Autoimmune Hepatitis Diagnostic Panel

**Test Code:** 19873(X)

**Specimen Requirements:** 2.5 mL refrigerated serum; 0.6 mL minimum

**CPT Codes**: 83516, 86038, 86255, 86376

**CLINICAL USE**
- Diagnose autoimmune hepatitis (AIH)
- Differentiate AIH from primary biliary cirrhosis (PBC)
- Monitor disease activity in children with AIH

**CLINICAL BACKGROUND**
AIH is a chronic disorder characterized by progressive hepatocellular loss and cell-mediated immunologic attack. Histologic inflammation is present and is usually accompanied by fibrosis, which can progress to cirrhosis and liver failure. AIH accounts for 11% to 23% of chronic liver disease in North America and about 4% to 6% of adult liver transplants in the United States and Europe. Early diagnosis and initiation of immunosuppressive therapy are essential to prevent severe liver damage.

Although patients may present with acute symptoms (eg, arthralgia), about 34% to 45% are asymptomatic and are identified subsequent to abnormal liver function tests such as increased alanine and/or aspartate aminotransferase (generally <500 U/L but occasionally 500 U/L to 1000 U/L). Elevated levels of globulin, gamma globulin, or immunoglobulin G (≥1.5 times the upper limit of the reference ranges) are typically present. Because the clinical features of AIH overlap with other forms of hepatitis, ruling out hereditary, infectious, and toxicity-related causes of liver disease is an important component of diagnosis. Interface hepatitis (piecemeal necrosis) in liver biopsy tissue is considered essential for diagnosis; portal plasma cell infiltration is typically present but not specific for AIH.

Once other causes of hepatitis have been excluded, several autoantibody markers are useful to support AIH diagnosis. The AIH Diagnostic Panel includes tests for actin (smooth muscle) antibody, antinuclear antibodies (ANAs), and liver/kidney microsome antibody (LKM-1). ANAs and actin antibody are associated with type 1 AIH, the most common form in adults in the United States, while LKM-1 antibody is associated with type 2 AIH, which is more commonly found in children. The panel also includes mitochondrial antibody, which can help differentiate AIH from PBC (see Interpretive Information below). Remission after initiation of immunosuppressive therapy confirms the diagnosis of AIH.

Antibody titers have been found to correlate with disease activity in pediatric AIH patients, whereas the correlation in adults is less clear.

**INDIVIDUALS SUITABLE FOR TESTING**
- Individuals with chronic or acute hepatitis of unknown cause
- Individuals with allograft dysfunction after liver transplantation

**METHOD**
- Actin (smooth muscle) antibody (IgG): enzyme-linked immunosorbent assay (ELISA)
- ANA screen: IFA with reflex to titer and pattern when screen is positive (at additional charge [CPT code 86039])
- Liver kidney microsomal (LKM-1) antibody (IgG): ELISA
- Mitochondrial antibody screen: immunofluorescence assay (IFA) with reflex to titer when screen is positive (at additional charge [CPT code 86256])

### Table. Antibody Frequencies (%) Observed in AIH and PBC

<table>
<thead>
<tr>
<th></th>
<th>Actin Antibody</th>
<th>ANA</th>
<th>LKM-1 Antibody</th>
<th>Mitochondrial Antibody</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIH type 1</td>
<td>72</td>
<td>67</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>AIH type 2</td>
<td>27b</td>
<td>--a</td>
<td>100</td>
<td>--a</td>
</tr>
<tr>
<td>PBC</td>
<td>30</td>
<td>50</td>
<td>--</td>
<td>85</td>
</tr>
</tbody>
</table>

AIH, autoimmune hepatitis; PBC, primary biliary cirrhosis; ANA, antinuclear antibody; LKM, liver kidney microsome.

Typically absent.

Data are from one study, n = 22.
Panel components can be ordered separately: actin (smooth muscle) antibody IgG (15043), ANA screen (249), LKM-1 antibody (15038), mitochondrial antibody screen (259).

**REFERENCE RANGE**

<table>
<thead>
<tr>
<th>Test Description</th>
<th>Negative</th>
<th>Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actin (smooth muscle) antibody (IgG)</td>
<td>&lt;20 U</td>
<td>≥20 U</td>
</tr>
<tr>
<td>ANA screen (IFA)</td>
<td>&lt;1:40</td>
<td>≥1:40 U</td>
</tr>
<tr>
<td>Liver kidney microsome (LKM-1) antibody (IgG)</td>
<td>&lt;20 U</td>
<td>20.1-24.9 U</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥25.0 U</td>
</tr>
<tr>
<td>Mitochondrial antibody screen</td>
<td>&lt;1:20</td>
<td>≥1:20 U</td>
</tr>
</tbody>
</table>

**INTERPRETIVE INFORMATION**

Antibody patterns associated with AIH types 1 and 2 and PBC are shown in the Table. During the course of AIH type 1, actin antibody and ANAs frequently disappear and reappear; thus, negative or weak positive antibody results do not rule out the presence of the disease. Furthermore, patients with negative results in whom other AIH diagnostic criteria are satisfied (13% of patients with AIH) may have soluble liver antigen and/or antineutrophil cytoplasmic antibodies.

The presence of LKM-1 antibody is consistent with AIH type 2. However, LKM-1 antibody has been detected in up to 10% of patients with chronic hepatitis C virus (HCV) infection; if not previously performed, testing for HCV infection should be considered for patients in whom LKM-1 is positive.

Detection of mitochondrial antibody, typically absent in AIH, has a sensitivity of 85% and specificity of 98% for PBC.

Since autoantibody levels in AIH types 1 and 2 are lower in children than in adults, a weak positive or equivocal antibody result in conjunction with other diagnostic criteria may be sufficient for diagnosis in children. Actin (smooth muscle) antibody, but not ANA, titers correlate with disease activity in children with type 1 AIH. For children with type 2 AIH, disease activity correlates with LKM-1 antibody titers.

The presence of immune complexes or other immunoglobulin aggregates in the specimen may lead to false-positive ELISA results. Antibody results should be interpreted in conjunction with other laboratory and clinical findings in patients with suspected AIH.

**References**


* The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.