MAYO CLINIC LABORATORIES

Test Definition: CIDP

Chronic Inflammatory Demyelinating Polyradiculoneuropathy/Nodopathy Evaluation, Serum

Overview

Useful For

Evaluating for chronic inflammatory demyelinating polyradiculoneuropathy and related demyelinating peripheral neuropathies

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
CIDPI	CIDP/NP Interpretation, S	No	Yes
CS1CS	CASPR1-IgG CBA, S	No	Yes
CONCS	Contactin-1 IgG CBA, S	No	Yes
NF4FS	Neurofascin-155 IgG4, S	No	Yes

Testing Algorithm

A thorough understanding of a patient's history along with clinical examination and laboratory testing are needed for a clinico-sero-pathological diagnosis of chronic demyelinating polyradiculoneuropathy (CIDP). To assess the probability of your patient having CIDP vs mimic disorders, see the Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) calculator.

Special Instructions

- Acquired Neuropathy Diagnostic Algorithm

Method Name

CS1CS, CONCS: Cell Binding Assay (CBA)
NF4FS: Flow Cytometry (FC)
CIDPI: Technical Interpretation

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

Multiple neurological phenotype-specific autoimmune/paraneoplastic evaluations are available. For more information

as well as phenotype-specific testing options, refer to Autoimmune Neurology Test Ordering Guide.

For a list of antibodies performed with each evaluation, see Autoimmune Neurology Antibody Matrix.

Specimen Required

Patient Preparation: For optimal antibody detection, specimen collection is recommended before initiation of immunosuppressant medication or intravenous immunoglobulin treatment.
Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Red top
Acceptable: Serum gel
Submission Container/Tube: Plastic vial
Specimen Volume: 3 mL Serum
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send a Neurology Specialty Testing Client Test Request (T732) with the specimen.

Specimen Minimum Volume

Serum: 2 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	28 days	
	Ambient	72 hours	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an acquired, immune-mediated condition effecting peripheral nerves and nerve roots and is characterized by electrodiagnostic features of demyelination with a chronic onset that leads to significant disability. The prevalence of CIDP is estimated at approximately 2 to 4 cases per

100,000 persons. Although a rarer cause of polyneuropathy, it is still important to recognize, as it is treatable with the appropriate use of immunomodulating therapies. Although the exact immunological trigger of CIDP remains unclear, a subset of patients with suspected CIDP have been identified with autoantibodies targeting nodal-paranodal proteins. These patients share common immunopathological mechanisms of disease, clinical features, and treatment responses that are distinct from classic CIDP. A common target of these autoantibodies is the neurofascin-155 (NF155):contactin-1 (CNTN1) complex. NF155 is expressed at the paranodal loops of Schwann cells where it interacts with CNTN1 expressed on adjacent axons. This interaction stabilizes and allows the proper organization of the paranodal axoglial junction. Antibody-mediated disruption of this interaction in animal models recapitulates the pathophysiology observed in humans.

Neurofascin-155 IgG antibodies are present in approximately 5% to 10% of patients with CIDP-like presentations and, more rarely, in those with more acute forms of demyelinating polyradiculoneuropathy. NF155 IgG positive cases are more likely to present with distal weakness, gait disturbance, tremor, and dysarthria as compared to classic CIDP. Most patients who are seropositive for NF155 IgG have been reported to be refractory to intravenous immunoglobulin (IVIg) therapy and often require second-line treatment that includes B-cell depleting therapies such as rituximab. Studies in animal models, as well as the disease pathology, indicate NF155 IgG4 antibodies directly disrupt the paranodal axoglial junction leading to demyelination. IgG4 is the predominant antibody subclass found in these patients and is associated with poorer treatment responses to IVIg. The detection of NF155 IgG4 is a highly specific finding and has not been reported in other disease mimics such as hereditary neuropathies, distal acquired demyelinating symmetric neuropathy, and motor neuron disease.

Contactin-1 IgG antibodies are present in approximately 2% of patients with CIDP-like presentations. CNTN1 IgG positive cases are more likely to present with neuropathic pain, sensory ataxia, and subacute progressive demyelinating polyradiculoneuropathy or polyradiculopathy. The majority of seropositive patients have been reported to be refractory to treatment with IVIg. However, some of these patients respond well to B-cell depleting therapies such as rituximab. Up to half of patients who are CNTN1 IgG positive with CIDP or CIDP-like presentations have been reported to develop membranous nephropathy; therefore, screening for proteinuria may be warranted.

Contactin-associated protein-1 (CASPR1) antibody is useful in the identification of autoimmune nodopathy cases, which can resemble CIDP. Detecting this antibody helps in selecting appropriate treatment. Patients who are CASPR1 IgG positive often do not respond well to IVIg, the standard CIDP therapy, but several have responded well to rituximab therapy. CASPR1 forms a complex with CNTN1, which is important for function. Autoantibodies have been identified that can target each protein (CASPR1 or CNTN1) alone, the CNTN1/CASPR1 complex, or both. Identifying the presence of these autoantibodies is useful in evaluating patients with suspected autoimmune peripheral neuropathy.

Reference Values

CONTACTIN-ASSOCIATED PROTEIN-1-IgG:
Negative

CONTACTIN-1 IgG:
Negative

NEUROFASCIN 155 IgG4:

Negative

Interpretation

Seropositivity for contactin-1 IgG is consistent with an immune-mediated demyelinating polyradiculoneuropathy/polyradiculopathy.

Seropositivity for neurofascin-155 IgG4 is consistent with an immune-mediated demyelinating polyradiculoneuropathy.

Seropositivity for contactin-associated protein-1 IgG is consistent with an immune-mediated demyelinating polyradiculoneuropathy.

Cautions

A negative result does not exclude an immune mediated demyelinating neuropathy.

This test should only be utilized in the appropriate clinical context.

The use of immunotherapy prior to specimen collection may negatively impact the sensitivity of this assay.

Clinical Reference

1. Dubey D, Honorat JA, Shelly S, et al. Contactin-1 autoimmunity: Serologic, neurologic, and pathologic correlates. Neurol Neuroimmunol Neuroinflamm. 2020;7(4):e771
2. Cortese A, Lombardi R, Briani C, et al. Antibodies to neurofascin, contactin-1, and contactin-associated protein 1 in CIDP: Clinical relevance of IgG isotype. Neurol Neuroimmunol Neuroinflamm. 2019;7(1):e639
3. Manso C, Querol L, Mekaouche M, Illa I, Devaux JJ. Contactin-1 IgG4 antibodies cause paranode dismantling and conduction defects. Brain. 2016;139(Pt 6):1700-1712
4. Le Quintrec M, Teisseyre M, Bec N, et al. Contactin-1 is a novel target antigen in membranous nephropathy associated with chronic inflammatory demyelinating polyneuropathy. Kidney Int. 2021;100(6):1240-1249
5. Ogata H, Yamasaki R, Hiwatashi A, et al. Characterization of IgG4 anti-neurofascin 155 antibody-positive polyneuropathy. Ann Clin Transl Neurol. 2015;2(10):960-971
6. Querol L, Nogales-Gadea G, Rojas-Garcia R, et al. Neurofascin IgG4 antibodies in CIDP associate with disabling tremor and poor response to IVIg. Neurology. 2014;82(10):879-886
7. Shelly S, Klein CJ, Dyck PJB, et al. Neurofascin-155 immunoglobulin subtypes: Clinicopathologic associations and neurologic outcomes. Neurology. 2021;97(24):e2392-e2403

Performance

Method Description

Contactin-associated protein-1-IgG and contactin-1 IgG:
Patient sample is applied to a composite slide containing transfected and nontransfected EU90 cells. After incubation and washing, fluorescein-conjugated goat-antihuman IgG is applied to detect the presence of patient IgG binding.(Package insert: IIFT: Neurology Mosaics, Instructions for the indirect immunofluorescence test. EUROIMMUN;

FA_112d-1_A_UK_C13, 02/25/2019)

Neurofascin-155 IgG4:
This cell-binding assay utilizes flow cytometry to detect neurofascin 155 (NF155) IgG4 antibodies in patient sample. Briefly, a stable HEK293 cell line expressing human NF155 on the cell surface is premixed with parental HEK293 cells that do not express human NF155. The 2 cell populations are distinguished using a green fluorescent protein marker, which is only expressed in NF155 expressing cells. The mixture of cells is incubated with diluted patient sera to allow antibodies present in the sample to bind target antigens. Next the cells are incubated with a human IgG4 specific secondary antibody conjugated to AlexaFluor 647 to detect cell bound human IgG4 antibodies. The AlexaFluor 647 signal intensity of the different cell populations is measured using a flow cytometer. The IBI (IgG binding index) is then calculated as the median fluorescent intensity (MFI) of AlexaFluor 647 of the NF155 expressing cells divided by the MFI of the parental non-NF155 expressing cells. When the IBI is greater than or equal to 2.0 the result is considered positive for NF155 IgG4 antibodies.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
CS1CS, CONCS: Monday through Thursday, Sunday
NF4FS: Monday, Friday

Report Available
5 to 10 days

Specimen Retention Time
2 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

Test Definition: CIDP

Chronic Inflammatory Demyelinating Polyradiculoneuropathy/Nodopathy Evaluation, Serum

86255 x 4

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CIDP	CIDP/NP Evaluation, S	101447-1

Result ID	Test Result Name	Result LOINC® Value
614591	Neurofascin-155 IgG4, S	100845-7
616444	CIDP/NP Interpretation, S	69048-7
616442	Contactin-1 IgG CBA, S	In Process
623393	CASPR1-IgG CBA, S	101448-9
624189	CASPR1/Contactin-1 Complex	In Process