

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

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

Antibody Components				
Primary Tests for Autoimmune Neuropathies				
Antibody	2007965 Sensory Antibody Panel	2007966 Motor & Sensory	2007967 Motor & Sensory with IFE	0051225 Motor Panel
Purkinje cell/neuronal nuclear IgG	✓	✓	✓	
Purkinje cell antibody titer	✓	✓	✓	
Neuronal nuclear (Hu, Ri, and Yo) IgG	✓	✓	✓	
Neuronal nuclear antibody (ANNA) IgG titer	✓	✓	✓	
MAG IgM	✓	✓	✓	✓
SGPG IgM	✓	✓	✓	✓
Asialo-GM1 IgG and IgM		✓	✓	✓
IgG and IgM for GM1, GD1a, GD1b		✓	✓	✓
GQ1b antibodies		✓	✓	✓
Total protein electrophoresis, serum			✓	✓
Albumin			✓	✓
Alpha-1 and alpha-2 globulins			✓	✓
Beta globulins			✓	✓
Gamma globulins			✓	✓
Immunoglobulins A, G, M			✓	✓

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 \(GM1\) Antibodies, IgG and IgM 0050591](#)

[Ganglioside \(GM1, GD1b, and GQ1b\) Antibodies, IgG and IgM 2004998](#)

[CV2.1 Screen by IFA with Reflex to Titer 2013956](#)

[Amphiphysin Antibody 2008893](#)

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

Table 1

Nonparaneoplastic Markers	
Autoantibody	Examples of Associated Neuropathic Syndromes
GM1	MMN, ALS/MND, GBS, AMAN
GM2	GBS-variants
GD1a	Axonal GBS
GD1b	Sensory peripheral neuropathy, MND, GBS
GQ1b	MFS, acute ophthalmoplegia, cerebellar ataxia
MAG/SGPG	Inflammatory (often demyelinating) neuropathy with IgM gammopathy, gait ataxia, hand tremor
Sulfatide	Chronic sensory peripheral neuropathy, GALOP syndrome (gait disorder, antibody, late-age onset polyneuropathy)

ALS, amyotrophic lateral sclerosis; AMAN, acute motor axonal neuropathy; GALOP syndrome, gait disorder, antibody, late-age onset polyneuropathy; GBS, Guillain-Barre syndrome; MAG, myelin-associated glycoprotein; MFS, Miller-Fisher syndrome; MMN, multifocal motor neuropathy; MND, motor neuron disease; SGPG, sulfate-3-glucuronyl paragloboside
Vernino, 2007

Table 2

Paraneoplastic Markers		
Autoantibody	Examples of Associated Neuropathic Syndromes	Associated Tumors
Hu (ANNA-1)	PN, limbic encephalitis, ataxia, sensory neuronopathy, autonomic and sensorimotor neuropathies, GI dysmotility	SCLC
CV2 (CRMP5)	PN, limbic encephalitis, ataxia, chorea, optic neuritis	SCLC, thymoma
Amphiphysin	Encephalomyelitis, neuropathy, stiff-person syndrome	Lung, breast
Ri (ANNA-2)	Ataxia, opsoclonus-myoclonus, neuropathy	Lung, breast
ANNA-3	Ataxia, limbic encephalitis, neuropathy	Lung, breast
N-type calcium channel antibodies	PN, other syndromes	Lung, breast

GI, gastrointestinal; PN, peripheral neuropathy; SCLC, small cell lung cancer
Vernino, 2007

Symptoms

- Motor symptoms are often mild and diagnosed only with electromyography
- Isolated sensory symptoms are not uncommon
 - Paresthesias, dysesthesias, and pain predominate
- Symptoms depend on type of syndrome
- May have rapid onset and include respiratory muscles

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

Vernino S, Wolfe GI. Antibody testing in peripheral neuropathies. *Neurologic Clin.* 2007;25(1):29-46