MAYO CLINIC LABORATORIES

Test Definition: PBCPN

Primary Biliary Cholangitis Antibody Panel, Serum

Overview

Useful For

Optimal diagnostic evaluation in at-risk patients for primary biliary cholangitis (PBC)

Early identification of patients at-risk PBC with or without incomplete feature of disease

Reevaluation of PBC patients with new features of other liver diseases or systemic autoimmune diseases

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
NAIFA	Antinuclear Ab, HEp-2 Substrate, S	Yes	Yes
SP100	SP100 Antibody, IgG, S	Yes	Yes
GP210	GP210 Antibody, IgG, S	Yes	Yes
AMA	Mitochondrial Ab, M2, S	Yes	Yes

Highlights

This is the recommended first-line autoantibody panel for the evaluation of at-risk individuals under investigation for primary biliary cholangitis with new features of other liver diseases or overlapping connective tissue disease.

Method Name

GP210, SP100: Enzyme-Linked Immunosorbent Assay (ELISA)
AMA: Enzyme Immunoassay (EIA)
NAIFA: Indirect Immunofluorescence

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: 1.5 mL Serum
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

Serum: 1.1 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

Primary biliary cholangitis (PBC) is a chronic and progressive autoimmune liver disease characterized by the destruction of 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 such as 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 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) In a recent study, the

prevalence of AMA and levels of ALP were both reported to vary by race and ethnicity, highlighting the need to incorporate the ANA PBC-specific autoantibodies and HE-2 IFA in disease evaluation.(6)

Positivity of AMA ranges from 90% to 95% in patients with PBC, while the PBC-specific ANA (anti-Sp100 and anti-gp210 antibodies) may occur in approximately 30% of all patients with PBC, and up to 50% of AMA-negative patients.(4,5) The M2-type AMA (AMA-M2) is the dominant target of the 9 subunits of the mitochondrial antigenic complex.(2) AMA-M2 target components of the 2-oxo-acid dehydrogenase complex: pyruvate dehydrogenase complex, 2-oxoglutarate dehydrogenase complex (OGDC), and branched-chain 2-oxoacid dehydrogenase complex. Although the sensitivities of the anti-Sp100 and anti-gp210 antibodies are low, their specificities for PBC are excellent, therefore both tests have been reported to be useful in confirming a diagnosis of PBC or predicting development of disease in preclinical cases with positive AMA.(4,5) 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.(7) In addition to MND and punctate nuclear envelope, the anticentromere (AC-3) and the speckled (AC-4 and AC-5) patterns can be found in variable prevalence in patients with PBC with overlapping connective tissue diseases (systemic sclerosis and Sjogren syndrome).(8) In the context of other liver diseases, the cytoplasmic fibrillar linear (AC-15) HEp-2 IFA pattern, associated with autoimmune hepatitis (AIH), may also be seen when PBC overlaps in patients with AIH or other liver diseases, such as hepatitis B virus infection, hepatitis C virus infection, and hepatic carcinoma.(9) In general, a mixed pattern composed of at least two HEp-2 IFA patterns is mostly found in patients with PBC than in other liver diseases.(9)

Traditionally, the IFA method was used for the detection of AMA; however, antigen-specific solid-phase immunoassays (SPA), such as enzyme-linked immunosorbent assay (ELISA), line blot immunoassay (LIA), and dot immunoassay (DIA) have been developed and are increasingly being used in the laboratory evaluation of PBC.(4,5,7-10) The AMA SPA use a variety of M2 antigens, including fusion protein combining the three E2 subunits, a mixture of recombinant E2 subunits or the three E2 recombinant subunits isolated, among others.(4,5,7,10) The anti-Sp100 and anti-gp210 antibodies can also be determined using analyte-specific ELISA, LIA, and DIA. In addition to the 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 dot 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. The use of SPA for ANA testing does not provide these additional diagnostic insights.

Reference Values

MITOCHONDRIAL ANTIBODY, M2
Negative: <0.1 Units
Borderline: 0.1-0.3 Units

Weakly positive: 0.4-0.9 Units
Positive: > or =1.0 Units
Reference values apply to all ages.

SP100 ANTIBODY, IgG
Negative: < or =20.0 Units
Equivocal: 20.1-24.9 Units
Positive: > or =25.0 Units

GP210 ANTIBODY, IgG
Negative: < or =20.0 Units
Equivocal: 20.1-24.9 Units
Positive: > or =25.0 Units

ANTINUCLEAR ANTIBODY, HEP-2 SUBSTRATE
Negative: <1:80

Interpretation

Positive results of anti-mitochondrial antibody, anti-Sp100 and/or anti-gp210 antibodies associated with features of cholestatic liver disease is highly suggestive of primary biliary cholangitis. Antinuclear antibody positivity for non-primary biliary cholangitis associated pattern may suggest a coexisting disease requiring additional testing for confirmation.

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). Correlations between anti-mitochondrial (AMA), anti-Sp100, or anti-gp210 antibodies for specific HEp-2 immunofluorescence assay (IFA) patterns (AMA, multiple nuclear dots, or nuclear punctate envelope) are variable. Positive correlation between PBC-specific autoantibody and their corresponding HEp-2 IFA pattern is likely to increase the likelihood of PBC.

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

Positive results for antimitochondrial antibodies of M2 specificity are found (infrequently) in patients with systemic sclerosis, relatives of patient with PBC, systemic lupus erythematosus, Sjogren syndrome, idiopathic inflammatory myopathies, as well as individuals who may appear healthy.

Some patients without clinical evidence of systemic autoimmune rheumatic disease (SARD) may be positive for anti-cellular antibody. This occurs at variable prevalence depending on the patient demographics. A positive result may also precede clinical manifestation of SARD or be associated with some viral or chronic infections, cancers, or use of certain medications. All results must be reported in the appropriate clinical context as the performance of the test can be variable.

Clinical Reference

1. Ali AH, Carey EJ, Lindor KD. Diagnosis and management of primary biliary cirrhosis. Expert Rev Clin Immunol. 2014;10(12):1667-1678
2. Lindor KD, Bowlus CL, Boyer J, Levy C, Mayo M. Primary biliary cholangitis: 2018 practice guidance 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 December 24, 2025. Updated September 2025. 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. Caines A, Lu M, Wu T, et al. Pre-Diagnosis Alkaline Phosphatase and Antimitochondrial Antibody Positivity Vary by Race/Ethnicity Among Patients With Primary Biliary Cholangitis. J Gastroenterol Hepatol. 2025;40(9):2209-2218. doi:10.1111/jgh.17035
7. 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
8. 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
9. Wei Q, Jiang Y, Xie J, et al. Investigation and analysis of HEp 2 indirect immunofluorescence titers and patterns in various liver diseases . Clin Rheumatol. 2020;39(8):2425-2432. doi:10.1007/s10067-020-04950-7
10. 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(3):697

Performance

Method Description

SP100 and GP210

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).

Antinuclear Antibodies, Hep-2 Substrate,

Antibodies to nuclear antigens in a human epithelial type 2 (HEp-2) cell line by an indirect immunofluorescent technique. Commercial slides prepared from HEp-2 cells are used as a substrate. IgG antibodies in serum specimens are detected after incubation of serum with the commercial slides by the addition of a fluorescein isothiocyanate (FITC)-labeled antihuman-IgG reagent. All patient specimens are initially screened at 1:80.(Package insert: NOVA Lite DAPI ANA. Inova Diagnostics; 05/2015)

Mitochondrial Antibodies, M2
A recombinant pyruvate dehydrogenase complex-E2 (M2) antigen for detection of antibodies against M2 is attached to the surface of a microplate. Diluted patient serum, standards, or controls are added to the wells, and the M2 specific IgG and IgM antibodies, if present, bind to the antigen. All unbound human antibodies are washed away, and a conjugate of enzyme-labeled polyclonal antibody to human IgG and IgM is added. The enzyme conjugate binds to the antibody complex. Excess enzyme-conjugate is washed away, and substrate is added. After a specified time, the enzyme reaction is stopped. The intensity of the color generated is proportional to the amount of anti-M2 IgG and/or IgM antibody in the sample. The results are read by a spectrophotometer producing a direct measurement of the anti-M2 IgG and IgM antibodies in the serum. Testing is performed on the Agility instrument by Dynex.(Package insert: Kallestad Anti-Mitochondrial Kit. Bio-Rad Laboratories, Inc; 04/2014)

PDF Report
No

Day(s) Performed
Tuesday

Report Available
2 to 8 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
86039
83516 x2
86381

Test Definition: PBCPN

Primary Biliary Cholangitis Antibody Panel, Serum

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PBCPN	PBC Comprehensive Antibody Panel, S	106054-0

Result ID	Test Result Name	Result LOINC® Value
AMA	Mitochondrial Ab, M2, S	51715-1
ANAH	Antinuclear Ab, HEp-2 Substrate, S	59069-5
1TANA	ANA Titer:	33253-6
1PANA	ANA Pattern:	49311-4
2TANA	ANA Titer 2:	33253-6
2PANA	ANA Pattern 2:	49311-4
CYTQL	Cytoplasmic Pattern:	55171-3
LCOM	Lab Comment:	77202-0
SP100	SP100 Antibody, IgG, S	96565-7
GP210	GP210 Antibody, IgG, S	96560-8