MAYO CLINIC LABORATORIES

Test Definition: PNEFC

Neuroimmunology Antibody Follow-up, Spinal Fluid

Overview

Useful For

Monitoring patients who have previously tested positive for 1 or more antibodies within the past 5 years in a Mayo Clinic Neuroimmunology Laboratory spinal fluid evaluation

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
AMPCC	AMPA-R Ab CBA, CSF	No	No
AMPIC	AMPA-R Ab IF Titer Assay, CSF	No	No
AMPHC	Amphiphysin Ab, CSF	No	No
ABLTC	Amphiphysin Western Blot, CSF	No	No
AGN1C	Anti-Glial Nuclear Ab, Type 1	No	No
ANN1C	Anti-Neuronal Nuclear Ab, Type 1	No	No
ANN2C	Anti-Neuronal Nuclear Ab, Type 2	No	No
ANN3C	Anti-Neuronal Nuclear Ab, Type 3	No	No
CS2CC	CASPR2-IgG CBA, CSF	No	No
CRMWC	CRMP-5-IgG Western Blot, CSF	No	No
CRMC	CRMP-5-IgG, CSF	No	No
GABCC	GABA-B-R Ab CBA, CSF	No	No
GABIC	GABA-B-R Ab IF Titer Assay, CSF	No	No
LG1CC	LGI1-IgG CBA, CSF	No	No
NMDCC	NMDA-R Ab CBA, CSF	No	No
NMDIC	NMDA-R Ab IF Titer Assay, CSF	No	No
WBNC	Paraneoplas Autoantibody WBlot,CSF	No	No
PCTRC	Purkinje Cell Cytoplasmc Ab Type Tr	No	No
PCA1C	Purkinje Cell Cytoplasmic Ab Type 1	No	No
PCA2C	Purkinje Cell Cytoplasmic	No	No

	Ab Type 2		
VGKCC	VGKC-complex Ab IPA, CSF	No	No
DPPCC	DPPX Ab CBA, CSF	No	No
DPPIC	DPPX Ab IFA, CSF	No	No
DPPTC	DPPX Ab IFA Titer, CSF	No	No
GL1CC	mGluR1 Ab CBA, CSF	No	No
GL1IC	mGluR1 Ab IFA, CSF	No	No
GL1TC	mGluR1 Ab IFA Titer, CSF	No	No

Method Name

ANN1C, ANN2C, ANN3C, AGN1C, PCA1C, PCA2C, PCTRC, AMPHC, CRMC, NMDIC, AMPIC, GABIC, DPPIC, DPPTC, GL1CC, GL1TC: Indirect Immunofluorescence (IFA)
NMDCC, AMPCC, GABCC, LG1CC, CS2CC, DPPCC, GL1CC: Cell-Binding Assay (CBA)
WBNC, ABLTC: Western Blot
VGKCC: Radioimmunoassay (RIA)

NY State Available

Yes

Specimen

Specimen Type

CSF

Ordering Guidance

This test is only appropriate for follow-up in patients who have previously tested positive in a spinal fluid test. If patients have not previously been positive in a spinal fluid test, order 1 of the following:
-PAC1 / Paraneoplastic, Autoantibody Evaluation, Spinal Fluid
-DMC1 / Dementia, Autoimmune Evaluation, Spinal Fluid
-ENC1 / Encephalopathy, Autoimmune Evaluation, Spinal Fluid
-EPC1 / Epilepsy, Autoimmune Evaluation, Spinal Fluid
-MDC1 / Movement Disorder Evaluation, Spinal Fluid

Specimen Required

Container/Tube: Sterile vial
Specimen Volume: 4 mL

Forms

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

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	
	Frozen	28 days	
	Ambient	72 hours	

Clinical & Interpretive

Clinical Information

Paraneoplastic autoimmune neurological disorders reflect a patient's humoral and cellular immune responses to cancer. The cancer may be new or recurrent, is usually limited in metastatic volume, and is often occult by standard imaging procedures. Autoantibodies specific for onconeural proteins found in the plasma membrane, cytoplasm, and nucleus of neurons or muscle are generated in this immune response, and serve as serological markers of paraneoplastic autoimmunity. The most commonly recognized cancers in this context are small-cell lung carcinoma (SCLC), thymoma, ovarian (or related mullerian) carcinoma, breast carcinoma, and Hodgkin lymphoma. Pertinent childhood neoplasms recognized thus far include neuroblastoma, thymoma, Hodgkin lymphoma, and chondroblastoma. An individual patient's autoantibody profile can predict a specific neoplasm with 90% certainty, but not the neurological syndrome.

Three classes of autoantibodies are recognized in the spinal fluid analysis:
-Neuronal nuclear (antineuronal nuclear antibody-type 1 [ANNA-1], ANNA-2, ANNA-3)
-Neuronal and muscle cytoplasmic (Purkinje cell cytoplasmic antibody, type 1 [PCA-1]; PCA-2; PCA-Tr, CRMP-5, and amphiphysin)
-Glial nuclear (antiglial nuclear antibody: AGNA)

Seropositive patients usually present with subacute neurological symptoms and signs. The patient may present with encephalopathy, cerebellar ataxia, myelopathy, radiculopathy, plexopathy, sensory, sensorimotor, or autonomic neuropathy, with or without coexisting evidence of a neuromuscular transmission disorder: Lambert-Eaton syndrome (LES), myasthenia gravis, or neuromuscular hyperexcitability. Initial signs may be subtle, but a subacute multifocal and progressive syndrome usually evolves. Sensorimotor neuropathy and cerebellar ataxia are common presentations, but the clinical picture in some patients is dominated by striking gastrointestinal dysmotility, limbic encephalopathy, basal ganglionitis, or cranial neuropathy (especially loss of vision, hearing, smell, or taste). Cancer risk factors include past or family history of cancer, history of smoking, or social/environmental exposure to carcinogens. Early diagnosis and treatment of the neoplasm favor less neurological morbidity and offer the best hope for survival.

Reference Values

Test ID	Reporting Name	Reference Value
AMPCC	AMPA-R Ab CBA, CSF	Negative
AMPIC	AMPA-R Ab IF Titer Assay, CSF	<1:2
AMPHC	Amphiphysin Ab, CSF	<1:2
ABLTC	Amphiphysin Western Blot, CSF	Negative
AGN1C	Anti-Glial Nuclear Ab, Type 1	<1:2
ANN1C	Anti-Neuronal Nuclear Ab, Type 1	<1:2
ANN2C	Anti-Neuronal Nuclear Ab, Type 2	<1:2
ANN3C	Anti-Neuronal Nuclear Ab, Type 3	<1:2
CS2CC	CASPR2-IgG CBA, CSF	Negative
CRMC	CRMP-5-IgG, CSF	<1:2
GABCC	GABA-B-R Ab CBA, CSF	Negative
GABIC	GABA-B-R Ab IF Titer Assay, CSF	<1:2
LG1CC	LGI1-IgG CBA, CSF	Negative
VGKCC	Neuronal (V-G) K+ Channel Ab, CSF	<0.02
NMDCC	NMDA-R Ab CBA, CSF	Negative
NMDIC	NMDA-R Ab IF Titer Assay, CSF	<1:2
NMOTC	NMO/AQP4 FACS Titer, CSF	<1:2
WBNC	Paraneoplastic Autoantibody WBlot, CSF	Negative
PCA1C	Purkinje Cell Cytoplasmic Ab Type 1	<1:2
PCA2C	Purkinje Cell Cytoplasmic Ab Type 2	<1:2
PCTRC	Purkinje Cell Cytoplasmic Ab Type Tr	<1:2

Interpretation

Antibodies directed at onconeural proteins shared by neurons, muscle, and certain cancers are valuable serological markers of a patient's immune response to cancer. They are not found in healthy subjects, and are usually accompanied by subacute neurological symptoms and signs. Several autoantibodies have a syndromic association, but no known autoantibody predicts a specific neurological syndrome. Conversely, a positive autoantibody profile has 80% to 90% predictive value for a specific cancer. It is not uncommon for more than 1 paraneoplastic autoantibodies to be detected, each predictive of the same cancer.

Cautions

This test should only be utilized when the presence of paraneoplastic autoantibodies has been previously documented.

This test should not be requested in 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.

Clinical Reference

Lancaster E, Martinez-Hernandez E, Dalmau J: Encephalitis and antibodies to synaptic and neuronal cell surface proteins. Neurology 2011;77(2):179-189

Performance

Method Description

Indirect Immunofluorescence Assay (IFA):
After applying patient's prepared specimen to a composite substrate of frozen mouse tissues (brain, kidney, and gut) and washing, fluorescein-conjugated goat-antihuman IgG is applied to detect the distribution and pattern of patient IgG binding.(Pittock SJ, Kryzer TJ, Lennon VA: Paraneoplastic antibodies coexist and predict cancer, not neurological syndrome. Ann Neurol 2004;56:715-719)

Radioimmunoprecipitation (RIA):
Goat-antihuman IgG and IgM is used as precipitant in all assays. Cation channel protein antigens are solubilized from neuronal or muscle membrane, in nonionic detergent, and complexed with a selective high-affinity ligand labeled with (125)I.(Griesmann GE, Kryzer TJ, Lennon VA: Autoantibody profiles of myasthenia gravis and Lambert-Eaton myasthenic syndrome. In Manual of Clinical and Laboratory Immunology, Sixth edition. Edited by NR Rose, RG Hamilton, et al. Washington, DC, ASM Press, 2002, pp 1005-1012)

Cell-Binding Assay (CBA):
Patient specimen is applied to a composite slide containing transfected and nontransfected HEK-293 cells. After incubation and washing, fluorescein-conjugated goat-antihuman IgG is applied to detect the presence of patient IgG binding.(Package insert: EUROIMMUN AG. Stocker W, et al. Differenzierte Autoantikorper-Diagnostik mit BIOCHIP-Mosaiken. U Conrad, K. (Hrsg) Autoantikorper. Pabst-Verlag 1998, 78-99)

Western Blot (WB):
A mixture of neuronal antigens extracted aqueously from adult rat cerebellum is denatured, reduced, and separated by electrophoresis on 10% polyacrylamide gel. Full-length recombinant human CRMP-5 antigen is used to confirm CRMP-5-IgG.(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]:145-154)

PDF Report

No

Day(s) Performed

ANN1C, ANN2C, ANN3C, AGN1C, PCA1C, PCA2C, PCTRC, AMPHC, CRMC, NMDIC, AMPIC, GABIC, DPPIC, DPPTC, GL1CC, GL1TC, VGKC: Monday through Sunday

AMPCC, GABCC, NMDCC, LG1CC, CS2CC, DPPCC, GL1CC: Monday through Friday

WBNC, ABLTC: Monday, Wednesday, Friday

Report Available

Varies

Specimen Retention Time

28 days

Performing Laboratory Location

Rochester

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. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

84182-Paraneoplastic autoantibody Western blot confirmation (if appropriate)
84182-Amphiphysin Western blot confirmation (if appropriate)
86255-Amphiphysin (if appropriate)
86255-ANNA-1 (if appropriate)
86255-ANNA-2 (if appropriate)
86255-ANNA-3 (if appropriate)
86255-CRMP-5-IgG (if appropriate)
86255-PCA-1 (if appropriate)
86255-PCA-2 (if appropriate)
86255-PCA-Tr (if appropriate)
86255-AGNA-1 (if appropriate)
86256-AMPIC (if appropriate)
86256-GABIC (if appropriate)
86256-NMDIC (if appropriate)
86255-DPPIC (if appropriate)
86256-DPPTC (if appropriate)
86255-GL1IC (if appropriate)
86256-GL1TC (if appropriate)
86255-AMPCC (if appropriate)
86255-GABCC (if appropriate)
86255-NMDCC (if appropriate)
83519-VGKCC (if appropriate)
86255-LG1CC (if appropriate)

86255-CS2CC (if appropriate)
86255-DPPCC (if appropriate)
86255-GL1CC (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PNEFC	Neuroimmunology Ab Follow-up, CSF	80615-8

Result ID	Test Result Name	Result LOINC® Value
84299	Neuroimmunology Ab Follow-up, CSF	80615-8