Autoimmune Neuropathies

Indications for Ordering

Evaluation of autoimmune neuropathies

**Test Description**

- Semiquantitative indirect fluorescent antibody (IFA)
  - Neuronal nuclear antibody (ANNA-1 and ANNA-2)
  - Purkinje cell cytoplasmic antibody-1 (PCCA-1)
- Qualitative immunoblot assay
  - Neuronal nuclear antibodies (Hu, Ri, and Yo)
- Semiquantitative enzyme-linked immunosorbent assay
  - Myelin-associated glycoprotein (MAG) antibodies
  - Sulfate-3-glucuronyl paragloboside (SGPG)
  - Ganglioside (Asialo-GM1, GM1, GM2, GD1a, GD1b, and GQ1b) antibodies

**Tests to Consider**

Typical testing strategy
Initial testing to rule out other, more common diseases

- Infectious
  - Complete blood count
  - Cerebral spinal fluid testing for protein, cell count, glucose, and culture
- Metabolic
  - Electrolytes
  - Vitamin B12
- Inflammatory
  - Erythrocyte sedimentation rate or C-reactive protein
  - Elevations in either might suggest connective tissue disease or vasculitis evaluation (eg, ANA, ANCA)
- Other testing based on individual presentation
  - *Campylobacter jejuni* (stool specimen)
  - *Mycoplasma pneumoniae*
  - Hepatitis virus
  - HIV

Neuronal marker testing

- Choice of panel – based on clinical manifestations
  - Sensory only (typical)
  - Sensorimotor
  - Motor predominant
- Age – aids in decision about whether to test for underlying cancer/tumor
- Risk or presence of specific malignancy – may determine appropriate antibody tests

### Antibody Components

<table>
<thead>
<tr>
<th>Primary Tests for Autoimmune Neuropathies</th>
<th>2007965 Sensory Antibody Panel</th>
<th>2007966 Motor &amp; Sensory</th>
<th>2007967 Motor &amp; Sensory with IFE</th>
<th>0051225 Motor Panel</th>
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</thead>
<tbody>
<tr>
<td>Purkinje cell/neuronal nuclear IgG</td>
<td>√</td>
<td>√</td>
<td>√</td>
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<td>Purkinje cell antibody titer</td>
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<tr>
<td>Neuronal nuclear (Hu, Ri, and Yo) IgG</td>
<td>√</td>
<td>√</td>
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<tr>
<td>Neuronal nuclear antibody (ANNA) IgG</td>
<td>√</td>
<td>√</td>
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<tr>
<td>MAG IgM</td>
<td>√</td>
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<tr>
<td>SGPG IgM</td>
<td>√</td>
<td>√</td>
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<tr>
<td>Asialo-GM1 IgG and IgM</td>
<td></td>
<td>√</td>
<td></td>
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<tr>
<td>IgG and IgM for GM1, GD1a, GD1b</td>
<td></td>
<td>√</td>
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<tr>
<td>GQ1b antibodies</td>
<td>√</td>
<td>√</td>
<td></td>
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<tr>
<td>Total protein electrophoresis, serum</td>
<td></td>
<td>√</td>
<td></td>
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<tr>
<td>Albumin</td>
<td></td>
<td>√</td>
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<tr>
<td>Alpha-1 and alpha-2 globulins</td>
<td></td>
<td>√</td>
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<tr>
<td>Beta globulins</td>
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<tr>
<td>Gamma globulins</td>
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<tr>
<td>Immunoglobulins A, G, M</td>
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*Primary tests*

**Sensory Neuropathy Antibody Panel with Reflex to Titer and Neuronal Immunoblot 2007965**
- Aid in diagnosis of a sensory neuropathy when malignancy, other than plasma cell dyscrasia, is suspected

**Motor and Sensory Neuropathy Evaluation with Reflex to Titer and Neuronal Immunoblot 2007966**
- Aid in diagnosis of combined motor/sensory neuropathy when malignancy, other than plasma cell dyscrasia, is suspected

**Motor and Sensory Neuropathy Evaluation with Immunofixation Electrophoresis and Reflex to Titer and Neuronal Immunoblot 2007967**
- Aid in diagnosis of combined motor/sensory neuropathy with suspicion for plasma cell dyscrasia or suspicion for other malignancy

**Motor Neuropathy Panel 0051225**
- Aid in diagnosis of motor neuropathy with suspicion for plasma cell dyscrasia
Related Tests
Paraneoplastic Reflexive Panel 2013955
Paraneoplastic Antibodies (PCCA/ANNA) by IFA with Reflex to Titer and Immunoblot 2007961
Myelin Associated Glycoprotein (MAG) Antibodies, IgM and Sulfate-3-Glucuronyl Paragloboside (SGPG) Antibodies, IgM 2004412
Ganglioside (Asialo-GM1, GM1, GM2, GD1a, GD1b, and GQ1b) Antibodies 0051033
Sulfate-3-Glucuronyl Paragloboside (SGPG) Antibody, IgM 0051284
Myelin Associated Glycoprotein (MAG) Antibody, IgM 0051285
Ganglioside (GM1, GD1b, and GQ1b) Antibodies, IgG and IgM 2004998
CV2.1 Screen by IFA with Reflex to Titer 2013956

Disease Overview

Classification
- Monoclonal gammopathy associated
- Polyclonal inflammatory polyneuropathy
- Guillain-Barré syndrome (GBS)
- Chronic inflammatory demyelinating polyneuropathy
- Multifocal motor neuropathy (MMN)
- Paraneoplastic neuropathy (PNS)

Antibody markers associated with syndromes
See Tables 1 and 2

Symptoms
- Motor symptoms are often mild and diagnosed only with electromyography
- Isolated sensory symptoms are not uncommon

Diagnostic issues
- Overlap of symptoms among syndromes often makes diagnosis difficult
- Antibody testing may aid in clarification of diagnosis, but cannot be used as sole diagnostic tool

Test Interpretation

Results
- Positive – marker(s) detected
  - In context of appropriate clinical setting, may suggest the presence of disease
  - Close clinical correlation is recommended
  - Suggests antibody-mediated neuropathy
- Negative – marker(s) not detected
  - Does not rule out disease and/or cancer

Limitations
Some antibodies may be associated with more than one disease and/or cancer

References

Table 1

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Associated neuropathic disorder/syndrome/disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>GM1</td>
<td>Motor – GBS, MMN, multiple sclerosis (MS)</td>
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<tr>
<td>GM2</td>
<td>Motor – GBS-variants, MMN, MS</td>
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<tr>
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<td>Sensory – demyelinating sensory neuropathy</td>
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<tr>
<td>GD1a</td>
<td>Motor – GBS-like syndrome (acute motor &amp; axonal), MMN, demyelinating motor neuropathy (with IgM M-protein)</td>
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<td>Combined – demyelinating sensory-motor neuropathy</td>
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<tr>
<td>GD1b</td>
<td>Motor – cranial nerve neuropathy</td>
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<td>Combined – sensory-motor neuropathy (ataxic)</td>
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<tr>
<td>GQ1b</td>
<td>Motor – Miller-Fisher syndrome, GBS with ataxia or ophthalmoplegia</td>
</tr>
<tr>
<td></td>
<td>Combined – sensory-motor neuropathy (ataxic)</td>
</tr>
<tr>
<td>Myelin-associated glycoprotein (MAG) and sulfate-3-glucuronyl paragloboside (SGPG)</td>
<td>Motor – multifocal motor neuropathy with conduction block (SGPG only); IgM-related neuropathy</td>
</tr>
<tr>
<td></td>
<td>Combined – chronic demyelinating sensory-motor polyneuropathy (MAG and SGPG); axonal sensory-motor neuropathy (SGPG only)</td>
</tr>
<tr>
<td>Sulfatide</td>
<td>Sensory – axonal, demyelinating</td>
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<tr>
<td></td>
<td>Combined – GALOP syndrome (gait disorder, antibody, late-age onset polyneuropathy)</td>
</tr>
</tbody>
</table>

Vernino 2007; Willison 2011
Table 2

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Associated neuropathic disorder/syndrome/disease</th>
<th>Associated tumor/cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hu (ANNA-1)</td>
<td>Sensory neuronopathy, encephalomyelitis, limbic encephalitis, opsoclonus-myoclonus, subacute cerebellar degeneration, autonomic neuropathy, enteric neuropathy (GI dysmotility)</td>
<td>Small-cell lung cancer (SCLC), neuroblastoma</td>
</tr>
<tr>
<td>Ri (ANNA-2)</td>
<td>Opsoclonus-myoclonus, brainstem encephalitis, cerebellar degeneration</td>
<td>SCLC, breast, ovary</td>
</tr>
<tr>
<td>Yo (PCA-1)</td>
<td>Subacute cerebellar degeneration, occasional GI dysmotility, chorea</td>
<td>Ovary, breast</td>
</tr>
<tr>
<td>CV2/CRMP5</td>
<td>Encephalomyelitis, chorea, limbic encephalitis, sensory neuronopathy, sensorimotor neuropathy, optic neuropathy (retinitis, optic neuritis, uveitis), subacute cerebellar degeneration, autonomic neuropathy, GI dysmotility</td>
<td>SCLC, thymoma</td>
</tr>
</tbody>
</table>

Dalmau 2008; Graus, 2004