MAYO CLINIC LABORATORIES

Test Definition: GB2GP

Beta-2 Glycoprotein 1 Antibodies, IgG, Serum

Overview

Useful For

Evaluating patients with suspected antiphospholipid syndrome by identification of beta-2 glycoprotein 1 IgG 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; MB2GP / Beta-2 Glycoprotein 1 Antibodies, IgM, 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

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterized by thrombosis and/or specific pregnancy-related death. Based on the 2006 revised Sapporo consensus classification criteria, the laboratory requirements for diagnosing APS include the presence of at least one of the following: lupus anticoagulant (LAC), anticardiolipin (aCL), and anti-beta-2 glycoprotein 1 (B2GP1) IgG or IgM antibodies.(1). To avoid overdiagnosis, and to exclude patients with transient antiphospholipid (aPL) levels, the APS guidance also recommends confirmation of any positive result at least 12 weeks after the initial evaluation. 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 2006 APS guidance, 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-B2GP1 IgA.(2)

B2GP1 is a 326-amino acid protein 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 for the protein.(4-6). Autoantibodies to B2GP1 may be detected by solid-phase immunoassays (SPA) and functional coagulation assays. Unlike LAC, the SPA provides quantitative measurements and antibody isotype class determinations that are important for risk assessment. Immunoassays for B2GP1 antibodies can be performed using either a composite substrate comprised of B2GP1 plus anionic phospholipid (ie, cardiolipin-dependent B2GP1) or B2GP1 alone. Antibodies detected using B2GP1 substrate without another phospholipid (direct assays) are referred to simply as "B2GP1 antibodies." Some B2GP1 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-B2GP1 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 B2GP1 antibody positivity.(7)

For detection of anti-B2GP1 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-B2GP1 IgA immunoassays, there is no consensus for their determination.(6) For aCL IgG and IgM testing, the APS classification guidance recommends antibody cutoff values greater than 40 IgG phospholipid (GPL) or IgM PL (units traceable to the Harris standards for aCL antibody assays) or more than the 99th percentile for the testing laboratory’s population for positivity.(1) The use of cutoff values greater than 40 GPL or MPL units to define positivity is not applicable to all aCL antibody immunoassays as the threshold used to distinguish

moderate-to-high positive from low positive results are test dependent.(4,5,7,8) In addition, the cutoff value used at the 99th percentile of a laboratory's testing population may not be consistent with kits from the same manufacturer or 40 GPL units in the case of aCL antibodies.(5-7).

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.(1,5-7) The APL antibodies were traditionally determined using the classic enzyme-linked immunosorbent assay, 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.(5-7) Based on these and other published studies, the interpretation and relevance of APL antibody tests are dependent on factors such as the type of aPL (LAC, aCL or anti-B2GP1), the source of cardiolipin and/or B2GP1, aPL antibody class (IgG, IgM or IgA) and level, as well as whether antibody positivity is single, double or triple.(1,5-8)

In conclusion, although the APS classification criteria were not established for routine clinical use, in the absence of formal diagnostic guidelines, these have widely been adopted to diagnose or assess risk for APS and the need for treatment or prophylaxis. 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 non-criteria aPL antibody tests such as the aCL IgA and anti-B2GP1 IgA recommended in 2012 SLICC guidance for SLE and/or evaluation of anti-phosphatidylserine/prothrombin IgG and IgM autoantibodies, amongst others.(2,6,8-10)

Reference Values

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

Reference values apply to all ages.

Interpretation

Positive results for beta-2 glycoprotein 1 (B2GP1) IgG antibodies, in association with specific clinical manifestations, may be diagnostic for antiphospholipid syndrome (APS). Low levels of B2GP1 IgG antibodies, especially in the absence of other criteria phospholipid antibodies, should be interpreted with a high degree of suspicion.

Documentation of persistent anti-B2GP1 IgG 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 B2GP1 antibodies using the enzyme-linked immunoassay 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 (B2GP1) 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 for aPL IgG and IgM antibodies in the 2006 revised Sapporo guidance for definite APS is required, 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.(1,5,7,8).

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 Feb;4(2): 295-306
2. 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 Aug;64(8):2677-2686
3. Sciascia S, Amigo MC, Roccatello D, Khamashta M: Diagnosing antiphospholipid syndrome: 'extra-criteria' manifestations and technical advances. Nat Rev Rheumatol. 2017 Sep;13(9):548-560
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 Jun;81(12):3640-3644. doi: 10.1073/pnas.81.12.3640
5. 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 Jan;64(1):1-10
6. Audrain MA, El-Kouri D, Hamidou MA, et al: Value of autoantibodies to beta(2)-glycoprotein 1 in the diagnosis of antiphospholipid syndrome. Rheumatology (Oxford). 2002 May;41(5):550-553
7. Pengo V, Bison E, Denas G, Jose SP, Zoppellaro G, Banzato A: Laboratory diagnostics of antiphospholipid syndrome. Semin Thromb Hemost. 2018 Jul;44(5):439-444
8. Devreese KMJ: Solid phase assays for antiphospholipid antibodies. Semin Thromb Hemost. 2022 Sep;48(6):661-671. doi: 10.1055/s-0042-1744364
9. Abisror N, Nguyen Y, Marozio L, et al: Obstetrical outcome and treatments in seronegative primary APS: data from European retrospective study. RMD Open. 2020 Aug;6(2):0. doi: 10.1136/rmdopen-2020-001340
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-beta 2 -glycoprotein I domain I and anti-phosphatidylserine/prothrombin complex antibodies tests. Arthritis Care Res (Hoboken). 2018 Apr;70(4):627-634

Performance

Method Description

Purified beta-2 glycoprotein 1 (B2GP1) antigen is bound to the wells of a polystyrene microwell plate under conditions that will preserve the antigen in its native state. Prediluted controls and diluted patient sera are added to separate wells, allowing any B2GPI IgG antibodies present to bind to the immobilized antigen. Unbound sample is washed away, and an enzyme-labeled antihuman IgG conjugate is added to each well. A second incubation allows the enzyme-labeled antihuman IgG to bind to any patient antibodies that have attached to the microwells. After washing away any unbound enzyme-labeled antihuman IgG, 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. The standard used to construct this curve is referenced to the reference calibrators for IgG beta-2-Glycoprotein I available from the

Rheumatology Lab, Seton Hall University, St. Joseph's Hospital and Medical Center. Semiquantitative results are reported in standard IgG anti-B2GPI units (SGU).(Package Insert: QUANTA Lite beta 2 GP1 IgG ELISA. Inova Diagnostics; Revision 19, 07/2020)

PDF Report
No

Day(s) Performed
Monday through Saturday

Report Available
2 to 6 days

Specimen Retention Time
14 days

Performing Laboratory Location
Rochester

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
GB2GP	Beta 2 GP1 Ab IgG, S	44448-9

Result ID	Test Result Name	Result LOINC® Value
GB2GP	Beta 2 GP1 Ab IgG, S	44448-9