MAYO CLINIC LABORATORIES

Test Definition: AB2GP

Beta-2 Glycoprotein 1 Antibodies, IgA, Serum

Overview

Useful For

Evaluating patients with suspected antiphospholipid syndrome by identification of beta-2 glycoprotein 1 IgA antibodies

Evaluating patients at-risk for antiphospholipid syndrome (APS) who are negative for criteria APS tests

Estimating the risk of thrombosis and/or pregnancy-related morbidity in patients with systemic lupus erythematosus

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

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.

Specimen Minimum Volume

0.4 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	OK
Heat-treated specimen	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Antiphospholipid syndrome (APS) has traditionally been described as a systemic autoimmune disease characterized by thrombosis or specific pregnancy-related morbidities associated with persistent documentation of "criterial" antiphospholipid antibody (aPL) tests.(1-2) Based on the 2006 revised Sapporo consensus classification, the "criterial" aPL antibody tests include lupus anticoagulant (LAC), and IgG/IgM antibodies to the cardiolipin (aCL) and beta-2-glycoprotein I (anti-B2GPI) with all tests carrying equal diagnostic significance for disease.(1) In 2023, the American College of Rheumatology (ACR)/European Alliance of Associations for Rheumatology (EULAR) published new classification criteria for APS, which includes an entry criterion of at least one positive aPL antibody test within 3 years of identification of an aPL-associated clinical criterion, followed by additive weighted criteria (score range 1-7 points each) clustered into 6 clinical domains (macrovascular venous thromboembolism, macrovascular arterial thrombosis, microvascular, obstetric, cardiac valve, and hematologic) and 2 laboratory domains (LAC functional coagulation assays and solid-phase enzyme-linked immunosorbent assays [ELISA] for IgG/IgM aCL and/or IgG/IgM anti-B2GPI).(3) Of note, aPL antibodies also occur in patients with autoimmune diseases with significant prevalence in systemic lupus erythematosus (SLE) as well as other clinical manifestations (eg, heart valve disease, livedo reticularis, thrombocytopenia, nephropathy and neurological) often associated with APS.(1-3) Thus, in addition to the 2023 APS classification criteria, the 2012 derivation and validation of the Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE recommends testing for the criteria aPL antibody tests as well as aCL IgA and anti-B2GPI IgA.(4)

B2GPI is a 326-amino acid protein that is synthesized by hepatocytes, endothelial cells, and trophoblast cells.(5) It contains 5 repetitive structures or "sushi domains," termed domain 1 through 5, for a combined molecular weight of 54 kDa.(5-7) Autoantibodies to B2GPI may be detected by solid-phase immunoassays (SPA) and functional coagulation assays. Unlike the LAC, the SPA provides quantitative measurements and antibody isotype class determinations that are important for risk assessment. Immunoassays for the detection and quantification of anti-B2GPI antibodies can be performed using either a composite substrate comprised of B2GPI plus anionic phospholipid (ie, cardiolipin-dependent B2GPI) or B2GPI alone. Antibodies detected using B2GPI substrate without another phospholipid (direct assays) are referred to simply as "anti-B2GPI 1 antibodies." Some anti-B2GPI antibodies are capable of inhibiting clot formation in functional coagulation assays that contain low concentrations of phospholipid cofactors.(6) Antibodies detected by functional coagulation assays are commonly referred to as LAC. Anti-B2GPI antibodies associated with thromboembolic events target domain 1 of the molecule and are responsible for LAC (functional, phospholipid-dependent prolongation of the clotting time) and aCL-dependent B2GPI antibody positivity.(2)

For the detection of anti-B2GPI IgG and IgM antibodies, the APS guidance advocates for the use of values above the 99th percentile of the laboratory's population in the establishment of reference intervals for tests. While this recommendation may be used for anti-B2GPI IgA immunoassays, there is no consensus for their determination.(6) aPL antibodies were traditionally determined using the classic ELISA, with more diverse methods recently developed and adapted for clinical testing. Recognizing the analytical and diagnostic challenges associated with aPL antibody testing, initiatives to support assay harmonization and utilization, including the development of calibrators, test development,

and validation efforts as well as preanalytical, analytical, and postanalytical measures have been published.(7) The interpretation and relevance of aPL antibody tests are dependent on factors such as the type of aPL (LAC, aCL or anti-B2GPI), the source of cardiolipin and/or B2GPI, aPL antibody class (IgG, IgM or IgA) and level, as well as whether antibody positivity is single, double or triple.(1-3,7,8)

The 2023 ACR/EULAR classification criteria for APS are meant for clinical studies and may not be appropriate for routine patient evaluation and management. Therefore, in clinical practice, if suspicion for disease is high but criteria aPL antibody tests are inconclusive or negative, deviation from the APS classification criteria may be justified. This may include testing for non-criteria aPL antibody tests, such the aCL IgA and anti-B2GPI IgA recommended in 2012 SLICC guidance for SLE or evaluation of other non-criteria aPL antibody tests.(4,9,10) However, there is no formal guidance for the measurement and interpretation of aCL and anti-B2GPI IgA antibodies in patients with APS or SLE. Some clinical relevance between APS-related clinical symptoms and the presence of aCL/anti-B2GPI IgA have been reported; however, the added value is minimal.(10,11) Isolated aPL IgA is rare, and these antibodies are usually found in association with IgG or IgM.

Reference Values

<15.0 SAU (negative)
15.0-39.9 SAU (weakly positive)
40.0-79.9 SAU (positive)
> or =80.0 SAU (strongly positive)
Results are reported in standard IgA anti-beta 2 glycoprotein 1 units (SAU).

Reference values apply to all ages.

Interpretation

The presence of anti-beta-2 glycoprotein 1 (anti-B2GPI) IgA antibodies may be associated with a diagnosis of antiphospholipid syndrome (APS) or systemic lupus erythematosus (SLE). In the absence of "criteria" aPL antibodies for APS and diagnostic tests for SLE, isolated anti-B2GPI IgA must be interpreted with a high degree of caution.

Documentation of persistence for anti-B2GPI IgA, as is the case for criteria B2GPI IgG and IgM antibodies, would be consistent with best clinical practice.

Detection of B2GPI antibodies is not affected by anticoagulant treatment.

Cautions

Immunoassays for the detection of antiphospholipid antibodies, including beta-2 glycoprotein 1 (B2GPI) may not completely distinguish between autoantibodies specific for antiphospholipid syndrome and those antibodies produced in response to infectious agents with or without thrombosis. Since these antibodies may be transiently produced, documentation of persistence as outlined in the 2006 revised Sapporo guidance for the criteria antibodies would constitute best practice, see Clinical Information.

Comparative studies and interlaboratory proficiency surveys indicate that results of phospholipid antibody tests can be highly variable, and results obtained with different commercial immunoassays may yield different results.(7,8,11)

Clinical Reference

1. Miyakis S, Lockshin MD, Atsumi T, et al. International consensus statement on an update of the classification criteria

for definite antiphospholipid syndrome (APS). J Thromb Haemost. 2006;4(2):295-306
2. Pengo V, Bison E, Denas G, Jose SP, Zoppellaro G, Banzato A. Laboratory diagnostics of antiphospholipid syndrome. Semin Thromb Hemost. 2018;44(5):439-444
3. Barbhaiya M, Zuily S, Naden R, et al. The 2023 ACR/EULAR antiphospholipid syndrome classification criteria. Arthritis Rheumatol. 2023;75(10):1687-1702
4. Petri M, Orbai AM, Alarcon GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum. 2012;64(8):2677-2686
5. Lozier J, Takahashi N, Putnam F W: Complete amino acid sequence of human plasma beta 2 glycoprotein 1. Proc Natl Acad Sci U S A. 1984;81(12):3640-3644
6. Audrain MAP, El-Kouri D, Hamidou MA, el al. Value of autoantibodies to beta(2)-glycoprotein 1 in the diagnosis of antiphospholipid syndrome. Rheumatology (Oxford). 2002;41(5):550-553
7. Lakos G, Favaloro EJ, Harris EN, et al. International consensus guidelines on anticardiolipin and anti-beta 2-glycoprotein I testing: report from the 13th International Congress on Antiphospholipid Antibodies. Arthritis Rheum. 2012;64(1):1-10
8. Devreese KMJ. Solid phase assays for antiphospholipid antibodies. Semin Thromb Hemost. 2022;48(6):661-671
9. Cousins L, Pericleous C, Khamashta M, et al. Antibodies to domain I of beta-2-glycoprotein I and IgA antiphospholipid antibodies in patients with ‘seronegative’ antiphospholipid syndrome. Ann Rheum Dis. 2015;74(01):317-319
10. Nakamura H, Oku K, Amengual O, et al. First-line, non-criterial antiphospholipid antibody testing for the diagnosis of antiphospholipid syndrome in clinical practice: A combination of anti-beta2 -glycoprotein I domain I and anti-phosphatidylserine/prothrombin complex antibodies tests. Arthritis Care Res (Hoboken). 2018;70(4):627-634
11. Meijide H, Sciascia S, Sanna G, Khamashta MA, Bertolaccini ML. The clinical relevance of IgA anticardiolipin and IgA anti-B2 glycoprotein I antiphospholipid antibodies: a systematic review. Autoimmun Rev. 2013;12(03):421-425

Performance

Method Description

Purified beta-2 glycoprotein 1 (B2GPI) antigen is bound to the wells of a polystyrene microwell plate under conditions that preserve the antigen in its native state. Prediluted controls and diluted patient sera are added to separate wells, allowing any B2GPIIgA antibodies present to bind to the immobilized antigen. Unbound sample is washed away, and an enzyme-labeled antihuman IgA conjugate is added to each well. A second incubation allows the enzyme-labeled antihuman IgA to bind to any patient antibodies that have attached to the microwells. After washing away any unbound enzyme-labeled antihuman IgA, the remaining enzyme activity is measured by adding a chromogenic substrate and measuring the intensity of the color that develops. The assay can be evaluated spectrophotometrically by measuring and comparing the color intensity that develops in the patient wells with that of a 5-point calibration curve. Semiquantitative results are reported in standard IgA anti-B2GPIunits (SAU).(Package insert: QUANTA Lite beta 2 GP1 IgA ELISA. Inova Diagnostics; Revision 11, 04/2020)

PDF Report

No

Day(s) Performed

Monday, Thursday

Report Available

4 to 6 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

86146

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
AB2GP	Beta 2 GP1 Ab IgA, S	44447-1

Result ID	Test Result Name	Result LOINC® Value
AB2GP	Beta 2 GP1 Ab IgA, S	44447-1