

Overview

Useful For

Evaluating 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 using spinal fluid specimens

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 cerebrospinal 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
AEECI	Encephalopathy, Interpretation, CSF	No	Yes
AMPCC	AMPA-R Ab CBA, CSF	No	Yes
AMPHC	Amphiphysin Ab, CSF	No	Yes
AGN1C	Anti-Glial Nuclear Ab, Type 1	No	Yes
ANN1C	Anti-Neuronal Nuclear Ab, Type 1	No	Yes
ANN2C	Anti-Neuronal Nuclear Ab, Type 2	No	Yes
ANN3C	Anti-Neuronal Nuclear Ab, Type 3	No	Yes
CS2CC	CASPR2-IgG CBA, CSF	No	Yes
CRMC	CRMP-5-IgG, CSF	No	Yes
DPPCC	DPPX Ab CBA, CSF	No	Yes
GABCC	GABA-B-R Ab CBA, CSF	No	Yes
GD65C	GAD65 Ab Assay, CSF	Yes	Yes

GFAIC	GFAP IFA, CSF	No	Yes
GL1IC	mGluR1 Ab IFA, CSF	No	Yes
IG5CC	IgLON5 CBA, CSF	No	Yes
LG1CC	LGI1-IgG CBA, CSF	No	Yes
NCDIC	Neurochondrin IFA, CSF	No	Yes
NIFIC	NIF IFA, CSF	No	Yes
NMDCC	NMDA-R Ab CBA, CSF	No	Yes
PCTRC	Purkinje Cell Cytoplasmic Ab Type Tr	No	Yes
PCA1C	Purkinje Cell Cytoplasmic Ab Type 1	No	Yes
PCA2C	Purkinje Cell Cytoplasmic Ab Type 2	No	Yes
PDEIC	PDE10A Ab IFA, CSF	No	Yes
SP7IC	Septin-7 IFA, CSF	No	Yes
T46IC	TRIM46 Ab IFA, CSF	No	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
AGNBC	AGNA-1 Immunoblot, CSF	No	No
AINCC	Alpha Internexin CBA, CSF	No	No
AMPIC	AMPA-R Ab IF Titer Assay, CSF	No	No
AMIBC	Amphiphysin Immunoblot, CSF	No	No
AN1BC	ANNA-1 Immunoblot, CSF	No	No
AN2BC	ANNA-2 Immunoblot, CSF	No	No
CRMWC	CRMP-5-IgG Western Blot, CSF	Yes	No
DPPTC	DPPX Ab IFA Titer, CSF	No	No
GABIC	GABA-B-R Ab IF Titer Assay, CSF	No	No
GFACC	GFAP CBA, CSF	No	No
GFATC	GFAP IFA Titer, CSF	No	No
IG5TC	IgLON5 IFA Titer, CSF	No	No
GL1CC	mGluR1 Ab CBA, CSF	No	No
GL1TC	mGluR1 Ab IFA Titer, CSF	No	No
NFHCC	NIF Heavy Chain CBA, CSF	No	No
NIFTC	NIF IFA Titer, CSF	No	No
NFLCC	NIF Light Chain CBA, CSF	No	No
NMDIC	NMDA-R Ab IF Titer Assay,	No	No

	CSF		
PC1BC	PCA-1 Immunoblot, CSF	No	No
PCTBC	PCA-Tr Immunoblot, CSF	No	No
AGNTC	AGNA-1 Titer, CSF	No	No
AN1TC	ANNA-1 Titer, CSF	No	No
AN2TC	ANNA-2 Titer, CSF	No	No
AN3TC	ANNA-3 Titer, CSF	No	No
APHTC	Amphiphysin Ab Titer, CSF	No	No
CRMTC	CRMP-5-IgG Titer, CSF	No	No
NCDCC	Neurochondrin CBA, CSF	No	No
NCDTC	Neurochondrin IFA Titer, CSF	No	No
PC1TC	PCA-1 Titer, CSF	No	No
PC2TC	PCA-2 Titer, CSF	No	No
PCTTC	PCA-Tr Titer, CSF	No	No
PDETC	PDE10A Ab IFA Titer, CSF	No	No
SP7CC	Septin-7 CBA, CSF	No	No
SP7TC	Septin-7 IFA Titer, CSF	No	No
T46CC	TRIM46 Ab CBA, CSF	No	No
T46TC	TRIM46 Ab IFA Titer, CSF	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 antigliial 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-1 immunoblot, and ANNA-2 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 the IFA pattern suggests PCA-2 antibody, then the PCA-2 IFA titer will be performed at an additional charge.

If the 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 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 result is positive, then 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 neurochondrin antibody, then the neurochondrin antibody CBA and neurochondrin IFA titer will be performed at an additional charge.

If the IFA pattern suggests septin-7 antibody, then the septin-7 antibody CBA and septin-7 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-Spinal Fluid](#)
[-Central Nervous System Demyelinating Disease Diagnostic Algorithm](#)

Special Instructions

- [Autoimmune/Paraneoplastic Encephalopathy Evaluation Algorithm-Spinal Fluid](#)
- [Meningitis/Encephalitis Panel Algorithm](#)
- [Central Nervous System Demyelinating Disease Diagnostic Algorithm](#)

Method Name

AEECI: Medical Interpretation

AGN1C, AGNTC, AMPIC, AMPHC, APHTC, ANN1C, AN1TC, ANN2C, AN2TC, ANN3C, AN3TC, CRMTC, CRMC, DPPTC, GABIC, GFAIC, GFATC, IG5TC, GL1IC, GL1TC, NCDIC, NCDTC, NIFIC, NIFTC, NMDIC, PCA1C, PC1TC, PCA2C, PC2TC, PCTRC, PCTTC, PDEIC, PDETC, SP7IC, SP7TC, T46IC, T26TC: Indirect Immunofluorescence Assay (IFA)

AMPCC, CS2CC, DPPCC, GABCC, GFACC, IG5CC, LG1CC, GL1CC, NCDCC, AINCC, NFLCC, NFHCC, NMDCC, SP7CC, T46CC: Cell Binding Assay (CBA)

CRMWC: Western Blot (WB)

AGNBC, AMIBC, AN1BC, AN2BC, PC1BC, PCTBC: Immunoblot (IB)

GD65C: Radioimmunoassay (RIA)

NY State Available

Yes

Specimen

Specimen Type

CSF

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 PCDEC / Pediatric Autoimmune Encephalopathy/CNS Disorder Evaluation, Spinal Fluid. The pediatric autoimmune CNS 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.

Necessary Information

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

Specimen Required

- Container/Tube: Sterile vial
- Preferred: Collection vial number 1
- Acceptable: Any collection vial
- Specimen Volume: 4 mL

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 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
CSF	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 the physician 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, LGI1 antibody was initially considered to be specific for autoimmune limbic encephalitis, but, over time, other presentations have been reported, including 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 profile autoantibody 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, though 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 more sensitive and specific. In contrast, serum testing for LGI1 antibody is more sensitive than CSF testing.

Reference Values

Test ID	Reporting name	Methodology*	Reference value
AEECI	Encephalopathy, Interpretation, CSF	Medical interpretation	Interpretive report
AMPCC	AMPA-R Ab CBA, CSF	CBA	Negative
AMPHC	Amphiphysin Ab, CSF	IFA	Negative
AGN1C	Anti-Glial Nuclear Ab, Type 1	IFA	Negative
ANN1C	Anti-Neuronal Nuclear Ab, Type 1	IFA	Negative
ANN2C	Anti-Neuronal Nuclear Ab, Type 2	IFA	Negative
ANN3C	Anti-Neuronal Nuclear Ab, Type 3	IFA	Negative
CS2CC	CASPR2-IgG CBA, CSF	CBA	Negative
CRMC	CRMP-5-IgG, CSF	IFA	Negative
DPPCC	DPPX Ab CBA, CSF	CBA	Negative
GABCC	GABA-B-R Ab CBA, CSF	CBA	Negative
GD65C	GAD65 Ab Assay, CSF	RIA	< or =0.02 nmol/L Reference values apply to all ages.
GFAIC	GFAP IFA, CSF	IFA	Negative
GL1IC	mGluR1 Ab IFA, CSF	IFA	Negative
IG5CC	IgLON5 CBA, CSF	CBA	Negative
LG1CC	LGI1-IgG CBA, CSF	CBA	Negative
NCDIC	Neurochondrin IFA, CSF	IFA	Negative
NIFIC	NIF IFA, CSF	IFA	Negative
NMDCC	NMDA-R Ab CBA, CSF	CBA	Negative
PCTRC	Purkinje Cell Cytoplasmc Ab Type Tr	IFA	Negative
PCA1C	Purkinje Cell Cytoplasmic Ab Type 1	IFA	Negative
PCA2C	Purkinje Cell Cytoplasmic Ab Type 2	IFA	Negative
PDEIC	PDE10A Ab IFA, CSF	IFA	Negative
SP7IC	Septin-7 IFA, CSF	IFA	Negative
T46IC	TRIM46 IFA, CSF	IFA	Negative

Reflex Information:

Test ID	Reporting name	Methodology*	Reference value
AGNBC	AGNA-1 Immunoblot, CSF	IB	Negative
AGNTC	AGNA-1 Titer, CSF	IFA	<1:2
AINCC	Alpha Internexin CBA, CSF	CBA	Negative
AMPIC	AMPA-R Ab IF Titer Assay, CSF	IFA	<1:2
AMIBC	Amphiphysin Immunoblot, CSF	IB	Negative
AN1BC	ANNA-1 Immunoblot, CSF	IB	Negative

AN1TC	ANNA-1 Titer, CSF	IFA	<1:2
AN2BC	ANNA-2 Immunoblot, CSF	IB	Negative
AN2TC	ANNA-2 Titer, CSF	IFA	<1:2
AN3TC	ANNA-3 Titer, CSF	IFA	<1:2
APHTC	Amphiphysin Ab Titer, CSF	IFA	<1:2
CRMTC	CRMP-5-IgG Titer, CSF	IFA	<1:2
CRMWC	CRMP-5-IgG Western Blot, CSF	WB	Negative
DPPTC	DPPX Ab IFA Titer, CSF	IFA	<1:2
GABIC	GABA-B-R Ab IF Titer Assay, CSF	IFA	<1:2
GFACC	GFAP CBA, CSF	CBA	Negative
GFATC	GFAP IFA Titer, CSF	IFA	<1:2
IG5TC	IgLON5 IFA Titer, CSF	IFA	<1:2
GL1CC	mGluR1 Ab CBA, CSF	CBA	Negative
GL1TC	mGluR1 Ab IFA Titer, CSF	IFA	<1:2
NCDCC	Neurochondrin CBA, CSF	CBA	Negative
NCDTC	Neurochondrin IFA Titer, CSF	IFA	<1:2
NFLCC	NIF Light Chain CBA, CSF	CBA	Negative
NFHCC	NIF Heavy Chain CBA, CSF	CBA	Negative
NIFTC	NIF IFA Titer, CSF	IFA	<1:2
NMDIC	NMDA-R Ab IF Titer Assay, CSF	IFA	<1:2
PC1BC	PCA-1 Immunoblot, CSF	IB	Negative
PC1TC	PCA-1 Titer, CSF	IFA	<1:2
PC2TC	PCA-2 Titer, CSF	IFA	<1:2
PCTBC	PCA-Tr Immunoblot, CSF	IB	Negative
PCTTC	PCA-Tr Titer, CSF	IFA	<1:2
PDETC	PDE10A Ab IFA Titer, CSF	IFA	<1:2
SP7CC	Septin-7 CBA, CSF	CBA	Negative
SP7IC	Septin-7 IFA Titer, CSF	IFA	<1:2
T46CC	TRIM46 CBA, CSF	CBA	Negative
T46TC	TRIM46 IFA Titer, CSF	IFA	<1:2

*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, ANNA-3, 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 1:2 are detectable by recombinant CRMP-5 Western blot analysis. CRMP-5 Western blot

analysis will be done on request on stored spinal fluid (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: These are all potential effectors of neurological dysfunction: 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.
- 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), or glutamic acid decarboxylase (GAD65).

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.

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 specimen 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 ambient temperature (18 to 28 degrees C) utilizing the EUROBlot One instrument. Diluted patient serum (1:12.5) is added to test strips (strips containing recombinant antigen manufactured and purified using biochemical methods) in individual channels and incubated for 30 minutes. Positive specimens will bind to the purified recombinant antigen and negative specimens 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.00000000000008472)

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 x23

86341 x1

- 84182 AGNBC (if appropriate)
- 86256 AGNTC (if appropriate)
- 86255 AINCC (if appropriate)
- 86256 AMPIC (if appropriate)
- 84182 AMIBC (if appropriate)
- 84182 AN1BC (if appropriate)
- 86256 AN1TC (if appropriate)
- 84182 AN2BC (if appropriate)
- 86256 AN2TC (if appropriate)
- 86256 AN3TC (if appropriate)
- 86256 APHTC (if appropriate)
- 86256 CRMTC (if appropriate)
- 84182 CRMWC (if appropriate)
- 86256 DPPTC (if appropriate)

- 86256 GABIC (if appropriate)
- 86255 GFACC (if appropriate)
- 86256 GFATC (if appropriate)
- 86256 IG5TC (if appropriate)
- 86255 GL1CC (if appropriate)
- 86256 GL1TC (if appropriate)
- 86255 NCDCC (if appropriate)
- 86256 NCDTC (if appropriate)
- 86255 NFHCC (if appropriate)
- 86256 NIFTC (if appropriate)
- 86255 NFLCC (if appropriate)
- 86256 NMDIC (if appropriate)
- 84182 PC1BC (if appropriate)
- 86256 PC1TC (if appropriate)
- 86256 PC2TC (if appropriate)
- 84182 PCTBC (if appropriate)
- 86256 PCTTC (if appropriate)
- 86256 PDETC (if appropriate)
- 86255 SP7CC (if appropriate)
- 86256 SP7TC (if appropriate)
- 86255 T46CC (if appropriate)
- 86256 T46TC (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ENC2	Enceph, Autoimm/Paraneo, CSF	94708-5

Result ID	Test Result Name	Result LOINC® Value
89079	AGNA-1, CSF	90827-7
5906	Amphiphysin Ab, CSF	90815-2
3852	ANNA-1, CSF	44768-0
7472	ANNA-2, CSF	56959-0
21633	ANNA-3, CSF	90836-8
21650	CRMP-5-IgG, CSF	63216-6
3988	PCA-1, CSF	90841-8
21632	PCA-2, CSF	90843-4
21631	PCA-Tr, CSF	90845-9
21702	GAD65 Ab Assay, CSF	94359-7
61513	NMDA-R Ab CBA, CSF	93502-3
61514	AMPA-R Ab CBA, CSF	93491-9
61515	GABA-B-R Ab CBA, CSF	93426-5
34256	Encephalopathy, Interpretation, CSF	69048-7
618895	IFA Notes	48767-8

64280	LGI1-IgG CBA, CSF	94288-8
64282	CASPR2-IgG CBA, CSF	94286-2
64927	mGluR1 Ab IFA, CSF	94361-3
64934	DPPX Ab CBA, CSF	94283-9
605156	GFAP IFA, CSF	94360-5
606965	NIF IFA, CSF	96490-8
606951	IgLON5 CBA, CSF	96481-7
615866	Neurochondrin IFA, CSF	101451-3
615874	Septin-7 IFA, CSF	101464-6
620067	PDE10A Ab IFA, CSF	103842-1
616446	TRIM46 Ab IFA, CSF	103843-9