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 2 – 0050148
  • Complement Component Level 3a – 2003304
  • Complement Component Level 4a – 2003180
  • Complement Component 5 – 0050156
  • Complement Component Level 6 – 0099072
  • Complement Component 7 – 0099073
  • Complement Component 8 – 0099074
  • Complement Component 9 – 0099076
  • Complement Factor B – 0051720
  • Complement Factor H Level (B-1H) – 2009416
  • Complement Factor I – 2009382

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
    o H. influenzae
    o S. pneumoniae
    o Neisseria spp.
    o Endocarditis
  • Immune complex diseases
    o Acute glomerulonephritis
    o Membranoproliferative glomerulonephritis
    o Systemic lupus erythematosus (SLE)
    o Serum sickness
    o Chronic hepatitis
  ▪ HBV
  ▪ HCV

Physiology

  • Complement system
    o Plays a role in host defense and inflammation response
    o Controls microbial infections
    o Prevents immune complex diseases
  • Plasma enzymes, regulatory proteins, and other proteins are activated in cascading fashion, leading to
    o Lysis of cell membranes
    o Subsequent cell death of infectious agent
  • Complement cascade activation can occur with several activating mechanisms via 3 pathways
    o Classical pathway
    o Alternative pathway
    o Lectin pathway
  • All 3 pathways converge into a final terminal pathway
  • Deficiencies of any of the proteins within these pathways will alter complement functionality
    o 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
    o 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

<table>
<thead>
<tr>
<th>Interpretation of Combined Testing</th>
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<tbody>
<tr>
<td>Complement pathway screening results*</td>
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<tr>
<td>-----------------------------------</td>
</tr>
<tr>
<td>• CAE – low or absent</td>
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<tr>
<td>• AH50 – normal</td>
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</tbody>
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* Available testing
CAE = Complement Activity Enzyme Immunoassay, Total, AH50 = Complement Activity, Alternative Pathway (AH50), MBL = Mannose Binding Lectin