MAYO CLINIC LABORATORIES

Test Definition: PCDEC

Pediatric Autoimmune Encephalopathy/CNS Disorder Evaluation, Spinal Fluid

Overview

Useful For

Evaluating children with autoimmune central nervous system disorders using spinal fluid specimens

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
PCCI	Peds Autoimmune CNS Interp, CSF	No	Yes
ANN1C	Anti-Neuronal Nuclear Ab, Type 1	No	Yes
CS2CC	CASPR2-IgG CBA, CSF	No	Yes
DPPIC	DPPX Ab IFA, 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
LG1CC	LGI1-IgG CBA, CSF	No	Yes
GL1IC	mGluR1 Ab IFA, CSF	No	Yes
NMDCC	NMDA-R Ab CBA, CSF	No	Yes
NMOFC	NMO/AQP4 FACS, CSF	Yes	Yes
PCTRC	Purkinje Cell Cytoplasmc Ab Type Tr	No	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
AGN1C	Anti-Glial Nuclear Ab, Type 1	No	No
AGNBC	AGNA-1 Immunoblot, CSF	No	No
AMIBC	Amphiphysin Immunoblot, CSF	No	No
AMPCC	AMPA-R Ab CBA, CSF	No	No
AMPHC	Amphiphysin Ab, CSF	No	No
AMPIC	AMPA-R Ab IF Titer Assay, CSF	No	No
AN1BC	ANNA-1 Immunoblot, CSF	No	No
AN2BC	ANNA-2 Immunoblot, CSF	No	No
ANN2C	Anti-Neuronal Nuclear Ab, Type 2	No	No
ANN3C	Anti-Neuronal Nuclear Ab,	No	No

	Type 3		
DPPCC	DPPX Ab CBA, CSF	No	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
GL1CC	mGluR1 Ab CBA, CSF	No	No
GL1TC	mGluR1 Ab IFA Titer, CSF	No	No
NMDIC	NMDA-R Ab IF Titer Assay, CSF	No	No
NMOTC	NMO/AQP4 FACS Titer, CSF	No	No
PC1BC	PCA-1 Immunoblot, CSF	No	No
PCA1C	Purkinje Cell Cytoplasmic Ab Type 1	No	No
PCA2C	Purkinje Cell Cytoplasmic Ab Type 2	No	No
PCTBC	PCA-Tr Immunoblot, CSF	No	No

Testing Algorithm

If indirect immunofluorescence assay (IFA) patterns suggest antineuronal nuclear antibodies (ANNA)-1, then ANNA-1 immunoblot and ANNA-2 immunoblot are performed at an additional charge.

If IFA patterns suggest ANNA-2 antibody, then ANNA-2 immunoblot, ANNA-1 immunoblot, and ANNA-2 antibody IFA are performed at an additional charged.

If IFA patterns suggest ANNA-3 antibody, then ANNA-3 IFA is performed at an additional charge.

If IFA patterns suggest Purkinje cytoplasmic antibody (PCA)-1, then PCA-1 immunoblot and PCA-1 IFA are performed at an additional charge.

If IFA patterns suggest PCA-2 antibody, then PCA-2 IFA is performed at an additional charge.

If IFA patterns suggest PCA-Tr antibody, then PCA-Tr immunoblot is performed at an additional charge.

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

If IFA pattern suggests anti-glial nuclear antibody (AGNA), then AGNA immunoblot and AGNA antibody IFA titer are performed at an additional charge.

If IFA pattern suggests N-methyl-D-aspartate receptor (NMDA-R) antibody, then NMDA-R IFA titer is performed at an additional charge.

If IFA pattern suggests alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptor (AMPA-R) antibody, then AMPA-R antibody cell-binding assay (CBA) and AMPA-R IFA are performed at an additional charge.

If IFA pattern suggests gamma-aminobutyric acid B receptor (GABA-B-R) antibody, then GABA-B-R IFA titer is performed at an additional charge.

If IFA pattern suggests dipeptidyl-peptidase-like protein-6 (DPPX) antibody, then DPPX antibody CBA and DPPX IFA titer are performed at an additional charge.

If IFA pattern suggests metabotropic glutamate receptor 1 (mGluR1) antibody, then mGluR1antibody CBA and mGluR1 IFA titer are performed at an additional charge.

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

If neuromyelitis optica/aquaporin-4-IgG (NMO/AQP4-IgG) fluorescence-activated cell sorting (FACS) screen assay requires further investigation, then NMO/AQP4-IgG FACS titration assay is performed at an additional charge.

For more information, see the following:
Pediatric Autoimmune Encephalopathy/Central Nervous System Disorders Evaluation Algorithm-Spinal Fluid
Pediatric Autoimmune Central Nervous System Demyelinating Disease Diagnostic Algorithm

Special Instructions

- Pediatric Autoimmune Encephalopathy/CNS Disorders Evaluation Algorithm-Spinal Fluid
- Pediatric Autoimmune Central Nervous System Demyelinating Disease Diagnostic Algorithm

Method Name

CS2CC, DPPCC, GABCC, AMPCC, GFACC, GL1CC, LG1CC, NMDCC: Cell-Binding Assay (CBA)

NMOFC, NMOTC: Flow Cytometry

AGN1C, AMPIC, ANN1C, ANN2C, ANN3C, DPPIC, DPPTC, GABIC, GFAIC, GFATC, GL1IC, GL1TC, NMDIC, PCA1C, PCA2C, PCTRC: Indirect Immunofluorescence (IFA)

GD65C: Radioimmunoassay (RIA)

AGNBC, AMIBC, AN1BC, AN2BC, PC1BC, PC2BC: Immunoblot (IB)

NY State Available

Yes

Specimen

Specimen Type
CSF

Ordering Guidance
Multiple neuroimmunology profile tests are available. For testing that is performed with each profile, see Autoimmune Neurology Antibody Matrix.

Necessary Information
Provide the following information:
-Relevant clinical information
-Ordering provider name, phone number, mailing address, and e-mail address

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
Autoimmune encephalitis and myelitis is increasingly recognized as a cause of central nervous system disease in children and adolescents. N-methyl-D-aspartate receptor antibody (NMDA-R) encephalitis and myelin oligodendrocyte glycoprotein (MOG) autoimmunity are most common, although other entities, including aquaporin-4 autoimmunity,

contactin-associated protein-like 2 (CASPR2) autoimmunity, autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy, and paraneoplastic encephalomyelopathies, may also occur in children.

Reference Values

Test ID	Reporting Name	Methodology	Reference Value
PCCI	Peds Autoimmune CNS Interp, CSF	Medical interpretation	NA
ANN1C	Anti-Neuronal Nuclear Ab, Type 1	IFA	Negative at <1:2*
CS2CC	CASPR2-IgG CBA, CSF	CBA	Negative
DPPIC	DPPX Ab IFA, CSF	IFA	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
LG1CC	LGI1-IgG CBA, CSF	CBA	Negative
NMDCC	NMDA-R Ab CBA, CSF	CBA	Negative
NMOFC	NMO/AQP4 FACS, CSF	FACS	Negative
PCTRC	Purkinje Cell Cytoplasmc Ab Type Tr	IFA	<1:2*

Reflex Information:

Test ID	Reporting Name	Methodology	Reference Value
AGN1C	Anti-Glial Nuclear Ab Type 1	IFA	<1:2
AGNBC	AGNA-1 Immunoblot, CSF	IB	Negative
AMIBC	Amphiphysin Immunoblot, CSF	IB	Negative
AMPCC	AMPA-R Ab CBA, CSF	CBA	Negative
AMPHC	Amphiphysin Ab, CSF	IFA	<1:2
AMPIC	AMPA-R Ab IF Titer Assay, CSF	IFA	<1:2
ANN2C	Anti-Neuronal Nuclear Ab, Type 2	IFA	<1:2*
AN1BC	ANNA-1 Immunoblot, CSF	IB	Negative
AN2BC	ANNA-2 Immunoblot, CSF	IB	Negative
ANN3C	Anti-Neuronal Nuclear Ab, Type 3	IFA	<1:2*
DPPCC	DPPX Ab CBA, CSF	CBA	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
GL1CC	mGluR1 Ab CBA, CSF	CBA	Negative
GL1TC	mGluR1 Ab IFA Titer, CSF	IFA	<1:2
NMDIC	NMDA-R Ab IF Titer Assay, CSF	IFA	<1:2
NMOTC	NMO/AQP4 FACS Titer, CSF	FACS	<1:2

PC1BC	PCA-1 Immunoblot, CSF	IB	Negative
PCA1C	Purkinje Cell Cytoplasmic Ab Type 1	IFA	<1:2*
PCA2C	Purkinje Cell Cytoplasmic Ab Type 2	IFA	<1:2*
PCTBC	PCA-Tr Immunoblot, CSF	IB	Negative

*Methodology abbreviations:
Immunofluorescence assay (IFA)
Cell-binding assay (CBA)
Fluorescence activated cell sorting assay (FACS)
Radioimmunoassay (RIA)
Immunoblot (IB)

*Neuron-restricted patterns of IgG staining that do not fulfill criteria for ANNA-1, ANNA-2, ANNA-3, PCA-1, PCA-2, or PCA-Tr may be reported as "unclassified antineuronal IgG." Complex patterns that include nonneuronal elements may be reported as "uninterpretable."

Interpretation

This profile is consistent with an autoimmune central nervous system disorder.

Cautions

Negative results do not exclude a diagnosis of an autoimmune central nervous system disorder.

Clinical Reference

1. Dubey D, Pittock SJ, Krecke KN, et al: Clinical, radiologic, and prognostic features of myelitis associated with myelin oligodendrocyte glycoprotein autoantibody. JAMA Neurol. 2019 Mar 1;76(3):301-309 doi: 10.1001/jamaneurol.2018.4053
2. McKeon A, Lennon VA, Lotze T, et al: CNS aquaporin-4 autoimmunity in children. Neurology. 2008 Jul 8;71(2):93-100
3. Dubey D, Hinson SR, Jolliffe EA, et al: Autoimmune GFAP astrocytopathy: Prospective evaluation of 90 patients in 1?year. J Neuroimmunol. 2018 Aug 15;321:157-163
4. Philipps G, Alisanski SB, Pranzatelli M, et al: Purkinje cell cytoplasmic antibody type 1 (anti-Yo) autoimmunity in a child with Down syndrome. JAMA Neurol. 2014 Mar;71(3):347-349
5. Lopez-Chiriboga AS, Klein C, Zekeridou A, et al: LGI1 and CASPR2 neurological autoimmunity in children. Ann Neurol. 2018 Sep;84(3):473-480
6. Lopez-Chiriboga AS, Majed M, Fryer J, et al: Association of MOG-IgG serostatus with relapse after acute disseminated encephalomyelitis and proposed diagnostic criteria for MOG-IgG-associated disorders. JAMA Neurol. 2018 Nov 1;75(11):1355-1363
7. Clardy SL, Lennon VA, Dalmau J: Childhood onset of stiff-man syndrome. JAMA Neurol. 2013 Dec;70(12):1531-1536
8. Banwell B, Tenembaum S, Lennon VA, et al: Neuromyelitis optica-IgG in childhood inflammatory demyelinating CNS disorders. Neurology. 2008 Jan 29;70(5):344-352

Performance

Method Description

Indirect Immunofluorescence Assay :
Before testing, patient's spinal fluid (CSF) is preabsorbed with liver powder to remove nonorgan-specific autoantibodies. After applying 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; Basal E, Zalewski N, Kryzer TJ, et al: Paraneoplastic neuronal intermediate filament autoimmunity. Neurology. 2018 Oct 30;91[18]:e1677-e1689)

Radioimmunoassay :
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. (125)I-labelled recombinant human glutamic acid decarboxylase-65 (GAD65) antigen is used to confirm GAD65 autoantibody (when suspected from immunofluorescent staining pattern).(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; 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 Nov;72[11]:1304-1312 doi: 10.1001/jamaneurol.2015.2378)

Cell-Binding Assay :
Patient CSF 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: IIFT: Neurology Mosaics, Instructions for the indirect immunofluorescence test. EUROIMMUN; FA_112d-1_A_UK_C13, 02/2019)

Immunoblot:
All steps are performed at ambient temperature (18-28 degrees C) utilizing the EUROBlot One instrument.
Diluted patient CSF (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 CSF samples will bind to the purified recombinant antigen and negative CSF samples will not bind. Strips are washed to remove unbound antibodies and then are incubated with antihuman IgG antibodies (alkaline phosphatase-labelled) for 30 minutes. The strips are again washed to remove unbound antihuman 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 Apr 4;6[3]:e552 doi: 10.1212/NXI.0000000000000552)

Fluorescence-Activated Cell Sorting Assay :
Human embryonic kidney cells (HEK 293) are transfected transiently with a plasmid (pIRES2- Aequorea coerulescens green fluorescent protein [AcGFP]) encoding both green fluorescent protein (AcGFP) and AQP4-M1. After 36 hours, a

mixed population of cells (transfected expressing AQP4 on the surface and AcGFP in the cytoplasm and nontransfected lacking AQP4 and AcGFP) are lifted and resuspended in live cell-binding buffer. Patient CSF is then added to cells. After incubation and washing, the cells are resuspended in secondary antibody (AlexaFluor 647-conjugated goat-antihuman IgG), held on ice, washed, fixed, and analyzed by flow cytometry (BD FACSCanto; Becton, Dickinson and Co). Two populations are gated on the basis of AcGFP expression: positive (high AQP4 expression) and negative (low or no AQP4 expression). The IgG-binding index is calculated as the ratio of the average MFI for duplicate aliquots of each cell population (MFI GFP positive/MFI GFP negative). (Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Profile tests: Monday through Sunday; Reflex tests: Varies

Report Available
8 to 11 days

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 Regional Manager. 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
86255 x 9
86053
86341

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PCDEC	Peds Autoimm Enceph CNS, CSF	In Process

Test Definition: PCDEC

Pediatric Autoimmune Encephalopathy/CNS Disorder Evaluation, Spinal Fluid

Result ID	Test Result Name	Result LOINC® Value
3852	ANNA-1, CSF	94356-3
36429	Reflex Added	77202-0
21631	PCA-Tr, CSF	94362-1
21702	GAD65 Ab Assay, CSF	94359-7
61513	NMDA-R Ab CBA, CSF	93502-3
61515	GABA-B-R Ab CBA, CSF	93426-5
38325	NMO/AQP4-IgG FACS, CSF	46718-3
64280	LGI1-IgG CBA, CSF	94288-8
64282	CASPR2-IgG CBA, CSF	94286-2
64929	DPPX Ab IFA, CSF	82989-5
64927	mGluR1 Ab IFA, CSF	94361-3
605156	GFAP IFA, CSF	94360-5
605132	Peds Autoimmune CNS Interp, CSF	69048-7
618906	IFA Notes	48767-8