MAYO CLINIC LABORATORIES

Test Definition: PCDES

Pediatric Autoimmune Encephalopathy/CNS Disorder Evaluation, Serum

Overview

Useful For

Evaluating children with autoimmune central nervous system disorders using serum specimens

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
PCSI	Peds Autoimmune CNS Interp, S	No	Yes
AMPCS	AMPA-R Ab CBA, S	No	Yes
ANN1S	Anti-Neuronal Nuclear Ab, Type 1	No	Yes
CS2CS	CASPR2-IgG CBA, 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
LG1CS	LGI1-IgG CBA, S	No	Yes
GL1IS	mGluR1 Ab IFA, S	No	Yes
MOGFS	MOG FACS, S	Yes	Yes
NCDIS	Neurochondrin IFA, S	No	Yes
NMDCS	NMDA-R Ab CBA, S	No	Yes
NMOFS	NMO/AQP4 FACS, S	Yes	Yes
PCATR	Purkinje Cell Cytoplasmic Ab Type Tr	No	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
AN1BS	ANNA-1 Immunoblot, S	No	No
AN2BS	ANNA-2 Immunoblot, S	No	No
DPPTS	DPPX Ab IFA Titer, S	No	No
GFACS	GFAP CBA, S	No	No
GFATS	GFAP IFA Titer, S	No	No
GL1CS	mGluR1 Ab CBA, S	No	No
GL1TS	mGluR1 Ab IFA Titer, S	No	No
MOGTS	MOG FACS Titer, S	No	No
NMDIS	NMDA-R Ab IF Titer Assay, S	No	No
NMOTS	NMO/AQP4 FACS Titer, S	No	No

PCTBS	PCA-Tr Immunoblot, S	No	No
AN1TS	ANNA-1 Titer, S	No	No
GABIS	GABA-B-R Ab IF Titer Assay, S	No	No
NCDCS	Neurochondrin CBA, S	No	No
NCDTS	Neurochondrin IFA Titer, S	No	No
PCTTS	PCA-Tr Titer, S	No	No
AMPIS	AMPA-R Ab IF Titer Assay, S	No	No

Testing Algorithm

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

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

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

If the gamma-aminobutyric acid B receptor (GABA-B-R) antibody CBA result is positive, then the GABA-B-R IFA titer 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 glial fibrillary acidic protein (GFAP) antibody, then the GFAP antibody CBA and GFAP IFA titer will be performed at an additional charge.

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

If the myelin oligodendrocyte glycoprotein (MOG) FACS screen assay requires further investigation, then the MOG FACS titration assay will be performed at an additional charge.

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

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

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

Special Instructions

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

Method Name

AMPCS, CS2CS, DPPCS, GABCS, GFACS, LG1CS, GL1CS, NCDCS, NMDCS: Cell-Binding Assay (CBA)

MOGFS, MOGTS, NMOFS, NMOTS: Flow Cytometry

AMPIS, ANN1S, AN1TS, DPPTS, GABIS, GFAIS, GFATS, GL1IS, GL1TS, NCDIS, NCDTS, NMDIS, PCATR, PCTTS: Indirect Immunofluorescence (IFA)

GD65S: Radioimmunoassay (RIA)

AN1BS, AN2BS, PCTBS: Immunoblot (IB)

PCSI: Medical Interpretation

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 **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 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
Serum	Refrigerated (preferred)	28 days	
	Ambient	72 hours	
	Frozen	28 days	

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, though 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
PCSI	Peds Autoimmune CNS Interp, S	Medical interpretation	Interpretive report
AMPCS	AMPA-R Ab CBA, S	CBA	Negative
ANN1S	Anti-Neuronal Nuclear Ab, Type 1	IFA	Negative
CS2CS	CASPR2-IgG CBA, S	CBA	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
LG1CS	LGI1-IgG CBA, S	CBA	Negative
GL1IS	mGluR1 Ab IFA, S	IFA	Negative
NCDIS	Neurochondrin IFA, S	IFA	Negative
MOGFS	MOG FACS, S	FACS	Negative
NMDCS	NMDA-R Ab CBA, S	CBA	Negative
NMOFS	NMO/AQP4 FACS, S	FACS	Negative
PCATR	Purkinje Cell Cytoplasmic Ab Type Tr	IFA	Negative

Reflex Information:

Test ID	Reporting name	Methodology	Reference value
AMPIS	AMPA-R Ab IF Titer Assay, S	IFA	<1:240
AN1BS	ANNA-1 Immunoblot, S	IB	Negative
AN1TS	ANNA-1 Titer, S	IFA	<1:240
AN2BS	ANNA-2 Immunoblot, S	IB	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
GL1CS	mGluR1 Ab CBA, S	CBA	Negative
GL1TS	mGluR1 Ab IFA Titer, S	IFA	<1:240
MOGTS	MOG FACS Titer, S	FACS	<1:20
NCDCS	Neurochondrin CBA, S	CBA	Negative

NCDTS	Neurochondrin IFA Titer, S	IFA	<1:240
NMDIS	NMDA-R Ab IF Titer Assay, S	IFA	<1:240
NMOTS	NMO/AQP4 FACS Titer, S	FACS	<1:5
PCTTS	PCA-Tr Titer, S	IFA	<1:240
PCTBS	PCA-Tr Immunoblot, S	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, or PCA-Tr may be reported as "unclassified anti-neuronal IgG." Complex patterns that include non-neuronal 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.

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

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;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;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;321:157-163. doi:10.1016/j.jneuroim.2018.04.016
4. Philipps G, Alisanski SB, Pranzatelli M, Clardy SL, Lennon VA, McKeon A. Purkinje cell cytoplasmic antibody type 1 (anti-Yo) autoimmunity in a child with Down syndrome. JAMA Neurol. 2014;71(3):347-349
5. Lopez-Chiriboga AS, Klein C, Zekeridou A, et al. LGI1 and CASPR2 neurological autoimmunity in children. Ann Neurol. 2018;84(3):473-480. doi:10.1002/ana.25310
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;75(11):1355-1363. doi:10.1001/jamaneurol.2018.1814
7. Clardy SL, Lennon VA, Dalmau J, Childhood onset of stiff-man syndrome. JAMA Neurol. 2013;70(12):1531-1536. doi:10.1001/jamaneurol.2013.4442
8. Banwell B, Tenembaum S, Lennon VA, et al. Neuromyelitis optica-IgG in childhood inflammatory demyelinating CNS disorders. Neurology. 2008;70(5):344-352. doi:10.1212/01.wnl.0000284600.80782.d5

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)

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 or MOG on the surface and AcGFP in the cytoplasm and nontransfected lacking AQP4 or MOG and AcGFP) are lifted and resuspended in live cell-binding buffer. Cells are incubated with patient sample and an AlexaFluor 647-labeled secondary antibody is added. Two populations are gated on the basis of AcGFP expression: positive (high AQP4 or MOG expression) and negative (low or no AQP4 or MOG expression). Positivity is based on the ratio (positive >2.0) of the average median fluorescence intensity (MFI) of each cell population (MFI GFP positive:MFI GFP negative).(Unpublished Mayo method)

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 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 sample. 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; 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)

Immunoblot:
All steps are performed at ambient temperature (18-28 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 antihuman IgG antibodies (alkaline phosphatase-labeled) for 30 minutes. The strips are again washed to remove unbound antihuman IgG antibodies and nitroblue tetrazolium chloride/5-bromo-4-chloro-3-indolyl phosphate (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)

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
86341
86363
86053
86255 x 11
86256 AMPIS (if appropriate)

84182 AN1BS (if appropriate)
86256 AN1TS (if appropriate)
84182 AN2BS (if appropriate)
86256 DPPTS (if appropriate)
86256 GABIS (if appropriate)
86255 GFACS (if appropriate)
86256 GFATS (if appropriate)
86255 GL1CS (if appropriate)
86256 GL1TS (if appropriate)
86363 MOGTS (if appropriate)
86255 NCDCS (if appropriate)
86256 NCDTS (if appropriate)
86256 NMDIS (if appropriate)
86053 NMOTS (if appropriate)
84182 PCTBS (if appropriate)
86256 PCTTS (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PCDES	Peds Autoimm Enceph CNS, S	101417-4

Result ID	Test Result Name	Result LOINC® Value
80150	ANNA-1, S	33615-6
81596	GAD65 Ab Assay, S	30347-9
83076	PCA-Tr, S	84926-5
61516	NMDA-R Ab CBA, S	93503-1
61518	AMPA-R Ab CBA, S	93489-3
61519	GABA-B-R Ab CBA, S	93428-1
38324	NMO/AQP4 FACS, S	43638-6
64279	LGI1-IgG CBA, S	94287-0
64281	CASPR2-IgG CBA, S	94285-4
65563	MOG FACS, S	90248-6
64933	DPPX Ab CBA, S	94676-4
64928	mGluR1 Ab IFA, S	94347-2
605155	GFAP IFA, S	94346-4
605131	Peds Autoimmune CNS Interp, S	69048-7
618907	IFA Notes	48767-8
615867	Neurochondrin IFA, S	101452-1