MAYO CLINIC LABORATORIES

Test Definition: PR3

Proteinase 3 Antibodies, IgG, Serum

Overview

Useful For

Evaluating patients with clinical features of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, specifically granulomatosis with polyangiitis (GPA), microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis

Distinguishing between GPA and other forms of ANCA-associated vasculitis, in conjunction with myeloperoxidase antibody and cytoplasmic neutrophil antibody testing

Following treatment response or monitoring disease activity in patients with proteinase 3 antibodies

Special Instructions

- Acquired Neuropathy Diagnostic Algorithm

Method Name

Multiplex Flow Immunoassay

NY State Available

Yes

Specimen

Specimen Type

Serum

Additional Testing Requirements

To distinguish between granulomatosis with polyangiitis and other forms of anti-neutrophil cytoplasmic antibody-associated vasculitis, also order MPO / Myeloperoxidase Antibodies, IgG, Serum and ANCA / Cytoplasmic Neutrophil Antibodies, Serum; alternatively, VASC / Antineutrophil Cytoplasmic Antibodies Vasculitis Panel, Serum may be ordered instead, which initially tests for MPO and proteinase 3 antibodies, with reflex to ANCA when appropriate.

Specimen Required

Supplies: Sarstedt Aliquot Tube 5 mL (T914)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 0.5 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:
-Kidney Transplant Test Request
-Renal Diagnostics Test Request (T830)

Specimen Minimum Volume

0.35 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	21 days	
	Frozen	21 days	

Clinical & Interpretive

Clinical Information

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitides are characterized by a pauci-immune inflammation within the walls of small blood vessels.(1) There are 3 specific diseases which are identified as ANCA-associated vasculitides: microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis (EGPA). The serological hallmark of these disorders is the presence of ANCA, which are antibodies that bind to cytoplasmic antigens found in the granules of neutrophils.(2) Patients with GPA frequently have antibodies specific for proteinase 3 (PR3), while individuals with MPA or EGPA are more likely to have antibodies that bind to myeloperoxidase (MPO). The presence of PR3-ANCA and MPO-ANCA can be detected using antigen-specific immunoassays or indirect immunofluorescence (IIF). IIF is typically performed using ethanol-fixed neutrophils. Using this substrate, anti-PR3 antibodies produce a granular cytoplasmic staining pattern, which is referred to as cANCA. In comparison, due to an artefact that is a result of the fixation process, anti-MPO antibodies display a perinuclear pattern (pANCA).

Patients with suspected ANCA-associated vasculitis should be evaluated for the presence of PR3-ANCA, MPO-ANCA and ANCA by IIF. A consensus guideline published in 2017 recommends that patients with possible GPA or MPA be tested for PR3-ANCA and MPO-ANCA using antigen-specific immunoassays.(3) ANCA by IIF should then be used in cases where there is a high degree of suspicion for GPA or MPA, but the PR3-ANCA and MPO-ANCA testing is negative. To improve specificity of the testing, this guideline also suggests that ANCA be used in situations where a low-positive PR3-ANCA or MPO-ANCA level is detected. The classification criteria for MPA, GPA, and EGPA published by the American College of Rheumatology and the European Alliance of Associations for Rheumatology include PR3-ANCA and MPO-ANCA detected by either antigen-specific immunoassay or IIF.(4-6) These classification criteria incorporate serological ANCA testing along with clinical symptoms, imaging, and biopsy results to determine a score that allows for the classification of the various ANCA-associated vasculitides.

Reference Values

<0.4 U (negative)
0.4-0.9 U (equivocal)
> or =1.0 U (positive)
Reference values apply to all ages.

Interpretation

Positive results for proteinase 3 (PR3) anti-neutrophil cytoplasmic antibodies (ANCA) by antigen-specific immunoassay and cytoplasmic ANCA by indirect immunofluorescence are consistent with the diagnosis of granulomatosis with polyangiitis (GPA), in patients with the appropriate clinical presentation.

The reactivity of PR3-ANCA may decline with treatment of patients with GPA.

Cautions

A positive result for proteinase 3 (PR3)-anti-neutrophil cytoplasmic antibodies (ANCA), myeloperoxidase (MPO)-ANCA, or ANCA by indirect immunofluorescence is not diagnostic for any ANCA-associated vasculitis and must be interpreted in the clinical context of the patient.

Negative results for PR3-ANCA, MPO ANCA, and ANCA by IIF do not exclude the possibility of ANCA-associated vasculitis.

Monitoring reactivity of PR3-ANCA or MPO-ANCA should not be relied upon exclusively to evaluate response to treatment or to assess for risk of disease flare.

Clinical Reference

1. Kitching AR, Anders HJ, Basu N, et al. ANCA-associated vasculitis. Nat Rev Dis Primers. 2020;6(1):71
2. Ramponi G, Folci M, De Santis M, et al. The biology, pathogenetic role, clinical implications, and open issues of serum anti-neutrophil cytoplasmic antibodies. Autoimmun Rev. 2021;20(3):102759
3. Bossuyt X, Cohen Tervaert JW, Arimura Y, et al. Position paper: Revised 2017 international consensus on testing of ANCAs in granulomatosis with polyangiitis and microscopic polyangiitis. Nat Rev Rheumatol. 2017;13(11):683-692
4. Suppiah R, Robson JC, Grayson PC, et al. 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for microscopic polyangiitis. Ann Rheum Dis. 2022;81(3):321-326. doi:10.1136/annrheumdis-2021-221796
5. Robson JC, Grayson PC, Ponte C, et al. 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for granulomatosis with polyangiitis. Ann Rheum Dis. 2022;81(3):315-320. doi:10.1136/annrheumdis-2021-221795
6. Grayson PC, Ponte C, Suppiah R, et al. 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for eosinophilic granulomatosis with polyangiitis. Ann Rheum Dis. 2022;81(3):309-314. doi:10.1136/annrheumdis-2021-221794

Performance

Method Description

Proteinase 3 (PR3) antigen is covalently coupled to polystyrene microspheres that are impregnated with fluorescent dyes to create a unique fluorescent signature. PR3 antibodies, if present in diluted serum, bind to the PR3 antigen on the microspheres. The microspheres are washed to remove extraneous serum proteins. Phycoerythrin (PE)-conjugated antihuman IgG antibody is then added to detect anti-PR3 IgG bound to the microspheres. The microspheres are washed

to remove unbound conjugate, and bound conjugate is detected by laser photometry. A primary laser reveals the fluorescent signature of each microsphere to distinguish it from microspheres that are labeled with other antigens. A secondary laser reveals the level of PE fluorescence associated with each microsphere. Results are calculated by comparing the median fluorescence response for PR3 microspheres to a 4-point calibration curve.(Package insert: Bio-Plex 2200 Vasculitis. Bio-Rad Laboratories; 12/2018)

PDF Report
No

Day(s) Performed
Monday through Saturday

Report Available
2 to 3 days

Specimen Retention Time
14 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Superior Drive

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 has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information
83516

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PR3	Proteinase 3 Ab (PR3), S	74106-6

Result ID	Test Result Name	Result LOINC® Value
PR3	Proteinase 3 Ab (PR3), S	74106-6