

Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

Overview

Useful For

Investigating new onset dementia and cognitive impairment plus 1 or more of the following accompaniments using cerebrospinal fluid specimens:

- -Rapid onset and progression
- -Fluctuating course
- -Psychiatric accompaniments (psychosis, hallucinations)
- -Movement disorder (myoclonus, tremor, dyskinesias)
- -Headache
- -Autoimmune stigmata (personal history or family history or signs of diabetes mellitus, thyroid disorder, vitiligo, poliosis [premature graying], myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus)
- -Smoking history (20 or more pack-years) or other cancer risk factors
- -History of cancer
- -Inflammatory cerebrospinal fluid
- -Neuroimaging findings atypical for degenerative etiology

Profile Information

| Test Id | Reporting Name | Available Separately | Always Performed |
|---------|-----------------------------|----------------------|------------------|
| ADMCI | Dementia, Interpretation, | No | Yes |
| | CSF | | |
| AMPCC | AMPA-R Ab CBA, CSF | No | Yes |
| AMPHC | Amphiphysin Ab, CSF | No | Yes |
| AGN1C | Anti-Glial Nuclear Ab, Type | No | Yes |
| | 1 | | |
| ANN1C | Anti-Neuronal Nuclear Ab, | No | Yes |
| | Type 1 | | |
| ANN2C | Anti-Neuronal Nuclear Ab, | No | Yes |
| | Type 2 | | |
| ANN3C | Anti-Neuronal Nuclear Ab, | No | Yes |
| | Type 3 | | |
| 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 |
| IG5CC | IgLON5 CBA, CSF | No | Yes |
| LG1CC | LGI1-IgG CBA, CSF | No | Yes |
| GL1IC | mGluR1 Ab IFA, CSF | No | Yes |



Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

| NCDIC | Neurochondrin IFA, CSF | No | Yes |
|-------|---------------------------|----|-----|
| NIFIC | NIF IFA, CSF | No | Yes |
| NMDCC | NMDA-R Ab CBA, CSF | No | Yes |
| PCTRC | Purkinje Cell Cytoplasmc | No | Yes |
| | Ab Type Tr | | |
| PCA2C | Purkinje Cell Cytoplasmic | No | Yes |
| | Ab Type 2 | | |
| PDEIC | PDE10A Ab 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, | No | No |
| | CSF | | |
| AMIBC | Amphiphysin Immunoblot, | No | No |
| | CSF | | |
| AN1BC | ANNA-1 Immunoblot, CSF | No | No |
| AN2BC | ANNA-2 Immunoblot, CSF | No | No |
| CRMWC | CRMP-5-IgG Western Blot, | Yes | No |
| | CSF | | |
| DPPTC | DPPX Ab IFA Titer, CSF | No | No |
| GABIC | GABA-B-R Ab IF Titer | No | No |
| | Assay, CSF | | |
| 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 | | |
| 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 |



Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

| CDNATC | CDMD F InC Titor CCF | NIC | NI |
|--------|--------------------------|-----|----|
| CRMTC | CRMP-5-IgG Titer, CSF | No | No |
| NCDCC | Neurochondrin CBA, CSF | No | No |
| NCDTC | Neurochondrin IFA Titer, | No | No |
| | CSF | | |
| PCTTC | PCA-Tr Titer, CSF | No | No |
| PC2TC | PCA-2 Titer, CSF | No | No |
| PDETC | PDE10A Ab 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 <u>Antibody Prevalence in Epilepsy and Encephalopathy (APE2) scorecard</u>.

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

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

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

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

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

If the IFA pattern suggests Purkinje cell antibody type 2 (PCA-2), then PCA-2 IFA titer will be performed at an additional charge.

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

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

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

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



Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

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

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

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

If IgLON5 antibody CBA result is positive, then IgLON5 IFA titer will be performed at an additional charge.

If the IFA pattern suggests neuronal intermediate filament (NIF) antibody, then 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 neurochondrin antibody CBA and neurochondrin 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 Autoimmune/Paraneoplastic Dementia Evaluation Algorithm-Spinal Fluid.

Special Instructions

• Autoimmune/Paraneoplastic Dementia Evaluation Algorithm-Spinal Fluid

Method Name

ADMCI: 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, PCA2C, PC2TC, PCTRC, PCTTC, PDEIC, PDETC, T46IC, T46TC: Indirect Immunofluorescence Assay (IFA)

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

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



Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

CRMWC: Western Blot (WB)

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 <u>Autoimmune Neurology Test Ordering Guide</u>.

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.

Necessary Information

Provide the following information:

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

Specimen Required

Container/Tube: Sterile vial

Preferred: Collection vial number 1 **Acceptable:** Any collection vial **Specimen Volume:** 4 mL

Forms

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

Specimen Minimum Volume

2 mL

Reject Due To

| Gross | Reject |
|---------------|--------|
| hemolysis | |
| Gross lipemia | Reject |



Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

| 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

The rapid identification of subacute cognitive decline as autoimmune dementia facilitates optimum treatment with immunotherapy and an expedited search for a limited stage of cancer in some patients. Traditionally, neurologists have been reluctant to consider a diagnosis of an autoimmune cognitive disorder in the absence of delirium. However, some recent case series and clinical-serologic observations have suggested a growing appreciation for autoimmune neurologic disorders presenting with features of a rapidly progressive dementia rather than delirium. These disorders can affect all age groups.

Unfortunately, these potentially reversible conditions may be misdiagnosed as being progressive neurodegenerative (currently irreversible) disorders with devastating consequences for the patient. In the evaluation of a patient with cognitive decline, clinicians should consider the possibility of an autoimmune etiology on their list of differential diagnoses. The importance of not overlooking this possibility rests in the experience that these patients have a potentially immunotherapy-responsive, reversible disorder. The development and widespread availability of neural antibody marker testing has changed this perspective so that other presenting symptoms, such as personality change, executive dysfunction, and psychiatric symptoms, are increasingly recognized in an autoimmune context.

Clues that are helpful in identifying patients with an autoimmune dementia can be summarized as a triad of:

- -Suspicious clinical features (a subacute onset of symptoms, a rapidly progressive course, and fluctuating symptoms) and radiological findings
- -Detection of cerebrospinal fluid (CSF) or serological biomarkers of autoimmunity
- -Response to immunotherapy

Detection of neural autoantibodies in serum or CSF serves 2 purposes: to inform the physician of a likely autoimmune etiology and to raise suspicion for a paraneoplastic cause. The neurological associations of neural autoantibodies tend to be diverse and multifocal, although certain syndromic associations may apply. For example, LGI1 (leucine-rich, glioma inactivated 1) 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.

Since neurological presentations are often multifocal and diverse, comprehensive antibody testing is usually more informative than testing for 1 or 2 selected antibodies. Some of the antibodies are highly predictive of an unsuspected



Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

underlying cancer. For example, small-cell lung carcinoma (antineuronal nuclear antibody-type 1 [ANNA-1]; collapsin response-mediator protein-5 neuronal [CRMP-5-IgG]), ovarian teratoma (N-methyl-D-aspartate receptor: NMDA-R), and thymoma (CRMP-5 IgG).

Also, a profile of seropositivity for multiple autoantibodies may be informative for cancer type. For example, in a patient presenting with a rapidly progressive dementia who has CRMP-5-IgG, and subsequent testing reveals muscle acetylcholine receptor (AChR) binding antibody, the findings should raise a high suspicion for thymoma. If an associated tumor is found, its resection or ablation optimizes the neurological outcome.

Antibody testing on CSF is additionally helpful particularly 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 more sensitive and specific.

Reference Values

| Test ID | Reporting name | Methodology* | Reference value |
|---------|-------------------------------------|----------------|---------------------------|
| ADMCI | Dementia, Interpretation, CSF | Medical | |
| | | interpretation | Interpretive report |
| AMPCC | AMPA-R Ab CBA, CSF | СВА | 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 | СВА | Negative |
| CRMC | CRMP-5-IgG, CSF | IFA | Negative |
| DPPCC | DPPX Ab CBA, CSF | СВА | Negative |
| GABCC | GABA-B-R Ab CBA, CSF | СВА | Negative |
| GD65C | GAD65 Ab Assay, CSF | RIA | < or =0.02 nmol/L |
| | | | Reference values apply to |
| | | | all ages. |
| GFAIC | GFAP IFA, CSF | IFA | Negative |
| IG5CC | IgLON5 CBA, CSF | СВА | Negative |
| LG1CC | LGI1-IgG CBA, CSF | СВА | Negative |
| NCDIC | Neurochondrin IFA, CSF | IFA | Negative |
| GL1IC | mGluR1 Ab IFA, CSF | IFA | Negative |
| NIFIC | NIF IFA, CSF | IFA | Negative |
| NMDCC | NMDA-R Ab CBA, CSF | СВА | Negative |
| PCTRC | Purkinje Cell Cytoplasmc Ab Type Tr | IFA | Negative |
| PCA2C | Purkinje Cell Cytoplasmic Ab Type 2 | IFA | Negative |
| PDEIC | PDE10A Ab IFA, CSF | IFA | Negative |
| T46IC | TRIM46 IFA, CSF | IFA | Negative |

Reflex Information:



Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

| 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 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 | СВА | 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 |
| NFHCC | NIF Heavy Chain CBA, CSF | CBA | Negative |
| NIFTC | NIF IFA Titer, CSF | IFA | <1:2 |
| NFLCC | NIF Light Chain CBA, CSF | СВА | Negative |
| NMDIC | NMDA-R Ab IF Titer Assay, 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 |
| T46CC | TRIM46 CBA, CSF | СВА | 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-2, or PCA-Tr may be reported as "unclassified anti-neuronal IgG." Complex patterns that include nonneuronal elements may be reported as "uninterpretable."



Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

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

Antibodies specific for neuronal, glial, or muscle proteins are valuable serological markers of autoimmune epilepsy and of a patient's immune response to cancer. These autoantibodies are not found in healthy subjects and are usually accompanied by subacute neurological symptoms and signs. It is not uncommon for more than 1 of the following autoantibodies to be detected in patients with autoimmune dementia:

- -Plasma membrane antibodies (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). These autoantibodies are all potential effectors of dysfunction.
- -Neuronal nuclear autoantibody type 1 (ANNA-1) or type 3 (ANNA-3)
- -Neuronal or muscle cytoplasmic antibodies (amphiphysin, Purkinje cell antibody-type 2 [PCA-2], collapsin response-mediator protein-5 neuronal [CRMP-5-IgG], or glutamic acid decarboxylase [GAD65] antibody).

Cautions

Negative results do not exclude autoimmune dementia or cancer.

This evaluation does not detect Ma1 or Ma2 antibodies (also known as MaTa). Ma2 antibody has been described in patients with brainstem and limbic encephalitis in the context of testicular germ cell neoplasms. Scrotal ultrasound is advisable in men who present with unexplained subacute encephalitis.

Clinical Reference

- 1. Sechi E, Flanagan EP. Diagnosis and management of autoimmune dementia. Curr Treat Options Neurol. 2019;21(3):11. Published 2019 Feb 27. doi:10.1007/s11940-019-0550-9
- 2. Bastiaansen AEM, van Steenhoven RW, de Bruijn MAAM, et al. Autoimmune encephalitis resembling dementia syndromes. Neurol Neuroimmunol Neuroinflamm. 2021;8(5):e1039. Published 2021 Aug 2. doi:10.1212/NXI.0000000000001039
- 3. 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
- 4. 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.000000000000151

Performance

Method Description

Indirect Immunofluorescence Assay:



Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

The patient's sample is tested by a standardized immunofluorescence assay that uses a composite frozen section of mouse cerebellum, kidney, and gut tissues. After incubation with sample and washing, fluorescein-conjugated goat-antihuman IgG is applied. Neuron-specific autoantibodies are identified by their characteristic fluorescence staining patterns. Samples 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. doi:10.1212/NXI.000000000000385)

Radioimmunoassay:

(125)I-labeled recombinant human antigens or labeled receptors are incubated with patient sample. 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, eds. Manual of Clinical and Laboratory Immunology. 6th ed. ASM Press; 2002:1005-1012; Walikonis JE, Lennon VA. Radioimmunoassay for glutamic acid decarboxylase [GAD65] autoantibodies as a diagnostic aid for stiff-man syndrome and a correlate of susceptibility to type 1 diabetes mellitus. Mayo Clin Proc. 1998;73[12]:1161-1166; 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)

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, 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)

Immunoblot:

All steps are performed at room temperature (18-28 degrees C) utilizing the EUROBlot One instrument. Diluted patient sample (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 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 produce 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)

Cell Binding Assay:

Patient sample is applied to a composite slide containing transfected and nontransfected EU90 cells. After incubation



Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

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)

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 <u>Test Prices</u> for detailed fee information.
- Clients without access to Test Prices can contact <u>Customer Service</u> 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact <u>Customer Service</u>.

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 21

86341

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)

SCALC VNATC (if appropriate)

86256 AN2TC (if appropriate)

86256 AN3TC (if appropriate)



Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

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 NCDCC (if appropriate)

86256 NCDTC (if appropriate)

86255-GL1CC (if appropriate)

86256-GL1TC (if appropriate)

86255-NFHCC (if appropriate)

86256-NIFTC (if appropriate)

86255-NFLCC (if appropriate)

86256-NMDIC (if appropriate)

86256 PC2TC (if appropriate)

84182-PCTBC (if appropriate)

86256 PCTTC (if appropriate)

86256 PDETC (if appropriate)

86255 T46CC (if appropriate)

86256 T46TC (if appropriate)

LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---------|--------------------------------|--------------------|
| DMC2 | Dementia, Autoimm/Paraneo, CSF | 94707-7 |

| 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 |
| 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 |
| 34254 | Dementia, Interpretation, CSF | 69048-7 |
| 618893 | IFA Notes | 48767-8 |
| 64280 | LGI1-IgG CBA, CSF | 94288-8 |



Dementia, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

| 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 |
| 620067 | PDE10A Ab IFA, CSF | 103842-1 |
| 616446 | TRIM46 Ab IFA, CSF | 103843-9 |