

Overview
Useful For

Evaluation of patients with suspected antiphospholipid syndrome by identification of beta-2 GP1 IgM antibodies

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available

Yes

Specimen
Specimen Type

Serum

Specimen Required
Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Specimen Volume: 0.5 mL

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 and Interpretive
Clinical Information

Beta-2 glycoprotein 1 (beta-2 GP1, also called apolipoprotein H) is a 326-amino acid polypeptide synthesized by hepatocytes, endothelial cells, and trophoblast cells. It contains 5 homologous domains of approximately 60 amino

acids each.(1,2) Domain 5, located at the C terminus, contains a hydrophobic core surrounded by 14 positively charged amino acid residues that promote electrostatic interactions with plasma membranes via interactions with negatively charged phospholipids. Complexes of beta 2 GP1 and phospholipid in vivo reveal epitopes that react with natural autoantibodies.(3) Plasma from normal individuals contains low concentrations of IgG autoantibodies to beta-2 GP1 (beta-2 GP1 antibodies) that are of moderate affinity and react with an epitope on the first domain near the N terminus.

Pathologic levels of beta 2 GP1 antibodies occur in patients with antiphospholipid syndrome (APS). APS is associated with a variety of clinical symptoms, notably, thrombosis, pregnancy complications, unexplained cutaneous circulatory disturbances (livedo reticularis or pyoderma gangrenosum), thrombocytopenia or hemolytic anemia, and nonbacterial thrombotic endocarditis. Beta 2 GP1 antibodies are found with increased frequency in patients with systemic rheumatic diseases, especially systemic lupus erythematosus.

Autoantibodies to beta-2 GP1 antibodies are detected in the clinical laboratory by different types of assays including immunoassays and functional coagulation assays. Immunoassays for beta-2 GP1 antibodies can be performed using either a composite substrate comprised of beta-2 GP1 plus anionic phospholipid (eg, cardiolipin or phosphatidylserine), or beta-2 GP1 alone. Antibodies detected by immunoassays that utilize composite substrates are commonly referred to as phospholipid or cardiolipin antibodies. Antibodies detected using beta-2 GP1 substrate without phospholipid (so called direct assays) are referred to simply as "beta-2 GP1 antibodies." Some beta-2 GP1 antibodies are capable of inhibiting clot formation in functional coagulation assays that contain low concentrations of phospholipid cofactors. Antibodies detected by functional coagulation assays are commonly referred to as lupus anticoagulants.

The diagnosis of APS requires at least 1 clinical criteria and 1 laboratory criteria be met.(4) The clinical criteria include vascular thrombosis (arterial or venous in any organ or tissue) and pregnancy morbidity (unexplained fetal death, premature birth, severe preeclampsia, or placental insufficiency). Other clinical manifestations, including heart valve disease, livedo reticularis, thrombocytopenia, nephropathy, neurological symptoms, are often associated with APS but are not included in the diagnostic criteria. The laboratory criteria for diagnosis of APS are the presence of lupus anticoagulant, the presence of IgG and/or IgM anticardiolipin antibody (>40 GPL, >40 MPL, or >99th percentile), and/or the presence of IgG and/or IgM beta-2 GP1 antibody (>99th percentile). All antibodies must be demonstrated on 2 or more occasions separated by at least 12 weeks. Direct assays for beta 2 GP1 antibodies have been reported to be somewhat more specific (but less sensitive) for disease diagnosis in patients with APS.(5) Anticardiolipin and beta 2 GP1 antibodies of the IgA isotype are not part of the laboratory criteria for APS due to lack of specificity.

Reference Values

<15.0 U/mL (negative)

15.0-39.9 U/mL (weakly positive)

40.0-79.9 U/mL (positive)

> or =80.0 U/mL (strongly positive)

Results are expressed in arbitrary units.

Reference values apply to all ages.

Interpretation

Strongly positive results for beta-2 glycoprotein 1 (beta-2 GPI) antibodies (>40 U/mL for IgG and/or IgM) are diagnostic criterion for antiphospholipid syndrome (APS). Lesser levels of beta-2 GP1 antibodies and antibodies of the IgA isotype may occur in patients with clinical signs of APS, but the results are not considered diagnostic. Beta-2

GP1 antibodies must be detected on 2 or more occasions at least 12 weeks apart to fulfill the laboratory diagnostic criteria for APS.

Detection of beta-2 GP1 antibodies is not affected by anticoagulant treatment.

Cautions

The immunoassay for beta-2 glycoprotein 1 (beta-2 GP1) antibodies does not distinguish between autoantibodies and antibodies produced in response to infectious agents or as epiphenomena following thrombosis. For this reason, a single positive test result is not sufficient to meet accepted serologic criteria for the diagnosis of antiphospholipid syndrome (see Clinical Information).

Comparative studies and interlaboratory proficiency surveys indicate that results of beta-2 GP1 antibody tests can be highly variable and results obtained with different commercial immunoassays may yield substantially different results.(4)

Clinical Reference

1. Caronti B, Calderaro C, Alessandri C, et al: Beta 2 glycoprotein 1 (beta 2 GP1) mRNA is expressed by several cell types involved in anti-phospholipid syndrome-related tissue damage. *Clin Exp Immunol* 1999;115:214-219
2. Lozier J, Takahashi N, Putnam F: Complete amino acid sequence of human plasma beta 2 glycoprotein 1. *Proc Natl Acad Sci USA* 1984;81:3640-3644
3. Kra-Oz Z, Lorber M, Shoenfeld Y, et al: Inhibitor(s) of natural anti-cardiolipin autoantibodies. *Clin Exp Immunol* 1993;93:265-268
4. Wong RCW, Flavaloro EJ, Adelstein S, et al: Consensus guidelines on anti-beta 2 glycoprotein I testing and reporting. *Pathology* 2008 Jan;40(1):58-63
5. 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;41:550-553

Performance

Method Description

Purified beta-2 GPI 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 beta-2 GPI 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 become 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. 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, February 2015 Revision 13)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Saturday; 8 a.m.

Analytic Time

Same day/1 day

Maximum Laboratory Time

6 days

Specimen Retention Time

14 days

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. For assistance, contact [Customer Service](#).

Test Classification

This test has been cleared, approved or is exempt by the U.S. 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