

AUTOIMMUNE AXONAL NEUROPATHY A COMPREHENSIVE TESTING APPROACH

Patients with neuropathy have variable sensory and motor disturbance (loss or exaggerated sensation) and can present with symptoms such as pain, weakness, and autonomic involvements like sweat abnormalities, gastrointestinal dysfunction, erectile dysfunction, and lightheadedness upon standing. These symptoms result from injury to the distal nerves, roots, ganglia, or their gathering points (nerve plexus in the thighs and arms). Patients may have symmetric or asymmetric involvements of the extremities, trunk, and head including extraocular muscles. Subacute onset and asymmetric involvements more commonly indicate inflammatory or immune causes rather than inherited or metabolic forms. Other parts of the nervous system may also be affected based on the specific inflammatory or immune-mediated causes.

THE VALUE OF A COMPREHENSIVE PHENOTYPE-SPECIFIC EVALUATION

Because of the overlap of clinical symptoms, we recommend a panel-based approach rather than individual antibody testing. Our comprehensive approach evaluates specific antibodies associated with autoimmune or paraneoplastic neuropathies.

Key testing

 AIAES | Axonal Neuropathy, Autoimmune/
Paraneoplastic Evaluation, Serum
TAT: 10 days

100%

100% SENSITIVITY IMPROVEMENT
FOR CRMP-5 ANTIBODY WHEN
INCLUDING BOTH IFA AND WB

95%

95% OF ACQUIRED
NEUROPATHIES ARE AXONAL¹²

When to consider testing

There are certain important clinical characteristics associated with the antibodies offered in this panel. The managing physician should consider ordering this test if the patient has one of the following clinical features:

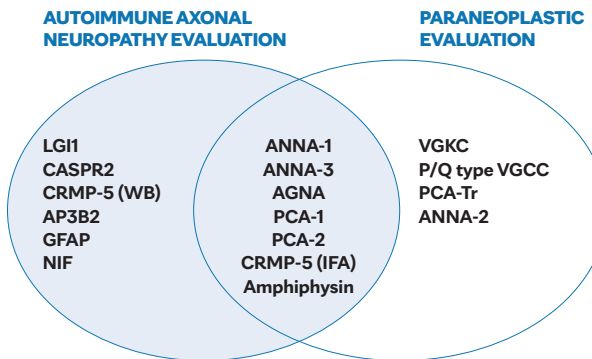
- Subacute axonal neuropathy with coexisting autonomic dysfunction or CNS involvement.
- Non-length-dependent or asymmetrical axonal neuropathies resembling either sensory neuronopathy, polyradiculoneuropathy, or another particular neuropathy.
- Progressive neuropathies with refractory pain or weight loss where an autoimmune or paraneoplastic etiology is suspected.
- Inflammatory CSF with an MRI demonstrating contrast enhancement of roots or nerves.
- Diffuse myokymia, cramp fasciculation syndromes, or neuromyotonia.
- Neuropathy developed as an immune-related adverse event of immune checkpoint inhibitors.

When to consider genetic testing

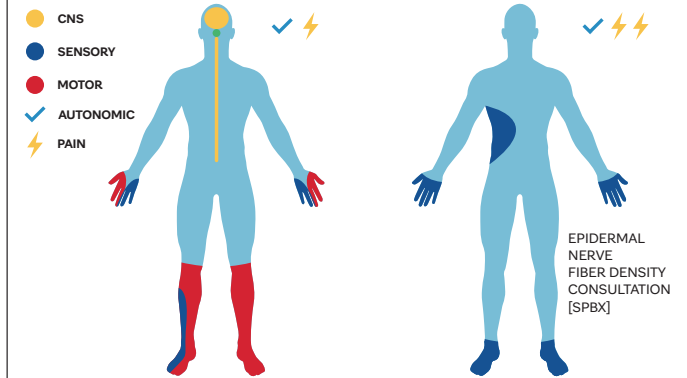
For those patients whose tests results are unclear and/or experience symptoms suggestive of an inherited neuropathy, genetic testing can be considered. Mayo Clinic Laboratories offers next-generation sequencing panels the full range of neuropathies.

PHENOTYPIC EVALUATIONS

Our autoimmune axonal neuropathy evaluation is part of an evolving approach to testing for autoimmune neurological disorders using phenotypic-specific evaluations that include multiple antibodies known for their disease association.



AUTOIMMUNE AXONAL NEUROPATHY PHENOTYPES



NEUROPATHY & POLYRADICULONEUROPATHY - SYMMETRIC & ASYMMETRIC

- +/- AUTONOMIC (GI, ORTHOSTASIS, HEART RATE)
- +/- PAIN
- +/- ENCEPHALOPATHY
- +/- SEIZURES

SMALL FIBER NEUROPATHY & IDIOPATHIC PAIN

- + PAIN
- + LENGTH DEPENDENT, PATCHY, DIFFUSE
- + SWEATING ABNORMALITIES

[Brackets indicate test code in Mayo test catalog]

¹Klein CJ. Autoimmune-mediated peripheral neuropathies and autoimmune pain. *Handb Clin Neurol*. 2016;133:417-46. ²Lucchinetti CF, Kimmel DW, Lennon VA. Paraneoplastic and oncologic profiles of patients seropositive for type 1 antineuronal nuclear autoantibodies. *Neurology*. 1998;50:652-657. ³Pittock SJ, Lucchinetti CF, Lennon VA. Anti-neuronal nuclear autoantibody type 2: paraneoplastic accompaniments. *Ann Neurol*. 2003;53:580-587. ⁴Chan KH, Vernino S, Lennon VA. ANNA-3 anti-neuronal nuclear antibody: marker of lung cancer-related autoimmunity. *Ann Neurol*. 2001;50:301-311. ⁵Dubey D, Lennon VA, Gadoth A, et al. Autoimmune CRMP5 neuropathy phenotype and outcome defined from 105 cases. *Neurology*. 2018;90:e103-e110. ⁶Gadoth A, Pittock SJ, Dubey D, et al. Expanded phenotypes and outcomes among 256 LGI1/CASPR2-IgG-positive patients. *Ann Neurol*. 2017;82:79-92. ⁷Bradshaw MJ, Haluska P, McKeon A, Klein CJ. Multifocal neuropathy as the presenting symptom of Purkinje cell cytoplasmic autoantibody-1. *Muscle Nerve*. 2013;48:827-831. ⁸Dubey D, Jitrapakulsan J, Bi H, et al. Amphiphysin-IgG autoimmune neuropathy: A recognizable clinicopathologic syndrome. *Neurology*. 2019;93(20):e1873-e1880. ⁹Jitrapakulsan J, Klein CJ, Pittock SJ, et al. Phenotypic presentations of paraneoplastic neuropathies associated with MAP1B-IgG. *J Neurol Neurosurg Psychiatry*. 2019;pii:jnnp-2019-322175. ¹⁰Stich O, Klages E, Bischler P, et al. SOX1 antibodies in sera from patients with paraneoplastic neurological syndromes. *Acta Neurol Scand*. 2012;125(5):326-31. ¹¹Cutsforth-Gregory JK, McKeon A, Coon EA, et al. Ganglionic antibody level as a predictor of severity of autonomic failure. *Mayo Clin Proc*. 2018;93:1440-1447. ¹²Hoffman ME, Staff NP, Robb JM, et al. Impairments and comorbidities of polyneuropathy revealed by population-based analyses. *Neurology*. 2015 Apr 21;84(16):1644-1651.

