Test Definition: ENS2

Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Serum

Overview

Useful For

Evaluating, using serum specimens, new onset encephalopathy (noninfectious or metabolic) comprising confusional states, psychosis, delirium, memory loss, hallucinations, movement disorders, sensory or motor complaints, seizures, dyssomnias, ataxias, nausea, vomiting, inappropriate antidiuresis, coma, dysautonomias, or hypoventilation

The following accompaniments should increase of suspicion for autoimmune encephalopathy:
-Headache
-Autoimmune stigmata (personal or family history or signs of diabetes mellitus, thyroid disorder, vitiligo, poliosis [premature graying], myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus)
-History of cancer
-Smoking history (20 or more pack-years) or other cancer risk factors
-Inflammatory cerebral spinal fluid (or isolated protein elevation)
-Neuroimaging signs suggesting inflammation

Evaluating limbic encephalitis (noninfectious)

Directing a focused search for cancer

Investigating encephalopathy appearing during or after cancer therapy and not explainable by metastasis or drug effect

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
AEESI	Encephalopathy, Interpretation, S	No	Yes
AMPCS	AMPA-R Ab CBA, 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
ANN2S	Anti-Neuronal Nuclear Ab, Type 2	No	Yes
ANN3S	Anti-Neuronal Nuclear Ab, Type 3	No	Yes
CS2CS	CASPR2-IgG CBA, S	No	Yes
CRMS	CRMP-5-IgG, S	No	Yes
DPPCS	DPPX Ab CBA, S	No	Yes
GABCS	GABA-B-R Ab CBA, S	No	Yes
GD65S	GAD65 Ab Assay, S	Yes	Yes

GFAIS	GFAP IFA, S	No	Yes
GL1IS	mGluR1 Ab IFA, S	No	Yes
IG5CS	IgLON5 CBA, S	No	Yes
LG1CS	LGI1-IgG CBA, S	No	Yes
NCDIS	Neurochondrin IFA, S	No	Yes
NIFIS	NIF IFA, S	No	Yes
NMDCS	NMDA-R Ab CBA, S	No	Yes
PCABP	Purkinje Cell Cytoplasmic Ab Type 1	No	Yes
PCAB2	Purkinje Cell Cytoplasmic Ab Type 2	No	Yes
PCATR	Purkinje Cell Cytoplasmic Ab Type Tr	No	Yes
PDEIS	PDE10A Ab IFA, S	No	Yes
SP7IS	Septin-7 IFA, S	No	Yes
T46IS	TRIM46 Ab IFA, S	No	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
AGNBS	AGNA-1 Immunoblot, S	No	No
AINCS	Alpha Internexin CBA, S	No	No
AMPIS	AMPA-R Ab IF Titer Assay, S	No	No
AMIBS	Amphiphysin Immunoblot, S	No	No
AN1BS	ANNA-1 Immunoblot, S	No	No
AN2BS	ANNA-2 Immunoblot, S	No	No
CRMWS	CRMP-5-IgG Western Blot, S	Yes	No
DPPTS	DPPX Ab IFA Titer, S	No	No
GABIS	GABA-B-R Ab IF Titer Assay, S	No	No
GFACS	GFAP CBA, S	No	No
GFATS	GFAP IFA Titer, S	No	No
IG5TS	IgLON5 IFA Titer, S	No	No
GL1CS	mGluR1 Ab CBA, S	No	No
GL1TS	mGluR1 Ab IFA Titer, S	No	No
NFHCS	NIF Heavy Chain CBA, S	No	No
NIFTS	NIF IFA Titer, S	No	No
NFLCS	NIF Light Chain CBA, S	No	No
NMDIS	NMDA-R Ab IF Titer Assay,	No	No

	S		
PC1BS	PCA-1 Immunoblot, S	No	No
PCTBS	PCA-Tr Immunoblot, S	No	No
AGNTS	AGNA-1 Titer, S	No	No
APHTS	Amphiphysin Ab Titer, S	No	No
AN1TS	ANNA-1 Titer, S	No	No
AN2TS	ANNA-2 Titer, S	No	No
AN3TS	ANNA-3 Titer, S	No	No
CRMTS	CRMP-5-IgG Titer, S	No	No
NCDCS	Neurochondrin CBA, S	No	No
NCDTS	Neurochondrin IFA Titer, S	No	No
PC1TS	PCA-1 Titer, S	No	No
PC2TS	PCA-2 Titer, S	No	No
PCTTS	PCA-Tr Titer, S	No	No
SP7CS	Septin-7 CBA, S	No	No
SP7TS	Septin-7 IFA Titer, S	No	No
PDETS	PDE10A Ab IFA Titer, S	No	No
T46CS	TRIM46 Ab CBA, S	No	No
T46TS	TRIM46 Ab IFA Titer, S	No	No

Testing Algorithm

To determine the necessity of laboratory testing for patients with suspected autoimmune encephalitis, epilepsy or dementia, see the Antibody Prevalence in Epilepsy and Encephalopathy (APE2) scorecard.

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

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

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

If the IFA pattern suggests 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 IFA pattern suggests ANNA-2 antibody, then the ANNA-2 IFA titer, ANNA-2 immunoblot, and ANNA-1 immunoblot will be performed at an additional charge.

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

If the IFA pattern suggests Purkinje cytoplasmic antibody type 1 (PCA-1), then the PCA-1 IFA titer and PCA-1 immunoblot

will be performed at an additional charge.

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

If the IgLON5 antibody cell binding assay (CBA) result is positive, then the IgLON5 IFA titer will be performed at an additional charge.

If the AMPA (alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid) receptor antibody CBA result is positive, then the AMPA-receptor antibody IFA titer assay will be performed at an additional charge.

If the gamma-aminobutyric acid B (GABA-B) receptor antibody CBA result is positive, then the GABA-B-receptor antibody IFA titer assay will be performed at an additional charge.

If the IFA pattern suggests glial fibrillary acidic protein (GFAP) antibody, then the GFAP IFA titer and GFAP CBA will be performed at an additional charge.

If the N-methyl-D-aspartate (NMDA) receptor antibody CBA is positive, then the NMDA-receptor antibody IFA titer assay will be performed at an additional charge.

If the dipeptidyl-peptidase-like protein-6 (DPPX) antibody CBA result is positive, then the DPPX IFA titer will be performed at an additional charge.

If the IFA pattern suggests metabotropic glutamate receptor 1 (mGluR1) antibody, then the mGluR1 antibody CBA and mGluR1 IFA titer will be performed at an additional charge.

If the IFA pattern suggests neuronal intermediate filament (NIF) antibody, then the alpha internexin CBA, NIF heavy chain CBA, NIF light chain CBA, and NIF IFA titer will be performed at an additional charge.

If the IFA pattern suggests tripartite motif-containing protein 46 (TRIM46) antibody, then the TRIM46 antibody CBA and TRIM46 IFA titer will be performed at an additional charge.

If the IFA pattern suggests phosphodiesterase 10A (PDE10A) antibody, then the PDE10A antibody IFA titer will be performed at an additional charge.

For more information, see the following algorithms:
-Autoimmune/Paraneoplastic Encephalopathy Evaluation Algorithm-Serum
-Central Nervous System Demyelinating Disease Diagnostic Algorithm

Special Instructions

- Autoimmune/Paraneoplastic Encephalopathy Evaluation Algorithm-Serum
- Meningitis/Encephalitis Panel Algorithm
- Central Nervous System Demyelinating Disease Diagnostic Algorithm

Method Name

AEESI: Medical Interpretation

AGN1S, AGNTS, AMPHS, APHTS, AMPIS, ANN1S, AN1TS, ANN2S, AN2TS, AN3TS, ANN3S, CRMS, CRMTS, DPPTS, GABIS, GFAIS, GFATS, IG5TS, GL1IS, GL1TS, NCDIS, NCDTS, NIFIS, NIFTS, NMDIS, PCABP, PC1TS, PCAB2, PC2TS, PCATR, PCTTS, PDEIS, PDETS, SP7IS, SP7TS, T46IS, T46TS: Indirect Immunofluorescence Assay (IFA)

AMPCS, CS2CS, DPPCS, GABCS, GFACS, IG5CS, LG1CS, GL1CS, NCDCS, AINCS, NFLCS, NFHCS, NMDCS, SP7CS, T46CS: Cell Binding Assay (CBA)

CRMWS: Western Blot (WB)

AGNBS, AMIBS, AN1BS, AN2BS, PC1BS, PCTBS: Immunoblot (IB)

GD65S: Radioimmunoassay (RIA)

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, see Autoimmune Neurology Test Ordering Guide.

When more than one evaluation is ordered on the same order number, the duplicate test will be canceled.

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

This test is intended to be ordered for **adult** patients. If this test is ordered for a patient younger than 18 years, it will be canceled and automatically reordered by the laboratory as PCDES / Pediatric Autoimmune Encephalopathy/CNS Disorder Evaluation, Serum. The pediatric autoimmune central nervous system disorders 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.

This test **should not be requested** for patients who have recently received radioisotopes, therapeutically or diagnostically, because of potential assay interference. The specific waiting period before specimen collection will depend on the isotope administered, the dose given, and the clearance rate in the individual patient. Specimens will be screened for radioactivity prior to analysis. Radioactive specimens received in the laboratory will be held 1 week and

assayed if sufficiently decayed or canceled if radioactivity remains.

Necessary Information

Provide the following information:
-Relevant clinical information
-Ordering healthcare professional's name, phone number, mailing address, and email address

Specimen Required

Patient Preparation: For optimal antibody detection, specimen collection is recommended 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: 4 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send 1 of the following with the specimen:
-Neurology Specialty Testing Client Test Request (T732)
-General Test Request (T239)
-Microbiology Test Request (T244)

Specimen Minimum Volume

2.5 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

Autoimmune encephalopathies extend beyond the classically recognized clinical and radiological spectrum of "limbic encephalitis." They encompass a diversity of neurological presentations with subacute or insidious onset, including confusional states, psychosis, delirium, memory loss, hallucinations, movement disorders, sensory or motor complaints, seizures, dyssomnias, ataxias, eye movement problems, nausea, vomiting, inappropriate antidiuresis, coma, dysautonomias, or hypoventilation. A diagnosis of autoimmune encephalopathy should be suspected based on the clinical course, coexisting autoimmune disorder (eg, thyroiditis, diabetes), serological evidence of autoimmunity, spinal fluid evidence of intrathecal inflammation, neuroimaging or electroencephalographic abnormalities, and favorable response to trial of immunotherapy.

Detection of one or more neural autoantibodies aids the diagnosis of autoimmune encephalopathy and may guide a search for cancer. Pertinent autoantibody specificities include:
-Neurotransmitter receptors and ion channels, such as neuronal voltage-gated potassium channels (and interacting synaptic and axonal proteins, leucine-rich glioma inactivated 1 [LGI1] protein and contactin associated protein 2 [CASPR2]), ionotropic glutamate receptors (N-methyl-D-aspartate receptor [NMDA] and 2-amino-3-[5-methyl-3-oxo-1,2-oxazol-4-yl] propanoic acid [AMPA]), metabotropic gamma-aminobutyric acid (GABA)-B receptors
-Enzymes, signaling molecules, and RNA-regulatory proteins in the cytoplasm and nucleus of neurons (glutamic acid decarboxylase 65 [GAD65], collapsin response-mediator protein-5 neuronal [CRMP-5], antineuronal nuclear antibody-type 1 [ANNA-1], and ANNA-2)

Importantly, autoimmune encephalopathies are reversible. Misdiagnosis as a progressive (currently irreversible) neurodegenerative condition is not uncommon and has devastating consequences for the patient. Clinicians must consider the possibility of an autoimmune etiology in the differential diagnoses of encephalopathy. For example, a potentially reversible disorder justifies a trial of immunotherapy for the detection of neural autoantibodies in patients presenting with symptoms of personality change, executive dysfunction, and psychiatric manifestations.

A triad of clues helps to identify patients with an autoimmune encephalopathy:
1. Clinical presentation (subacute symptoms, onset rapidly progressive course, and fluctuating symptoms) and radiological findings consistent with inflammation
2. Detection of neural autoantibodies in serum or cerebrospinal fluid (CSF)
3. Favorable response to a trial of immunotherapy

Detection of neural autoantibodies in serum or CSF informs healthcare professionals of a likely autoimmune etiology, may heighten suspicion for a paraneoplastic basis, and guide the search for cancer. Neurological accompaniments of neural autoantibodies are generally not syndromic but diverse and multifocal. For example, the LGI1 antibody was initially considered to be specific for autoimmune limbic encephalitis, but, over time, other presentations have been reported, including a rapidly progressive course of cognitive decline mimicking neurodegenerative dementia. Comprehensive antibody testing is more informative than selective testing for 1 or 2 neural antibodies. Some antibodies strongly predict an underlying cancer. For example, small-cell lung carcinoma (ANNA-1, CRMP-5-IgG), ovarian teratoma (NMDA-R), and thymoma (CRMP-5 IgG).

An individual patient's autoantibody profile may be informative for a specific cancer type. For example, in a patient presenting with encephalitis who has CRMP 5 IgG, and subsequent testing reveals muscle acetylcholine receptor (AChR) binding antibody, the findings should raise a high suspicion for thymoma. Testing of CSF for autoantibodies is particularly

helpful when serum testing is negative, although in some circumstances testing both serum and CSF simultaneously is pertinent. Testing of CSF is recommended for some antibodies (eg, NMDA-R antibody and glial fibrillary acidic protein [GFAP]-IgG) because CSF testing is both more sensitive and specific. In contrast, serum testing for LGI1 antibody is more sensitive than CSF testing.

Reference Values

est ID	Reporting name	Methodology*	Reference value
AEESI	Encephalopathy, Interpretation, S	Medical interpretation	Interpretive report
AMPCS	AMPA-R Ab CBA, S	CBA	Negative
AMPHS	Amphiphysin Ab, S	IFA	Negative
AGN1S	Anti-Glial Nuclear Ab, Type 1	IFA	Negative
ANN1S	Anti-Neuronal Nuclear Ab, Type 1	IFA	Negative
ANN2S	Anti-Neuronal Nuclear Ab, Type 2	IFA	Negative
ANN3S	Anti-Neuronal Nuclear Ab, Type 3	IFA	Negative
CS2CS	CASPR2-IgG CBA, S	CBA	Negative
CRMS	CRMP-5-IgG, S	IFA	Negative
DPPCS	DPPX Ab CBA, S	CBA	Negative
GABCS	GABA-B-R Ab CBA, S	CBA	Negative
GD65S	GAD65 Ab Assay, S	RIA	< or =0.02 nmol/L Reference values apply to all ages.
GFAIS	GFAP IFA, S	IFA	Negative
GL1IS	mGluR1 Ab IFA, S	IFA	Negative
IG5CS	IgLON5 CBA, S	CBA	Negative
LG1CS	LGI1-IgG CBA, S	CBA	Negative
NCDIS	Neurochondrin IFA, S	IFA	Negative
NIFIS	NIF IFA, S	IFA	Negative
NMDCS	NMDA-R Ab CBA, S	CBA	Negative
PCABP	Purkinje Cell Cytoplasmic Ab Type 1	IFA	Negative
PCAB2	Purkinje Cell Cytoplasmic Ab Type 2	IFA	Negative
PCATR	Purkinje Cell Cytoplasmic Ab Type Tr	IFA	Negative
PDEIS	PDE10A Ab IFA, S	IFA	Negative
SP7IS	Septin-7 IFA, S	IFA	Negative
T46IS	TRIM46 IFA, S	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
AINCS	Alpha Internexin CBA, S	CBA	Negative
AMPIS	AMPA-R Ab IF Titer Assay, 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
AN2TS	ANNA-2 Titer, S	IFA	<1:240
AN3TS	ANNA-3 Titer, S	IFA	<1:240
CRMTS	CRMP-5-IgG Titer, S	IFA	<1:240
CRMWS	CRMP-5-IgG Western Blot, S	WB	Negative
DPPTS	DPPX Ab IFA Titer, S	IFA	<1:240
GABIS	GABA-B-R Ab IF Titer Assay, S	IFA	<1:240
GFACS	GFAP CBA, S	CBA	Negative
GFATS	GFAP IFA Titer, S	IFA	<1:240
IG5TS	IgLON5 IFA Titer, S	IFA	<1:240
GL1CS	mGluR1 Ab CBA, S	CBA	Negative
GL1TS	mGluR1 Ab IFA Titer, S	IFA	<1:240
NCDCS	Neurochondrin CBA, S	CBA	Negative
NCDTS	Neurochondrin IFA Titer, S	IFA	<1:240
NFHCS	NIF Heavy Chain CBA, S	CBA	Negative
NIFTS	NIF IFA Titer, S	IFA	<1:240
NFLCS	NIF Light Chain CBA, S	CBA	Negative
NMDIS	NMDA-R Ab IF Titer Assay, S	IFA	<1:240
PC1BS	PCA-1 Immunoblot, S	IB	Negative
PC1TS	PCA-1 Titer, S	IFA	<1:240
PC2TS	PCA-2 Titer, S	IFA	<1:240
PCTBS	PCA-Tr Immunoblot, S	IB	Negative
PCTTS	PCA-Tr Titer, S	IFA	<1:240
PDETS	PDE10A Ab IFA Titer, S	IFA	<1:240
SP7CS	Septin-7 CBA, S	CBA	Negative
SP7TS	Septin-7 IFA Titer, S	IFA	<1:240
T46CS	TRIM46 CBA, S	CBA	Negative
T46TS	TRIM46 IFA Titer, S	IFA	<1:240

*Methodology abbreviations:
Immunofluorescence assay (IFA)
Cell-binding assay (CBA)
Western blot (WB)
Radioimmunoassay (RIA)
Immunoblot (IB)

Neuron-restricted patterns of IgG staining that do not fulfill criteria for ANNA-1, ANNA-2, CRMP-5-IgG, PCA-1, PCA-2, or PCA-Tr may be reported as "unclassified anti-neuronal IgG." Complex patterns that include nonneuronal elements may be reported as "uninterpretable."

Note: CRMP-5 titers lower than 1:240 are detectable by recombinant CRMP-5 Western blot analysis. CRMP-5 Western

blot analysis will be done on request on stored serum (held 4 weeks). This supplemental testing is recommended in cases of chorea, vision loss, cranial neuropathy, and myelopathy. Call the Neuroimmunology Laboratory at 800-533-1710 to request CRMP-5 Western blot.

Interpretation

Neuronal, glial, and muscle autoantibodies are valuable serological markers of autoimmune encephalopathy and of a patient's immune response to cancer. These autoantibodies are usually accompanied by subacute neurological symptoms and signs are not found in healthy subjects. It is not uncommon for more than 1 of the following autoantibody specificities to be detected in patients with an autoimmune encephalopathy:
-Plasma membrane autoantibodies: N-methyl-D-aspartate (NMDA) receptor; 2-amino-3-(5-methyl-3-oxo-1,2-oxazol-4-yl) propanoic acid (AMPA) receptor; gamma-amino butyric acid (GABA-B) receptor; neuronal acetylcholine receptor. These are all potential effectors of neurological dysfunction.
-Neuronal nuclear autoantibodies: Type 1 (ANNA-1), type 2 (ANNA-2), or type 3 (ANNA-3)
-Neuronal or muscle cytoplasmic antibodies: Amphiphysin, Purkinje cell antibodies (PCA-1 and PCA-2), collapsin response-mediator protein-5 (CRMP-5), glutamic acid decarboxylase (GAD65), or striational

Cautions

Negative results do not exclude autoimmune encephalopathy or cancer.

This test does not detect Ma1 or Ma2 antibodies (also known as MaTa), which are sometimes associated with brainstem and limbic encephalitis in the context of testicular germ cell neoplasms. Scrotal ultrasound is advised for men who present with unexplained subacute encephalitis.

Intravenous immunoglobulin (IVIg) treatment prior to the serum collection may cause a false-positive result.

Clinical Reference

1. Orozco E, Valencia-Sanchez C, Britton J, et al. Autoimmune encephalitis criteria in clinical practice. Neurol Clin Pract. 2023;13(3):e200151. doi:10.1212/CPJ.0000000000200151
2. Flanagan EP, Geschwind MD, Lopez-Chiriboga AS, et al. Autoimmune encephalitis misdiagnosis in adults. JAMA Neurol. 2023;80(1):30-39. doi:10.1001/jamaneurol.2022.4251
3. Budhram A, Dubey D, Sechi E, et al. Neural Antibody Testing in Patients with Suspected Autoimmune Encephalitis. Clin Chem. 2020;66(12):1496-1509. doi:10.1093/clinchem/hvaa254
4. Abboud H, Probasco JC, Irani S, et al. Autoimmune encephalitis: proposed best practice recommendations for diagnosis and acute management. J Neurol Neurosurg Psychiatry. 2021;92(7):757-768. doi:10.1136/jnnp-2020-325300
5. Dubey D, Pittock SJ, Kelly CR, et al. Autoimmune encephalitis epidemiology and a comparison to infectious encephalitis. Ann Neurol. 2018;83(1):166-177. doi:10.1002/ana.25131

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)

Indirect 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)

Radioimmunoassay:
(125)I-labeled recombinant human antigens or labeled receptors are incubated with patient specimen. After incubation, anti-human IgG is added to form an immunoprecipitate. The amount of (125)I-labeled antigen in the immunoprecipitate is measured using a gamma-counter. The amount of gamma emission in the precipitate is proportional to the amount of antigen-specific IgG in the specimen. Results are reported as units of precipitated antigen (nmol) per liter of patient sample.(Griesmann GE, Kryzer TJ, Lennon VA. Autoantibody profiles of myasthenia gravis and Lambert-Eaton myasthenic syndrome. In: Rose NR, Hamilton RG, et al, eds. Manual of Clinical and Laboratory Immunology. 6th ed. ASM Press; 2002:1005-1012; Jones AL, Flanagan EP, Pittock SJ, et al. Responses to and outcomes of treatment of autoimmune cerebellar ataxia in adults. JAMA Neurol. 2015;72[11]:1304-1312. doi:10.1001/jamaneurol.2015.2378)

Immunoblot:
All steps are performed at room temperature (18 to 28 degrees C) utilizing the EUROBlot One instrument. Diluted patient sample (1:101) is added to test strips (strips containing recombinant antigen manufactured and purified using biochemical methods) in individual channels and incubated for 30 minutes. Positive samples will bind to the purified recombinant antigen and negative samples will not bind. Strips are washed to remove unbound antibodies and then incubated with anti-human IgG antibodies (alkaline phosphatase-labelled) for 30 minutes. The strips are again washed to remove unbound anti-human IgG antibodies and nitroblue tetrazolium chloride/5-bromo-4-chloro-3-indolylphosphate (NBT/BCIP) substrate is added. Alkaline phosphatase enzyme converts the soluble substrate into a colored insoluble product on the membrane to produces a black band. Strips are digitized via picture capture on the EUROBlot One instrument and evaluated with the EUROLineScan software.(O'Connor K, Waters P, Komorowski L, et al. GABAA receptor autoimmunity: A multicenter experience. Neurol Neuroimmunol Neuroinflamm. 2019;6[3]:e552. doi:10.1212/NXI.0000000000000552)

Western Blot:
Neuronal antigens extracted aqueously from adult rat cerebellum, full-length recombinant human collapsin response-mediator protein-5 (CRMP-5), or full-length recombinant human amphiphysin protein is denatured, reduced, and separated by electrophoresis on 10% polyacrylamide gel. IgG is detected autoradiographically by enhanced chemiluminescence.(Yu Z, Kryzer TJ, Griesmann GE, Kim K, Benarroch EE, Lennon VA. 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
Profile tests: Monday through Sunday; Reflex tests: Varies

Report Available
8 to 12 days

Specimen Retention Time
28 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
86255 x 23
86341 x 1
84182-AGNBS (if appropriate)
86256 AGNTS (if appropriate)
86255-AINCS (if appropriate)
86256-AMPIS (if appropriate)
86256 APHTS (if appropriate)
84182-AMIBS (if appropriate)
84182-AN1BS (if appropriate)
86256 AN1TS (if appropriate)
84182-AN2BS (if appropriate)
86256 AN2TS (if appropriate)
86256 AN3TS (if appropriate)
86256 CRMTS (if appropriate)
84182-CRMWS (if appropriate)

86256-DPPTS (if appropriate)
86256-GABIS (if appropriate)
86255-GFACS (if appropriate)
86256-GFATS (if appropriate)
86256-IG5TS (if appropriate)
86255-GL1CS (if appropriate)
86256-GL1TS (if appropriate)
86255 NCDCS (if appropriate)
86256 NCDTS (if appropriate)
86255-NFHCS (if appropriate)
86256-NIFTS (if appropriate)
86255-NFLCS (if appropriate)
86256-NMDIS (if appropriate)
84182-PC1BS (if appropriate)
86256 PC1TS (if appropriate)
86256 PC2TS (if appropriate)
84182-PCTBS (if appropriate)
86256 PCTTS (if appropriate)
86256 PDETCS (if appropriate)
86255 SP7CS (if appropriate)
86256 SP7TS (if appropriate)
86255 T46CS (if appropriate)
86256 T46TS (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ENS2	Encephalopathy, Autoimm/Paraneo, S	94697-0

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
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