MAYO CLINIC LABORATORIES

Test Definition: PBC2

SP100 and GP210 Antibodies, IgG, Serum

Overview

Useful For

Evaluating the risk of primary biliary cholangitis in anti-mitochondrial antibody (AMA)-negative patients by identification of Sp100 and gp210 antibodies

Estimating risk in AMA-positive patients with incomplete feature of disease

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
SP100	SP100 Antibody, IgG, S	Yes	Yes
GP210	GP210 Antibody, IgG, S	Yes	Yes

Testing Algorithm

For more information see First-Line Screening for Autoimmune Liver Disease Algorithm.

Special Instructions

- First-Line Screening for Autoimmune Liver Disease Algorithm

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Additional Testing Requirements

This is a first line test when primary biliary cholangitis is strongly suspected. It should be ordered in conjunction with AMA / Mitochondrial Antibodies (M2), 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: 1.0 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send a Gastroenterology and Hepatology Test Request (T728) with the specimen.

Specimen Minimum Volume

0.4 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
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

Primary biliary cholangitis (PBC) is a chronic and progressive autoimmune liver disease characterized by the destruction of the small intrahepatic bile ducts and a variable clinical course, which may include fatigue and pruritus. Untreated patients with PBC have a high risk of liver cirrhosis and related complications, liver failure, and death.(1,2) The serological hallmark of PBC is the presence of anti-mitochondrial antibody (AMA) characterized by cytoplasmic reticular/AMA (anti-cell 21 [AC-21] based on the International Consensus on Antinuclear Antibody Patterns [ICAP] nomenclature) staining pattern on HEp-2 substrate by indirect immunofluorescence assay (IFA).(3) In addition, autoantibodies associated with the HEp-2 IFA nuclear patterns have been reported in a subset of patients with PBC who are seronegative for AMA or may be positive for AMA but have uncertain clinical or phenotypic attributes.(1,2,4,5) The HEp-2 IFA nuclear patterns in PBC include multiple nuclear dots (MND or AC-6) and punctate nuclear envelope (AC-12), which are associated with anti-Sp100 and anti-gp210 antibodies, respectively.(3) The diagnosis of PBC can be established if 2 out of the 3 following criteria are met: sustained elevated levels of alkaline phosphatase (ALP), evidence AMA or specific antinuclear antibody (ANA) (anti-Sp100 and anti-gp210 antibodies) and diagnostic liver histology.(2) Based on these criteria, a biopsy can be avoided in case of high ALP levels and detection of these PBC-specific autoantibodies.(1,2) Therefore, reliable and accurate serologic determination of PBC-specific autoantibodies play a critical role in disease evaluation.

Of the PBC-specific antibodies, the AMA is the most common, with the M2-type AMA (AMA-M2) the dominant target of the 9 subunits of the mitochondrial antigenic complex.(1,2) AMA-M2 target components of the 2-oxo-acid dehydrogenase complex: pyruvate dehydrogenase complex (PDC), 2-oxoglutarate dehydrogenase complex (OGDC), and branched-chain 2-oxoacid dehydrogenase complex (BCOADC). Specifically, autoantibodies mainly recognize the E2 subunits of these complexes: PDC-E2 (80%-90% of cases), BCOADC-E2 (50%-80% of cases) and OGDC-E2 (20%-60% of cases) and, to a lesser extent, the E1 and E3 subunits.(2). In addition to the diagnostic relevance of anti-gp210 IgG antibody, a few studies have suggested a role for their use in the risk stratification and prognosis in PBC; however, the significance of these remain contentious. In one study, the presence of anti-gp210 antibodies was reported to pose a significant risk for hepatic failure type progression, more severe interface hepatitis, and lobular inflammation compared to those with centromere antibodies who had relatively higher ductular reaction.(6) In other investigations, anti-gp210 and/or anti-Sp100 antibodies were reported to be useful in confirming a diagnosis of PBC or predicting development of disease in the context of AMA positivity in nonestablished PBC cases.(5,7)

The anti-Sp100 and anti-gp210 antibodies can also be determined using analyte-specific enzyme-linked immunosorbent assay, line blot immunoassay, and dot immunoassay.(4-8) In addition to the solid-phase immunoassays (SPA) for detecting antibodies to AMA, Sp100 and gp210, the use HEp-2 substrate by IFA provides a simple and strategic approach for confirming the presence of AMA cytoplasmic staining if positive by enzyme immunoassay (EIA) with the possibility of identifying patients who may be AMA-negative but positive to nuclear antibodies. In PBC patients, the nuclear envelope pattern is associated with anti-gp210 antibody, while the multiple nuclear dots pattern is specific for anti-Sp100 antibodies. However, expression of the multiple nuclear dot and the nuclear envelope patterns may not be easily identified in the presence of other antibodies. Testing for these antibodies is indicated in patients who are AMA positive by EIA as well as patients at-risk for PBC but are AMA negative. In addition to providing additional support for PBC diagnosis in AMA-positive and AMA-negative patients, the use of HEp-2 substrate offers the possibility to identify patients at-risk for PBC who may present with coexisting systemic autoimmune rheumatic diseases (systemic lupus erythematosus, systemic sclerosis, and Sjogren syndrome) or autoimmune liver disease (autoimmune hepatitis) through additional pattern recognition.(9,10) The use of SPA for ANA testing do not provide these additional diagnostic insights.

For more information see First-Line Screening for Autoimmune Liver Disease Algorithm.

Reference Values

Negative: < or =20.0 Units
Equivocal: 20.1-24.9 Units
Positive: > or =25.0 Units

Interpretation

A positive result for anti-gp210 antibodies or anti-Sp100 antibodies in the setting of chronic cholestasis after exclusion of other causes of liver disease is highly suggestive of primary biliary cholangitis.

Cautions

Serologic tests for autoantibodies, including anti-gp210 and anti-Sp100, should not be relied upon exclusively to determine the etiology or prognosis of patients with primary biliary cholangitis (PBC).

A negative result for anti-gp210 antibodies and/or anti-Sp100 antibodies does not exclude a diagnosis of PBC.

Results of this assay should be used in conjunction with clinical findings and other serological tests.

Clinical Reference

1. Younossi ZM, Bernstein D, Shiffman ML, et al. Diagnosis and management of primary biliary cholangitis. Am J Gastroenterol. 2019;114(1):48-63
2. Lindor KD, Bowlus CL, Boyer J, Levy C, Mayo M. Primary biliary cholangitis: 2018 practice guidance update from the American Association for the Study of Liver Diseases. Hepatology. 2019;69(1):394-419
3. International Consensus on ANA Patterns. AC-20 Cytoplasmic fine speckled. ICAP; 2015. Accessed August 18, 2023. Available at www.anapatterns.org/view_pattern.php?pattern=20
4. Zhang Q, Liu Z, Wu S, et al. Meta-analysis of antinuclear antibodies in the diagnosis of antimitochondrial antibody-negative primary biliary cholangitis. Gastroenterol Res Pract. 2019;2019:8959103
5. Dahlqvist G, Gaouar F, Carrat F, et al. Large-scale characterization study of patients with antimitochondrial antibodies but nonestablished primary biliary cholangitis. Hepatology. 2017;65(1):152-163
6. Nakamura M, Kondo H, Mori T, et al. Anti-gp210 and anti-centromere antibodies are different risk factors for the progression of primary biliary cirrhosis. Hepatology. 2007;45(1):118-127
7. Jaskowski TD, Nandakumar V, Novis CL, Palmer M, Tebo AE. Presence of anti-gp210 or anti-sp100 antibodies in AMA-positive patients may help support a diagnosis of primary biliary cholangitis. Clin Chim Acta. 2023;540:117219
8. Munoz-Sanchez G, Perez-Isidro A, Ortiz de Landazuri I, et al. Working algorithms and detection methods of autoantibodies in autoimmune liver disease: A nationwide study. Diagnostics (Basel). 2022;12:697
9. Favoino E, Grapsi E, Barbuti G, et al. Systemic sclerosis and primary biliary cholangitis share an antibody population with identical specificity. Clin Exp Immunol. 2023;212(1):32-38
10. Wei Q, Jiang Y, Xie J, et al. Investigation and analysis of HEp 2 indirect immunofluorescence titers and patterns in various liver diseases [published correction appears in Clin Rheumatol. 2021 Apr;40(4):1667]. Clin Rheumatol. 2020;39(8):2425-2432. doi:10.1007/s10067-020-04950-7

Performance

Method Description

These tests are intended for the semi-quantitative detection of anti-gp210 or anti-Sp100 antibody of the IgG class in human serum. A purified peptide corresponding to a portion of the gp210 or Sp100 protein is bound to the wells of a polystyrene microwell plate. Pre-diluted controls and diluted patient sera are added to separate wells, allowing any gp210 or Sp100 antibodies present to bind to the immobilized antigen. Unbound sample is washed away, and an enzyme labeled anti-human IgG conjugate is added to each well. A second incubation allows the enzyme labeled anti-human IgG to bind to any patient antibodies, which have become attached to the microwells. After washing away any unbound enzyme labeled anti-human 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 the control in the control wells.(Package inserts: QUANTA Lite gp210 ELISA 708995. INOVA Diagnostics; Rev. 5, 04/2019; QUANTA Lite sp100 ELISA 708990. INOVA Diagnostics; Rev. 3, 12/2018)

PDF Report

No

Day(s) Performed

Tuesday

Report Available
2 to 8 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
83516 x 2

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PBC2	SP100 and GP210 Antibodies, IgG, S	106055-7

Result ID	Test Result Name	Result LOINC® Value
SP100	SP100 Antibody, IgG, S	96565-7
GP210	GP210 Antibody, IgG, S	96560-8