

Overview

Useful For

Evaluating patients with suspected autoimmune liver disease, specifically autoimmune hepatitis or primary biliary cholangitis

Evaluating patients with liver disease of unknown etiology

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
AMA	Mitochondrial Ab, M2, S	Yes	Yes
NAIFA	Antinuclear Ab, HEp-2 Substrate, S	Yes	Yes
SMAS	Smooth Muscle Ab Screen, S	Yes	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
SMAT	Smooth Muscle Ab Titer, S	No	No

Testing Algorithm

If smooth muscle antibody (SMA) screen is positive, then the SMA titer will be performed at an additional charge.

For more information see [First-Line Screening for Autoimmune Liver Disease Algorithm](#).

Special Instructions

- [First-Line Screening for Autoimmune Liver Disease Algorithm](#)

Method Name

AMA: Enzyme Immunoassay (EIA)
NAIFA, SMAS, SMAT: Indirect Immunofluorescence

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

For evaluating patients at-risk for antinuclear antibody-associated systemic autoimmune rheumatic disease, particularly systemic lupus erythematosus, Sjogren syndrome, or mixed connective tissue disease, order CTDC / Connective Tissue Disease Cascade, Serum.

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)

Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Submission Container/Tube: Plastic vial

Specimen Volume: 1.5 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

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

Autoimmune liver diseases result from damage to hepatocytes or cholangiocytes caused by an inflammatory immune reaction. Included within this disease group are autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), and primary sclerosing cholangitis (PSC).(1) In some cases, patients with these diseases may present asymptotically, with increases in various liver enzymes being identified incidentally during an unrelated clinical evaluation. On the other end

of the spectrum are patients who present with clinical evidence of liver disease, including fatigue, hepatomegaly, ascites, esophageal varices, and jaundice.

Diagnosis of an autoimmune liver disease first requires that other etiologies of liver injury, including viral, drug, and metabolic causes, be excluded. In some situations, a liver biopsy may be indicated. For those patients in whom an autoimmune liver disease is suspected, autoantibody serology testing may be considered. These assays include markers that may support a diagnosis of an autoimmune liver disease, specifically AIH or PBC. Unfortunately, there are no known autoantibodies specific for PSC that are useful as diagnostic markers.(1)

Patients with AIH may be positive for smooth muscle antibodies (SMA) and/or antinuclear antibodies (ANA).(2) SMA are generally identified by indirect immunofluorescence using a smooth muscle substrate. The antigen specificity of SMA in the context of AIH has been identified as filamentous-actin (F-actin). SMA and F-actin antibodies with liver histology and thorough clinical evaluation are useful in the evaluation of patients with suspected autoimmune hepatitis.(3) SMA have a specificity of 80% to 90% for AIH, although the sensitivity is only in the range of 70% to 80%. In contrast, ANA, although relatively sensitive for AIH, lack specificity, being associated with a variety of autoimmune diseases.(4) Both SMA and ANA, along with other lab markers and biopsy evaluation, are included in the international diagnostic criteria for AIH.(5)

In association with chronic cholestasis after exclusion of known causes of liver disease, antimitochondrial antibodies (AMA) are strongly suggestive of a diagnosis of PBC.(6) AMA have a variable prevalence in other autoimmune diseases that can also be found in some apparently healthy individuals.(7,8) AMA are found in more than 90% of patients with PBC, with a specificity of greater than 95%. AMA are included in the clinical practice guidelines for PBC, which were developed through an international collaborative effort.(9)

For more information see [First-Line Screening for Autoimmune Liver Disease Algorithm](#).

Reference Values

MITOCHONDRIAL ANTIBODIES (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.

ANTINUCLEAR ANTIBODIES

Negative: <1:80

SMOOTH MUSCLE ANTIBODIES

Negative

If positive, results are titered.

Reference values apply to all ages.

Interpretation

The presence of smooth muscle antibodies (SMA) or antinuclear antibodies (ANA) is consistent with a diagnosis of chronic autoimmune hepatitis, in patients with clinical or laboratory evidence of hepatocellular damage.

A positive result for antimitochondrial antibodies (AMA) of M2 specificity in the setting of chronic cholestasis after exclusion of other causes of liver disease is highly suggestive of primary biliary cholangitis.

Negative results for SMA, ANA, or AMA does not exclude a diagnosis of an autoimmune liver disease.

This test is **not useful for** indicating the stage or prognosis of the disease or for monitoring the course of disease.

Cautions

Smooth muscle antibodies (SMA) may be found in patients with active hepatitis caused by alcohol or drug exposure.

Positive results for antimitochondrial antibodies (AMA) are found (infrequently) in patients with CREST (calcinosis, Raynaud phenomenon, esophageal hypomotility, sclerodactyly, and telangiectasia) syndrome, relatives of patients with primary biliary cholangitis, and other autoimmune diseases.

Antinuclear antibodies (ANA) occur in patients with a variety of systemic autoimmune diseases, including systemic lupus erythematosus, rheumatoid arthritis, Sjogren syndrome, and systemic sclerosis.

ANA may also be detectable following viral illnesses, in chronic infections, or in patients treated with many different medications.

The presence of SMA, ANA, and AMA should not be exclusively relied upon to diagnose an autoimmune liver disease. Correlation with clinical presentation and other laboratory parameters of liver disease is required.

Clinical Reference

1. Terziroli Beretta-Piccoli B, Mieli-Vergani G, Vergani D: The clinical usage and definition of autoantibodies in immune-mediated liver disease: A comprehensive overview. *J Autoimmun.* 2018 Dec;95:144-158. doi: 10.1016/j.jaut.2018.10.0046
2. Mieli-Vergani G, Vergani D, Czaja AJ, et al: Autoimmune hepatitis. *Nat Rev Dis Primers.* 2018 Apr 12;4:18017
3. Invernizzi P, Lleo A, Podda M: Interpreting serological tests in diagnosing autoimmune liver diseases. *Sem Liver Dis.* 2007 May;27(2):161-172
4. Terziroli Beretta-Piccoli B, Mieli-Vergani G, Vergani D: Serology in autoimmune hepatitis: A clinical-practice approach. *Eur J Intern Med.* 2018 Feb;48:35-43
5. Hennes EM, Zeniya M, Czaja AJ, et al: Simplified criteria for the diagnosis of autoimmune hepatitis. *Hepatol.* 2008 Jul;48(1):169-176
6. Muratori L, Granito A, Muratori P, Pappas G, Bianchi FB: Antimitochondrial antibodies and other antibodies in primary biliary cirrhosis: diagnostic and prognostic value. *Clin Liver Dis.* 2008 May;12(2):261-276
7. Colapietro F, Lleo A, Generali E: Antimitochondrial antibodies: From bench to bedside. *Clin Rev Allergy Immunol.* 2022 Oct;63(2):166-177. doi: 10.1007/s12016-021-08904-y
8. Leung PSC, Choi J, Yang G, Woo E, Kenny TP, Gershwin ME: A contemporary perspective on the molecular characteristics of mitochondrial autoantigens and diagnosis in primary biliary cholangitis. *Expert Rev Mol Diagn.* 2016 Jun;16(6):697-705. doi: 10.1586/14737159.2016.1164038
9. European Association for the Study of the Liver: EASL Clinical Practice Guidelines: The diagnosis and management of patients with primary biliary cholangitis. *J Hepatol.* 2017 Jul;67(1):145-172

Performance

Method Description

Mitochondrial Antibodies:

This method is an enzyme immunosorbent assay that detects both IgG and IgM antibodies to M2 antigens. A dilution of patient serum is added to the wells coated with M2 antigen and incubated. After incubation and washing, all unbound human antibodies are washed away, and enzyme-conjugated IgG and IgM anti-human is added. The enzyme conjugate binds to the antibody complex. Excess enzyme-conjugate is washed away, and substrate is added. After incubation, the enzyme substrate reaction is stopped. The complete assay is measured on a spectrophotometer plate reader. The intensity of the color generated is proportional to the amount of IgG and IgM specific antibody in the sample.(Package insert: Kallestad Anti-Mitochondrial Kit. Bio-Rad Laboratories; 10/2014)

Antinuclear Antibodies:

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; 06/2018)

Smooth Muscle Antibody:

The patient's serum in 1:20 and 1:40 dilutions is added to fresh tissue from mouse stomach/kidney and incubated; fluorescein-conjugated antiglobulin is then added. The slides are read with a fluorescence microscope.(Package insert: Kallestad Mouse Stomach/Kidney. Bio-Rad Laboratories, Inc; 06/2015)

PDF Report

No

Day(s) Performed

Monday through Saturday

Report Available

3 to 4 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

See Individual Test IDs

CPT Code Information

- 86381
- 86039
- 86015
- 86015-Titer (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
ALDG2	Autoimmune Liver Disease Panel, S	94700-2

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
609515	Smooth Muscle Ab Screen, S	26971-2