MAYO CLINIC LABORATORIES

Test Definition: CNES

Peripheral Nervous System Comprehensive Neuropathy, Autoimmune Evaluation, Serum

Overview

Useful For

Evaluating patients with suspected immune mediate peripheral neuropathy

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
CNEI	Comprehensive Neuropathy Interp, S	No	Yes
AMPHS	Amphiphysin Ab, S	No	Yes
AGN1S	Anti-Glial Nuclear Ab, Type 1	No	Yes
ANN1S	Anti-Neuronal Nuclear Ab, Type 1	No	Yes
ANN3S	Anti-Neuronal Nuclear Ab, Type 3	No	Yes
APBIS	AP3B2 IFA, S	No	Yes
CS1CS	CASPR1-IgG CBA, S	No	Yes
CS2CS	CASPR2-IgG CBA, S	No	Yes
CONCS	Contactin-1 IgG CBA, S	No	Yes
CRMS	CRMP-5-IgG, S	No	Yes
GQ1ES	GQ1b-IgG ELISA, S	Yes	Yes
IGG_D	IgG Disialo. GD1b	No	Yes
IGG_M	IgG Monos. GM1	No	Yes
IG5CS	IgLON5 CBA, S	No	Yes
IGM_D	IgM Disialo. GD1b	No	Yes
IGM_M	IgM Monos. GM1	No	Yes
LG1CS	LGI1-IgG CBA, S	No	Yes
MAGES	MAG IgM, S	Yes	Yes
NF4FS	Neurofascin-155 IgG4, S	No	Yes
PCAB2	Purkinje Cell Cytoplasmic Ab Type 2	No	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
AGNBS	AGNA-1 Immunoblot, S	No	No
AGNTS	AGNA-1 Titer, S	No	No
APHTS	Amphiphysin Ab Titer, S	No	No
AMIBS	Amphiphysin Immunoblot,	No	No

	S		
AN1BS	ANNA-1 Immunoblot, S	No	No
AN1TS	ANNA-1 Titer, S	No	No
AN2BS	ANNA-2 Immunoblot, S	No	No
AN3TS	ANNA-3 Titer, S	No	No
APBCS	AP3B2 CBA, S	No	No
APBTS	AP3B2 IFA Titer, S	No	No
CRMTS	CRMP-5-IgG Titer, S	No	No
CRMWS	CRMP-5-IgG Western Blot, S	No	No
IGDTS	IgG Disialo GD1b Titer, S	No	No
IGMTS	IgG Monos GM1 Titer, S	No	No
IG5TS	IgLON5 IFA Titer, S	No	No
IMDTS	IgM Disialo GD1b Titer, S	No	No
IMMTS	IgM Monos GM1 Titer, S	No	No
MP1BS	MAP1B Immunoblot, S	No	No
PC2TS	PCA-2 Titer, S	No	No

Testing Algorithm

To assess the probability of your patient having chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) vs mimic disorders, see the Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) calculator.

If the indirect immunofluorescence assay (IFA) patterns suggest amphiphysin antibody, then the amphiphysin antibody IFA titer and amphiphysin antibody immunoblot will be performed at an additional charge.

If the IFA patterns suggest antiglial nuclear antibody-1 (AGNA-1), then the AGNA-1 antibody IFA titer and AGNA-1 antibody immunoblot will be performed at an additional charge.

If the IFA patterns suggest antineuronal nuclear antibody type 1 (ANNA-1), then the ANNA-1 IFA titer, ANNA-1 immunoblot, and ANNA-2 immunoblot will be performed at an additional charge.

If the client requests or the IFA pattern suggests ANNA-3 antibody, then the ANNA-3 IFA titer will be performed at an additional charge.

If the IFA patterns suggest collapsin response-mediator protein-5 (CRMP-5)-IgG, then the CRMP-5 antibody IFA titer and CRMP-5 antibody Western blot will be performed at an additional charge.

Screening tests are performed for IgG and IgM antibodies to GM1 and GD1b. If positive, the appropriate titer assay will be performed at an additional charge.

If the IFA pattern suggests PCA-2 antibody, then the PCA-2 antibody IFA titer and MAP1B immunoblot will be performed at an additional charge.

For more information see:
-Comprehensive Neuropathy Evaluation Algorithm
-Acquired Neuropathy Diagnostic Algorithm

Special Instructions

- Acquired Neuropathy Diagnostic Algorithm
- Comprehensive Neuropathy Evaluation Algorithm

Method Name

CNEI: Technical Interpretation
CS1CS, CS2CS, CONCS, IG5CS, LG1CS, APBCS: Cell Binding Assay (CBA)
GQ1ES, IGG_D, IGG_M, IGM_D, IGM_M, MAGES, IGDTS, IGMTS, IMDTS, IMMTS: Enzyme-Linked Immunosorbent Assay (ELISA)
NF4FS: Flow Cytometry
AMPHS, AGN1S, ANN1S, ANN3S, APBIS, CRMS, PCAB2, AGNTS, APHTS, AN1TS, AN3TS, APBTS, CRMTS, IG5TS, PC2TS: Indirect Immunofluorescence Assay (IFA)
CRMWS: Western Blot (WB)
AGNBS, AMIBS, AN1BS, AN2BS, MP1BS: Immunoblot (IB)

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 to occur before starting immunosuppressant medication or intravenous immunoglobulin (IVIg) 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.

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

This evaluation detects autoantibodies associated with autoimmune and paraneoplastic neuropathies. The panel includes antibodies targeting peripheral nerve, dorsal root ganglia, and nodal/paranodal antigens, improving detection across diverse neuropathy phenotypes.

Reflex testing is performed to confirm and further characterize antibody reactivity, enhancing diagnostic sensitivity.

Appropriate for patients with subacute or progressive neuropathy, atypical or asymmetric presentations, autonomic involvement, or suspected immune-mediated or paraneoplastic etiologies.

Reference Values

Test ID	Reporting Name	Methodology	Reference Value
CNEI	Comprehensive Neuropathy Interp, S	Interpretation	N/A
AMPHS	Amphiphysin Ab, S	IFA	Negative
AGN1S	Anti-Glial Nuclear Ab, Type 1	IFA	Negative
ANN1S	Anti-Neuronal Nuclear Ab, Type 1	IFA	Negative
ANN3S	Anti-Neuronal Nuclear Ab, Type 3	IFA	Negative
APBIS	AP3B2 IFA, S	IFA	Negative

CS1CS	CASPR1-IgG CBA, S	CBA	Negative
CS2CS	CASPR2-IgG CBA, S	CBA	Negative
CONCS	Contactin-1 IgG CBA, S	CBA	Negative
CRMS	CRMP-5-IgG, S	IFA	Negative
GQ1ES	GQ1b ELISA, S	ELISA	Negative
IGG_D	IgG Disialo. GD1b	ELISA	Negative
IGG_M	IgG Monos. GM1	ELISA	Negative
IG5CS	IgLON5 CBA, S	CBA	Negative
IGM_D	IgM Disialo. GD1b	ELISA	Negative
IGM_M	IgM Monos. GM1	ELISA	Negative
LG1CS	LGI1-IgG CBA, S	CBA	Negative
MAGES	MAG IgM, S	ELISA	<1500
NF4FS	Neurofascin-155 IgG4, S	FC	Negative
PCAB2	Purkinje Cell Cytoplasmic Ab Type 2	IFA	Negative

Reflex Information:

Test ID	Reporting Name	Methodology	Reference Value
AGNBS	AGNA-1 Immunoblot, S	IB	Negative
AGNTS	AGNA-1 Titer, S	IFA	<1:240
APHTS	Amphiphysin Ab Titer, S	IFA	<1:240
AMIBS	Amphiphysin Immunoblot, S	IB	Negative
AN1BS	ANNA-1 Immunoblot, S	IB	Negative
AN1TS	ANNA-1 Titer, S	IFA	<1:240
AN2BS	ANNA-2 Immunoblot, S	IB	Negative
AN3TS	ANNA-3 Titer, S	IFA	<1:240
APBCS	AP3B2 CBA, S	CBA	Negative
APBTS	AP3B2 IFA Titer, S	IFA	<1:240
CRMTS	CRMP-5-IgG Titer, S	IFA	<1:240
CRMWS	CRMP-5-IgG Western Blot, S	WB	Negative
IGDTS	IgG Disialo GD1b Titer, S	ELISA	<1:2000
IGMTS	IgG Monos GM1 Titer, S	ELISA	<1:2000
IG5TS	IgLON5 IFA Titer, S	IFA	<1:240
IMDTS	IgM Disialo GD1b Titer, S	ELISA	<1:2000
IMMTS	IgM Monos GM1 Titer, S	ELISA	<1:4000
MP1BS	MAP1B Immunoblot, S	IB	Negative
PC2TS	PCA-2 Titer, S	IFA	<1:240

*Methodology abbreviations:
Cell-binding assay (CBA)
Enzyme-linked immunosorbent assay (ELISA)
Flow cytometry (FC)
Immunoblot (IB)
Immunofluorescence assay (IFA)

Western blot (WB)

Interpretation

The presence of specific autoantibodies and/or combinations of antibodies in this panel provides supportive evidence of an immune-mediated peripheral neuropathy. However, these results must be interpretated in the appropriate clinical context. A negative result does not exclude the possibility of an immune mediated peripheral neuropathy.

Cautions

Negative results do not exclude a diagnosis of an immune-mediated neuropathy. Autoantibody results should always be correlated with the clinical phenotype. The use of immunotherapy prior to sample collection may result in either false positive or false negative results.

The use of immunotherapy prior to sample collection may result in either false-positive or false-negative results.

Clinical Reference

1. Shelly S, Klein CJ, Dyck PJB, et al. Neurofascin-155 immunoglobulin subtypes: Clinicopathologic associations and neurologic outcomes. Neurology. 2021;97(24): e2392-e2403
2. Dubey D, Honorat JA, Shelly S, et al. Contactin-1 autoimmunity: Serologic, neurologic, and pathologic correlates. Neurol Neuroimmunol Neuroinflamm. 2020;7(4)e771
3. Paramasivan NK, Basal E, LaFrance-Corey RG, et al. Clinical insights Into CASPR1 and CASPR1/contactin-1 complex autoimmune nodopathies. Neurology. 2026;106(5):e214403. doi:10.1212/WNL.0000000000214403
4. Klein CJ, Triplett JD, Murray DL, et al. Optimizing anti-myelin-associated glycoprotein and IgM-gammopathy testing for neuropathy treatment evaluation. Neurology. 2024;103(11):e210000. doi:10.1212/WNL.0000000000210000
5. Dubey D, Lennon VA, Gadoth A, et al. Autoimmune CRMP5 neuropathy phenotype and outcome defined from 105 cases. Neurology. 2018;90(2):e103-e110. doi:10.1212/WNL.0000000000004803
6. Dubey D, Jitprapaikulsan J, Bi H, et al. Amphiphysin-IgG autoimmune neuropathy: A recognizable clinicopathologic syndrome. Neurology. 2019;93(20):e1873-e1880. doi:10.1212/WNL.0000000000008472
7. Dubey D. Autoimmune neuromuscular disorders associated with neural antibodies. Continuum (Minneap Minn). 2024;30(4):1136-1159. doi:10.1212/CON.0000000000001461

Performance

Method Description

Cell-Binding Assay
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)

Ganglioside Antibodies: IgG/IgM Disialo, GD1b; IgG/IgM Monos, GM1 Enzyme-Linked Immunosorbent Assays: Antiganglioside antibodies are detected by enzyme-linked immunosorbent assays (ELISA). Microwells are precoated with GM1 or GD1b antigen. The calibrator, controls, and diluted patient samples are added to the wells, and autoantibodies recognizing GM1 or GD1b bind during the first incubation. After washing the wells to remove all unbound proteins,

purified alkaline phosphatase-conjugated antihuman IgG or IgM is added. The conjugated secondary IgG or IgM binds to the captured human autoantibody, and the excess unbound conjugated IgG or IgM is removed by a further wash step. The bound conjugated IgG or IgM is visualized with 4-nitrophenyl phosphate substrate, which gives a yellow reaction product, the intensity of which is proportional to a concentration of autoantibody in the sample. A base is added to each well to stop the reaction, and the final product is read at 405 nm. For screening assays, patient results are calculated by dividing the optical density (OD) of patient samples or controls by the average OD of the calibrator. Any sample with a ratio of patient to calibrator OD greater than 2.0 is considered positive. Any positive sample on screening is then titered. For titer assays, patient samples are diluted, and the last dilution where the ratio of patient to calibrator OD is greater than 2.0 is reported as the end-point titer.(Unpublished Mayo method)

Ganglioside GQ1b Antibody, IgG ELISA:
Microwells are precoated with GQ1b antigen. The calibrator, controls, and diluted patient samples are added to the wells, and autoantibodies recognizing GQ1b bind during the first incubation. After washing the wells to remove all unbound proteins, purified horseradish peroxidase-labeled anti-human IgG conjugate is added. The conjugated IgG binds to the captured human autoantibody, and the excess unbound conjugated IgG is removed by a further wash step. The bound conjugated IgG is visualized with 3,3',5,5'-tetramethylbenzidine substrate, which gives a blue reaction product, the intensity of which is proportional to a concentration of autoantibody in the sample. Acid is added to each well to stop the reaction. This produces a yellow end-product color, which is read at 450 nm. Patient results are calculated as a cutoff index (COI) by dividing the OD of patient samples or controls by the average OD of the calibrator. Any sample with a COI greater than or equal to 1.0 is considered positive. Any sample with a COI less than 1.0 is considered negative. Results are reported qualitatively as positive or negative.(Unpublished Mayo method)

Myelin-Associated Glycoprotein Autoantibodies, IgM ELISA:
Microwells are precoated with human myelin-associated glycoprotein (MAG) antigen. The calibrators, controls, and diluted patient samples are added to the wells, and autoantibodies recognizing the MAG antigen bind during the first incubation. After washing the wells to remove all unbound proteins, purified horseradish peroxidase-labeled anti-human IgM conjugate is added. The secondary antibody conjugate binds to captured human autoantibody, and the excess unbound conjugate is removed by a further wash step. The bound secondary antibody conjugate undergoes an enzymatic reaction with a chemical substrate to generate a colormetric reaction. Absorbance is measured on a plate reader and patient sample signal is compared to a calibration curve to generate Buhlmann titer units.(Package insert: anti-MAG Autoantibodies ELISA. Buhlmann Laboratories AG; 10/2018)

Flow Cytometry
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)

Immunoblot
Test strips are incubated with appropriately diluted sample, prepared to meet the assay's required end-dilution for each specimen type. Samples and controls are added directly to the strips, ensuring they are fully covered with dilution buffer, then mixed gently and incubated for 60 minutes at room temperature on a rocking platform. After incubation, the strips undergo a series of wash steps using diluted wash buffer, followed by a 30-minute incubation with a ready-to-use alkaline phosphatase-labeled IgG conjugate. The strips are washed again using the same procedure, then incubated with a ready-to-use substrate solution for 20 minutes at room temperature. The reaction is stopped by rinsing with distilled water through several wash cycles. Strips are then placed on absorbent material and allowed to dry fully, generally requiring at least two hours. Results are interpreted only after the strips have dried completely, and dried strips are stored protected from light.(Package insert: PCA-2 line assay. ravo Diagnostika GmbH; 05/2023)

Immunofluorescence Assay
The patient's specimen is tested by a standardized immunofluorescence assay that uses a composite frozen section of mouse cerebellum, kidney, and gut tissues. After incubation with the specimen and washing, fluorescein-conjugated goat-antihuman IgG is applied. Neuron-specific autoantibodies are identified by their characteristic fluorescence staining patterns. Specimens that are scored positive for any neuronal nuclear or cytoplasmic autoantibody are titrated. Interference by coexisting non-neuron-specific autoantibodies can usually be eliminated by serologic absorption.(Honorat JA, Komorowski L, Josephs KA, et al. IgLON5 antibody: Neurological accompaniments and outcomes in 20 patients. Neurol Neuroimmunol Neuroinflamm. 2017;4[5]:e385. Published 2017 Jul 18. doi:10.1212/NXI.0000000000000385)

Western Blot
Western blot is performed on denatured full-length recombinant human collapsin response-mediator protein-5 (CRMP-5), reduced and subjected to electrophoresis on 10% polyacrylamide gel. IgG is detected autoradiographically by enhanced chemiluminescence.(Yu Z, Kryzer TJ, Griesmann GE, et al. CRMP-5 neuronal autoantibody: marker of lung cancer and thymoma-related autoimmunity. Ann Neurol. 2001;49[2]:146-154; Dubey D, Jitprapaikulsan J, Bi H, et al. Amphiphysin-IgG autoimmune neuropathy: A recognizable clinicopathologic syndrome. Neurology. 2019;93[20]:e1873-e1880. doi:10.1212/WNL.0000000000008472)

PDF Report
No

Day(s) Performed
Monday through Sunday

Report Available
8 to 12 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

86255x14
83516x5
83520
84182 AGNBS (if appropriate)
86256 AGNTS (if appropriate)
86256 APHTS (if appropriate)
84182 AMIBS (if appropriate)
84182 AN1BS (if appropriate)
86256 AN1TS (if appropriate)
84182 AN2BS (if appropriate)
86256 AN3TS (if appropriate)
86255 APBCS (if appropriate)
86256 APBTS (if appropriate)
86256 CRMTS (if appropriate)
84182 CRMWS (if appropriate)
83520 IGDTS (if appropriate)
83520 IGMTS (if appropriate)
86256 IG5TS (if appropriate)
83520 IMDTS (if appropriate)
83520 IMMTS (if appropriate)
84182 MP1BS (if appropriate)
86256 PC2TS (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CNES	Comprehensive Neuropathy Ab Eval, S	In Process

Result ID	Test Result Name	Result LOINC® Value
89080	AGNA-1, S	84927-3

81722	Amphiphysin Ab, S	72327-0
80150	ANNA-1, S	33615-6
83137	ANNA-3, S	43102-3
83077	CRMP-5-IgG, S	72504-4
4416	IgG Disialo. GD1b	94868-7
4412	IgG Monos. GM1	63243-0
4417	IgM Disialo. GD1b	94870-3
4413	IgM Monos. GM1	63247-1
83138	PCA-2, S	84925-7
64279	LGI1-IgG CBA, S	94287-0
64281	CASPR2-IgG CBA, S	94285-4
606950	IgLON5 CBA, S	96478-3
607034	MAG IgM, S	39087-2
614591	Neurofascin-155 IgG4, S	100845-7
616442	Contactin-1 IgG CBA, S	In Process
615863	AP3B2 IFA, S	101907-4
621107	GQ1b-IgG ELISA, S	63254-7
621106	Comprehensive Neuropathy Interp, S	69048-7
624190	IFA Notes	48767-8
623393	CASPR1-IgG CBA, S	101448-9
624189	CASPR1/Contactin-1 Complex	In Process