, S</td>
<td>24351-9</td>
</tr>
</tbody>
</table>
### Test Definition: SPEP
Electrophoresis, Protein, S

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TPE</td>
<td>Total Protein</td>
<td>2885-2</td>
</tr>
<tr>
<td>602837</td>
<td>Albumin</td>
<td>2862-1</td>
</tr>
<tr>
<td>602838</td>
<td>Alpha-1 Globulin</td>
<td>2865-4</td>
</tr>
<tr>
<td>602839</td>
<td>Alpha-2 Globulin</td>
<td>2868-8</td>
</tr>
<tr>
<td>602840</td>
<td>Beta-Globulin</td>
<td>2871-2</td>
</tr>
<tr>
<td>602841</td>
<td>Gamma-Globulin</td>
<td>2874-6</td>
</tr>
<tr>
<td>602842</td>
<td>A/G Ratio</td>
<td>44429-9</td>
</tr>
<tr>
<td>602843</td>
<td>M spike</td>
<td>51435-6</td>
</tr>
<tr>
<td>602844</td>
<td>M spike</td>
<td>35559-4</td>
</tr>
<tr>
<td>602836</td>
<td>Impression</td>
<td>49296-7</td>
</tr>
</tbody>
</table>