

Antiphospholipid Syndrome (APS) Testing

REVISED GUIDELINES FOR THE DIAGNOSIS OF DEFINITE APS

Test Highlights

New panel created to match the diagnostic recommendations of a recent international consensus statement on antiphospholipid antibody syndrome.¹

Clinical Background

- Antiphospholipid syndrome (APS) is an autoimmune disorder characterized by recurrent venous or arterial thrombosis and/or pregnancy morbidity in the presence of persistent antiphospholipid antibodies (aPLs).
- An international consensus statement has issued revised guidelines for the diagnosis of definite antiphospholipid syndrome (APS).¹
- The guidelines adopted in the Sapporo criteria have been modified to include testing for anti-beta-2 glycoprotein 1 (anti- β_2 GP1) IgG and IgM antibodies with the preservation of lupus anticoagulant (LA) and anticardiolipin (aCL) IgG and IgM antibody assays.^{1,2}

Pathophysiology

- Antiphospholipid antibodies represent a heterogeneous group of autoantibodies that recognize various phospholipids (PL), PL-binding plasma proteins, and/or PL-protein complexes.
- The involved plasma proteins include beta-2 glycoprotein 1 (β_2 GP1), prothrombin, protein C, protein S, and annexin V.

Epidemiology

The LA and aCL antibodies occur in varying percentages in patients with APS and systemic lupus erythematosus (SLE) disease. Approximately 3–10 percent of APS patients will test positive for only anti- β_2 GP1 antibodies.^{1,3,4}

Indications for Ordering

- Vascular thrombosis: one or more clinical episodes of arterial, venous, or small vessel thrombosis.
- Unexplained pregnancy loss:
 - One or more unexplained deaths of a morphologically normal fetus at or beyond the 10th week of gestation.
 - One or more premature births of a morphologically normal neonate before the 34th week of gestation because of eclampsia or severe preeclampsia, or recognized features of placental insufficiency.

- Three or more unexplained, consecutive, spontaneous abortions before the 10th week of gestation (maternal anatomic or hormonal abnormalities and chromosomal causes excluded).

Interpretation

- The diagnostic criteria for definite APS requires at least one of the clinical criteria (see indications) and one of the following laboratory findings on at least two occasions, at least 12 weeks apart:
 - Lupus anticoagulant (defined as prolongation of at least one phospholipid-dependent clotting test, continued prolongation after mixing with normal pooled plasma, shortening of clotting time by addition of excess phospholipids, and exclusion of other coagulopathies).
 - Presence of aCL, IgG, IgM, or both at titers >19 GPL or MPL units.
 - Presence of anti- β_2 GP1 IgG, IgM, or both at titers >20 GPL or MPL units.

Limitations

- Positive test results alone are not diagnostic and must be interpreted in conjunction with the patient's clinical presentation.
- Patients must be tested at least twice and at least 12 weeks apart to demonstrate antibody persistence.

Methodology

- Lupus Anticoagulant Reflexive Panel (0030181) includes functional, clot-based assays designed to detect LA and the presence of heparin (e.g., PTT, dilute Russell's viper venom time, thrombin time, reptilase time, heparin neutralization PTT, hexagonal phospholipid neutralization, and platelet neutralization).
- The aCL and anti- β_2 GP1 antibody tests are enzyme-linked immunosorbent assays (ELISA).
- The Cardiolipin Antibodies, IgG & IgM (0099344) assay uses purified cardiolipin antigen bound in conditions that preserve the antigen in its native state.
- The Beta-2 Glycoprotein I Antibodies, IgG & IgM (0050321) assay employs a purified β_2 GP1 antigen.

Related Tests

- There are reports that some patients with clinical features for APS will test negative for LA, aCL IgG/IgM, and anti-β₂GPI IgG/IgM, but positive for some of the non-criteria aPLs listed below.
- The clinical significance and standardization of these aPLs are still lacking; therefore, their application as routine diagnostic tools is not currently recommended.
 - Cardiolipin Antibody, IgA (0098358)
 - Beta-2 Glycoprotein 1 Antibody, IgA (0050324)
 - Phosphatidylserine Antibodies, IgG, IgM, and IgA (0050905)
 - Phosphatidylcholine Antibodies, IgG, IgM, & IgA (0051590)
 - Prothrombin Antibody, IgG (0051302) and IgM (0051303)
 - Phosphatidylethanolamine Antibodies, IgG, IgM, & IgA (0051622)
 - Phosphatidylglycerol Antibodies, IgG, IgM, & IgA (0051623)

- Phosphatidylinositol Antibodies, IgG, IgM, & IgA (0051624)

- These additional tests should not be used in the initial evaluation of a patient suspected of having APS.

References

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; 4:295–306.
2. Wilson WA, Gharavi AE, Koike T, et al. International consensus statement on preliminary classification criteria for definite antiphospholipid syndrome. *Arthritis Rheum* 1999; 42:1309–11.
3. Uthman I, Khamashta M. Ethnic and geographical variation in antiphospholipid (Hughes) syndrome. *Ann Rheum Dis* 2005; 64:1671–6.
4. Lee EY, Lee CK, Lee TH, et al. Does the anti-beta2-glycoprotein I antibody provide additional information in patients with thrombosis? *Thromb Res* 2003; 111:29–32.

Test Information

0051600

Phospholipid Antibodies, IgG, IgM, & IgA

For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult[®] at www.arupconsult.com.