Complement Testing

Indications for Ordering

Individuals with recurring infections and/or symptoms of autoimmune and antigen complex diseases

Test Description

Complement Activity Enzyme Immunoassay, Total
- Semiquantitative enzyme-linked immunosorbent assay

Complement Activity, Alternative Pathway (AH50)
- Semiquantitative radial immunodiffusion

Mannose Binding Lectin
- Quantitative enzyme-linked immunosorbent assay

Tests to Consider

Primary tests
Initial screening for functional ability of the complement system

Complement Activity Enzyme Immunoassay, Total 0050198
- Tests for defects in the classical complement pathway

Complement Activity, Alternative Pathway (AH50) 2005373
- Tests for defects in the alternative complement pathway

Mannose Binding Lectin 0051692
- Tests for defects in the lectin complement pathway

Related tests
The following tests should be ordered based on presentation, initial test results, and clinical suspicion for deficiency:
- Complement Component 5 0050156
- Complement Component 7 0099073
- Complement Component 8 0099074
- Complement Component 9 0099076
- Complement Factor B 0051720

Disease Overview

Prevalence and/or incidence – complement deficiency accounts for ~2% of immunodeficiency, autoimmune, and immune complex syndromes

Symptoms
- Recurring infections, predominantly with pyogenic organisms:
  - H. influenza
  - S. pneumoniae
  - Neisseria spp
  - Endocarditis
- Immune complex diseases:
  - Acute glomerulonephritis
  - Membranoproliferative glomerulonephritis
  - Systemic lupus erythematosus (SLE)
  - Serum sickness
  - Chronic hepatitis:
    - HBV
    - HCV

Physiology
- Complement system
  - Plays a role in host defense and inflammation response
  - Controls microbial infections
  - Prevents immune complex diseases
- Plasma enzymes, regulatory proteins, and other proteins are activated in cascading fashion, leading to
  - Lysis of cell membranes
  - Subsequent cell death of infectious agent
- Complement cascade activation can occur with several activating mechanisms via three pathways:
  - Classical pathway
  - Alternative pathway
  - Lectin pathway
- All three pathways converge into a final terminal pathway
- Deficiencies of any of the proteins within these pathways will alter complement functionality
  - Often leads to recurring infections, or autoimmune or immune complex diseases
### Test Interpretation

#### Results

**Complement Activity Enzyme Immunoassay, Total**
- Normal – 60-144 CAE units
- Low – ≤59 CAE units
  - Suspect defect in classical or terminal complement pathway

**Complement Activity, Alternative Pathway (AH50)**
- Normal – ≥59% of control
- Abnormal – <59% of control
  - Suspect defect in alternative or terminal complement pathway

**Mannose Binding Lectin**
- Normal – 60-144 CAE units
- Low – ≤59 CAE units
  - Suspect defect in lectin complement pathway
- High – ≥145 CAE units

#### Limitations
- Does not evaluate individual components of the alternative pathway
- Complement activation can occur during blood draw
  - Rare

### Interpretation of Combined Testing

<table>
<thead>
<tr>
<th>Complement pathway screening results</th>
<th>Complement pathway likely affected</th>
<th>Suggested follow-up testing for levels and/or function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAE – low or absent</td>
<td>Classical</td>
<td>C1, C2, C4, depending on clinical presentation</td>
</tr>
<tr>
<td>AH50 – normal</td>
<td></td>
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<tr>
<td>MBL – normal</td>
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<td></td>
</tr>
<tr>
<td>CAE – low or absent</td>
<td>Terminal</td>
<td>C3, C5-C9, factors H and I, depending on clinical presentation</td>
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<tr>
<td>AH50 – low or absent</td>
<td></td>
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<tr>
<td>MBL – normal</td>
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</tr>
<tr>
<td>CAE – normal</td>
<td>Alternative</td>
<td>Factors B and D, properdin, depending on clinical presentation</td>
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<tr>
<td>AH50 – low</td>
<td></td>
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<tr>
<td>MBL – normal</td>
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<td></td>
</tr>
<tr>
<td>CAE – normal</td>
<td>Lectin</td>
<td>n/a</td>
</tr>
<tr>
<td>AH50 – normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MBL – low or absent</td>
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</tr>
</tbody>
</table>

*Available testing

AH50, complement alternative pathway; CAE, complement activity enzyme; MBL, mannose binding lectin