# 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 |
| AMPCC | AMPA-R Ab CBA, CSF | No | Yes |
| ANN1C | Anti-Neuronal Nuclear Ab, Type 1 | No | Yes |
| CS2CC | CASPR2-IgG CBA, 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 |
| LG1CC | LGI1-IgG CBA, CSF | No | Yes |
| GL1IC | mGluR1 Ab IFA, CSF | No | Yes |
| NCDIC | Neurochondrin 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 |
|---|---|---|---|
| AMPIC | AMPA-R Ab IF Titer Assay, CSF | No | No |
| AN1BC | ANNA-1 Immunoblot, CSF | No | No |
| AN2BC | ANNA-2 Immunoblot, 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, | No | No |

| | | | |
|---|---|---|---|
| | CSF | | |
| NMOTC | NMO/AQP4 FACS Titer, CSF | No | No |
| PCTBC | PCA-Tr Immunoblot, CSF | No | No |
| AN1TC | ANNA-1 Titer, CSF | No | No |
| NCDCC | Neurochondrin CBA, CSF | No | No |
| NCDTC | Neurochondrin IFA Titer, CSF | No | No |
| PCTTC | PCA-Tr Titer, CSF | No | No |

## Testing Algorithm

If the indirect immunofluorescence assay (IFA) pattern suggests antineuronal nuclear antibodies (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 cell 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 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-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

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

NMOFC, NMOTC: Flow Cytometry

AMPIC, ANN1C, AN1TC, DPPTC, GABIC, GFAIC, GFATC, GL1IC, GL1TC, NCDIC, NCDTC, NMDIC, PCTRC, PCTTC: Indirect Immunofluorescence Assay (IFA)

GD65C: Radioimmunoassay (RIA)

AN1BC, AN2BC, PCTBC: Immunoblot (IB)

PCCI: Medical Interpretation

### 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, refer to 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.

### 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

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 | |
| | 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, 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 | Interpretive report |
| AMPCC | AMPA-R Ab CBA, CSF | CBA | Negative |
| ANN1C | Anti-Neuronal Nuclear Ab, Type 1 | IFA | Negative |
| CS2CC | CASPR2-IgG CBA, CSF | CBA | 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 |
| LG1CC | LGI1-IgG CBA, CSF | CBA | Negative |
| NCDIC | Neurochondrin IFA, CSF | IFA | Negative |
| NMDCC | NMDA-R Ab CBA, CSF | CBA | Negative |
| NMOFC | NMO/AQP4 FACS, CSF | FACS | Negative |
| PCTRC | Purkinje Cell Cytoplasmc Ab Type Tr | IFA | Negative |

**Reflex Information:**

| Test ID | Reporting name | Methodology | Reference value |
|---|---|---|---|
| AMPIC | AMPA-R Ab IF Titer Assay, CSF | IFA | <1:2 |
| AN1BC | ANNA-1 Immunoblot, CSF | IB | Negative |
| AN1TC | ANNA-1 Titer, CSF | IFA | <1:2 |
| AN2BC | ANNA-2 Immunoblot, CSF | IB | 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 |
| NCDCC | Neurochondrin CBA, CSF | CBA | Negative |
| NCDTC | Neurochondrin 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 |
| PCTTC | PCA-Tr Titer, CSF | 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 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;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
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;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
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
7. Clardy SL, Lennon VA, Dalmau J. Childhood onset of stiff-man syndrome. JAMA Neurol. 2013;70(12):1531-1536
8. Banwell B, Tenembaum S, Lennon VA, et al. Neuromyelitis optica-IgG in childhood inflammatory demyelinating CNS disorders. Neurology. 2008;70(5):344-352

## 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. 1983[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

86255 x 11
86341
86053
86256 AMPIC (if appropriate)
84182 AN1BC (if appropriate)
86256 AN1TC (if appropriate)
84182 AN2BC (if appropriate)
86256 DPPTC (if appropriate)
86256 GABIC (if appropriate)
86255 GFACC (if appropriate)
86256 GFATC (if appropriate)
86255 GL1CC (if appropriate)
86256 GL1TC (if appropriate)
86255 NCDCC (if appropriate)
86256 NCDTC (if appropriate)
86256 NMDIC (if appropriate)
86053 NMOTC (if appropriate)
84182 PCTBC (if appropriate)
86256 PCTTC (if appropriate)

### LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| PCDEC | Peds Autoimm Enceph CNS, CSF | 101416-6 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 3852 | ANNA-1, CSF | 44768-0 |

| | | |
|---|---|---|
| 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 |
| 38325 | NMO/AQP4-IgG FACS, CSF | 46718-3 |
| 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 |
| 605132 | Peds Autoimmune CNS Interp, CSF | 69048-7 |
| 618906 | IFA Notes | 48767-8 |
| 615866 | Neurochondrin IFA, CSF | 101451-3 |