MAYO CLINIC LABORATORIES

# Test Definition: PVLE

Paraneoplastic Vision Loss Evaluation, Serum

## Overview

### Useful For

Evaluating patients with rapidly progressive vision loss where a paraneoplastic cause for vision loss (retinopathy or optic neuritis with other findings [eg, retinitis] is suspected)

Evaluating patients with small-cell carcinoma who develop vision loss

### Profile Information

| Test Id | Reporting Name | Available Separately | Always Performed |
|---|---|---|---|
| PVLEI | Paraneoplas Vision Loss Interp, S | No | Yes |
| CRMS | CRMP-5-IgG, S | No | Yes |
| RCVBS | Recoverin Immunoblot, S | Yes | Yes |

### Reflex Tests

| Test Id | Reporting Name | Available Separately | Always Performed |
|---|---|---|---|
| CRMWS | CRMP-5-IgG Western Blot, S | Yes | No |
| CRMTS | CRMP-5-IgG Titer, S | No | No |

### Testing Algorithm

If the indirect immunofluorescence assay (IFA) patterns suggest collapsin response-mediator protein-5 (CRMP-5) antibody, then CRMP-5 IFA titer and CRMP-5 Western blot will be performed at an additional charge.

### Method Name

PVLEI: Medical Interpretation
CRMTS, CRMS: Indirect Immunofluorescence Assay (IFA)
CRMWS: Western Blot (WB)
RCVBS: Immunoblot (IB)

### 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, refer to Autoimmune Neurology Test Ordering Guide.

For a list of antibodies performed with each evaluation, 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

**Patient Preparation:**
1. For optimal antibody detection, specimen collection is recommended prior to initiation of immunosuppressant medication.
2. 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.
**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

There are 2 recognized forms of paraneoplastic vision loss: paraneoplastic autoimmune optic neuropathy with retinopathy accompanying collapsin response-mediator protein-5 (CRMP-5)-IgG and cancer associated retinopathy (CAR) accompanying recoverin antibody. Both occur in the setting of occult small-cell carcinoma of the lung or other body region.

Patients with CRMP-5-IgG associated optic neuropathy commonly present with painless bilateral visual loss over weeks to months. At onset, there is typically bilateral optic disc edema without evidence of enhancement of the optic nerve on magnetic resonance imaging or elevated opening pressure on lumbar puncture. Visual acuity can range from 20/20 to hand motion. In most cases, patients have coexisting vitritis or retinitis. In addition, patients can have diplopia, usually from cerebellar involvement. The majority of patients with CRMP-5 associated optic neuropathy will have other neurologic deficits from CRMP-5 autoimmunity, such as asymmetric axonal polyradiculoneuropathy. CAR presents with subacute painless progressive bilateral (although asymmetry has been described) progressive vision loss over weeks to months, reflecting both rod and cone retinal dysfunction in most patients. Accordingly, symptoms often include nyctalopia (inability to see in dim light or at night), impaired dark adaptation, photopsia (flashes of light in the field of vision), photosensitivity, dyschromatopsia, and, ultimately, severe visual acuity loss.

Patients with CRMP-5-IgG-related ophthalmitis may have improvements with intra-ocular or systemic corticosteroid treatment. Patients with recoverin-related retinopathy are unlikely to have vision improvement with treatment.

### Reference Values

COLLAPSIN RESPONSE-MEDIATOR PROTEIN-5-IgGNegative

RECOVERIN IMMUNOBLOT
Negative

COLLAPSIN RESPONSE-MEDIATOR PROTEIN-5 TITER
<1:240

COLLAPSIN RESPONSE-MEDIATOR PROTEIN-5 WESTERN BLOT
Negative
Titers lower than 1:240 are detectable by recombinant CRMP-5 Western blot analysis. CRMP-5 Western blot analysis will be done on request on stored serum (held 4 weeks). This supplemental testing is recommended in cases of chorea, vision loss, cranial neuropathy, and myelopathy. Call 1-800-533-1710 to request CRMP-5 Western blot.
Neuron-restricted patterns of IgG staining that do not fulfill criteria for CRMP-5-IgG may be reported as "unclassified antineuronal IgG." Complex patterns that include non-neuronal elements may be reported as "uninterpretable."

### Interpretation

Recoverin IgG:

Seropositivity is consistent with a diagnosis of paraneoplastic retinopathy. Considerations include small-cell carcinoma, pulmonary, or extrapulmonary.

Collapsin response-mediator protein-5 IgG:
Seropositivity is consistent with a diagnosis of paraneoplastic retinitis or ophthalmitis. Considerations include small-cell carcinoma, pulmonary, or extrapulmonary.

### Cautions

Negative results do not exclude the diagnosis of paraneoplastic eye disease.

### Clinical Reference

1. Cross SA, Salomao DR, Parisi JE, et al: Paraneoplastic autoimmune optic neuritis with retinitis defined by CRMP-5-IgG. Ann Neurol. 2003 Jul;54(1):38-50 doi: 10.1002/ana.10587
2. Lopez A, McKeon A, Lachance D, et al: Recoverin antibody: Ophthalmologic and oncologic significance. Neurology. 2016 Apr 5;86(16 Supplement)P6.131

## Performance

### Method Description

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)

Immunoblot:
All steps are performed at ambient temperature (18-28 degrees C) utilizing the EUROBlot One instrument. Diluted patient specimen (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 specimens will bind to the purified recombinant antigen and negative specimens 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 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)

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]:145-154; Dubey D, Jitprapaikulsan J, Bi H, et al: Amphiphysin-IgG autoimmune neuropathy: A recognizable clinicopathologic syndrome. Neurology. 2019 Nov 12;93(20):e1873-e1880. doi: 10.1212/WNL.0000000000008472)

### PDF Report
No

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

### Report Available
8 to 10 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 x1
84182 x1
84182 CRMWS (if appropriate)
86256 CRMTS (if appropriate)

### LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| PVLE | Paraneoplastic Vision Loss Eval, S | 104992-3 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|

| | | |
|---|---|---|
| 83077 | CRMP-5-IgG, S | 72504-4 |
| 610009 | Recoverin Immunoblot, S | 83003-4 |
| 607411 | Paraneoplas Vision Loss Interp, S | 104993-1 |
| 618908 | IFA Notes | 48767-8 |