Test Definition: MB2GP

Beta-2 Glycoprotein 1 Antibodies, IgM, Serum

Overview

Useful For

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

First-line test when antiphospholipid syndrome is strongly suspected in conjunction with cardiolipin antibodies (IgG and IgM) and lupus anticoagulant testing

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

Additional Testing Requirements

Diagnostic criteria for antiphospholipid syndrome include the presence of at least one of the following: lupus anticoagulant, anticardiolipin, and anti-beta-2 glycoprotein 1 IgG or IgM antibodies. Consider ordering CLPMG / Phospholipid (Cardiolipin) Antibodies, IgG and IgM, Serum; GB2GP / Beta-2 Glycoprotein 1 Antibodies, IgG, Serum; and ALUPP / Lupus Anticoagulant Profile, Plasma concurrently with this test.

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 specimens	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-glyocoprotein 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)

B2GPI is a 326-amino acid protein that is synthesized by hepatocytes, endothelial cells, and trophoblast cells.(4) 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 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.(5) 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)

Thrombosis and obstetric complications are common clinical events in the general population and are not unique to APS; therefore, the presence of aPL antibodies is an absolute requirement for the diagnosis of definite APS.(1,5,7) Furthermore, aPL antibodies are heterogeneous with overlapping tendencies; the lack of aPL test harmonization or standardization requires the use of all 3 tests for optimal APS diagnosis.(1,3,6,7)

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.(6-8) Overall, 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.(1-3,6-8)

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 diagnostic criteria may be justified. This may include testing for noncriteria aPL antibody tests, such the aCL IgA, anti-B2GPI IgA and anti-phosphatidylserine/prothrombin complex IgG and IgM antibodies.(2,6,9,10) However, there is no formal guidance for the measurement and interpretation of these non-criterial aPL antibodies in patients with APS or SLE.

Reference Values

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

Reference values apply to all ages.

Interpretation

Positive results for beta-2 glycoprotein 1 (B2GPI) IgM antibodies in association with specific clinical manifestations may be diagnostic for antiphospholipid syndrome (APS).

Compared to IgG antibodies B2GPI, the presence of isolated and low levels of B2GPI IgM antibodies have been reported to demonstrate a low risk for APS.

Documentation of persistent anti- B2GPI IgM antibodies is a requirement for the diagnosis of definite APS. Antibodies must be detected on 2 or more occasions at least 12 weeks apart to fulfill the laboratory diagnostic criteria for APS.

Detection of B2GPI antibodies using the enzyme-linked immunosorbent assay method or other solid-phase immunoassays is not affected by anticoagulant treatment.

Cautions

Immunoassays for the detection of antiphospholipid (aPL) antibodies, including beta-2 glycoprotein 1 (B2GPI) may not

completely distinguish between autoantibodies specific for antiphospholipid syndrome (APS) 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.(6-8)

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. 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
5. 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
6. 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
7. Devreese KMJ. Solid phase assays for antiphospholipid antibodies. Semin Thromb Hemost. 2022;48(6):661-671
8. Tebo AE. Laboratory evaluation of antiphospholipid syndrome: An update on autoantibody testing. Clin Lab Med. 2019;39(4):553-565
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

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 B2GPI IgM antibodies present to bind to the immobilized antigen. Unbound sample is washed away, and an enzyme-labeled antihuman IgM conjugate is added to each well. A second incubation allows the enzyme-labeled antihuman IgM to bind to any patient antibodies that have attached to the microwells. After washing away any unbound enzyme-labeled antihuman IgM, 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 out semiquantitatively in standard IgM anti-beta-2 GPI units (SMU).(Package insert: QUANTA Lite

beta 2 GP1 IgM ELISA. Inova Diagnostics; Revision 16, 09/2018)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
2 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
MB2GP	Beta 2 GP1 Ab IgM, S	44449-7

Result ID	Test Result Name	Result LOINC® Value
MB2GP	Beta 2 GP1 Ab IgM, S	44449-7