Test Definition: ACLIP

Phospholipid (Cardiolipin) Antibodies, IgA, Serum

Overview

Useful For

May be of diagnostic significance for patients at risk for antiphospholipid syndrome or systemic lupus erythematosus who test negative for criterial antiphospholipid antibodies

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
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 and/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 and beta2-glyocoprotein I (anti-B2 GPI) with all tests carrying equal diagnostic significance for disease.(1) In 2023, the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) published new classification criteria for APS that 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 for IgG/IgM aCL and/or IgG/IgM anti-B2 GPI).(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)

Unlike LAC, which is evaluated using functional assays, diverse solid-phase immunoassays, such as enzyme-linked immunosorbent assay, multiplex bead assay, chemiluminescent immunoassay, and fluorescence enzyme immunoassay are used in the clinical laboratories for the detection and measurement of aCL and anti-B2GPI IgA, IgG, and IgM antibodies.(5,6) For aCL IgG and IgM determinations, the APS classification guidance recommends antibody cutoff values greater than 40 IgG phospholipid (GPL) or IgM phospholipid (MPL) units (units traceable to the Harris standards for aCL antibody assays) or more than the 99th percentile for the testing laboratory's population for positivity. It also advocates for the use of values greater than the 99th percentile for the laboratory's population in the establishment of reference intervals for anti-B2GPI IgG and IgM antibody tests.(1) The use of cutoff values greater than 40 GPL or MPL units to define positivity is not be applicable to all aCL antibody immunoassays, as the threshold used to distinguish moderate-to-high positive from low positive results are test dependent.(6-8) In addition, the cutoff 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.(2,6-8)

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 classification criteria may be justified. This may include testing for noncriteria aPL antibody tests such the aCL IgA and anti-B2GPI IgA recommended in 2012 SLICC guidance for SLE or evaluation of other noncriteria aPL antibody tests.(4-6,9,10) 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 and/or IgM.

Reference Values

APL refers to IgA phospholipid units. One APL unit is 1 microgram of IgA antibody.

Negative: <15.0 APL
Weakly positive: 15.0-39.9 APL
Positive: 40.0-79.9 APL
Strongly positive: > or =80.0 APL

Reference values apply to all ages.

Interpretation

The presence of anticardiolipin (aCL) IgA antibodies (greater than 15 IgA phospholipid units [APL]) may be associated with a diagnosis of antiphospholipid syndrome (APS) and/or systemic lupus erythematosus (SLE). In the absence "criteria" aPL antibodies for APS and diagnostic tests for SLE, isolated aCL IgA must be interpreted with a high degree of caution.

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

Detection of anticardiolipin antibodies using the method is not affected by anticoagulant treatment.

Cautions

Immunoassays for the detection of certain antibodies including anticardiolipin (aCL) 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).

Data from systemic review suggest that results of antiphospholipid antibody tests can be highly variable, and results obtained with different commercial immunoassays may yield different results.(11)

Clinical Reference

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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
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7. Ruffatti A, Olivieri S, Tonello M, et al: Influence of different IgG anticardiolipin antibody cut-off values on antiphospholipid syndrome classification. J Thromb Haemost. 2008;6(10):1693-1696
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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;70(4):627-634
11. Meijide H, Sciascia S, Sanna G, Khamashta MA, Bertolaccini ML. The clinical relevance of IgA anticardiolipin and IgA anti-ß2 glycoprotein I antiphospholipid antibodies: a systematic review. Autoimmun Rev. 2013;12(03):421-425

Performance

Method Description

Purified cardiolipin 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 cardiolipin 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 become 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. After stopping the enzymatic production of colored product, the presence or absence of cardiolipin antibody is determined by comparing the sample optical density with that of a 5-point calibration curve. Results are reported out semiquantitatively in standard IgA anticardiolipin units.(Package insert: QUANTA Lite ACA IgA III. Inova Diagnostics; Version 22, 08/2020)

PDF Report

No

Day(s) Performed

Monday, Thursday

Report Available

3 to 5 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

86147

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ACLIP	Phospholipid Ab IgA, S	5076-5

Result ID	Test Result Name	Result LOINC® Value
ACLIP	Phospholipid Ab IgA, S	5076-5