MAYO CLINIC LABORATORIES

Test Definition: AMA

Mitochondrial Antibodies (M2), Serum

Overview

Useful For

Establishing the diagnosis of primary biliary cholangitis

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

Method Name

Enzyme Immunoassay (EIA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Collection Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Submission Container/Tube: Plastic vial

Specimen Volume: 0.5 mL

Forms

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

-General Request (T239)

-Gastroenterology and Hepatology Client Test Request (T728)

Specimen Minimum Volume

0.4 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	OK
Heat-treated	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	21 days	
	Frozen	21 days	

Clinical & Interpretive

Clinical Information

The presence of antimitochondrial antibodies (AMA) in association with chronic cholestasis after exclusion of known causes of liver disease is strongly suggestive of a diagnosis of primary biliary cholangitis (PBC).(1) AMA have a variable prevalence in other autoimmune diseases such as systemic sclerosis, Sjogren syndrome, autoimmune thyroid disease, rheumatoid arthritis, systemic lupus erythematosus, celiac disease, psoriasis, inflammatory bowel disease, antiphospholipid syndrome, and idiopathic inflammatory myopathy.(2-4) AMA can also be found in some apparently healthy individuals as well as patients with hepatic diseases such as nonalcoholic steatohepatitis and viral hepatitis.(2,3,5)

AMA recognize mitochondrial antigens classified numerically as M1 through M9 with an immunodominance to the M2 antigen in patients with PBC. The M2 antigens comprise of 2-oxo acid dehydrogenase complexes, which are key enzymes in the mitochondrial respiratory chain, namely the pyruvate dehydrogenase complex (PDC), the E3 binding protein of PDC, the 2-oxoglutarate dehydrogenase complex (OADC), and the branched-chain 2-oxo acid dehydrogenase complex.(5) These are multienzyme complexes consist of a minimum of three enzymes, namely E1, E2, and E3, which have a common structure. The identification of the E2 subunit of the PDC (PDC-E2) located on the inner mitochondrial membrane was a major advance in the study of PBC, leading to the development of solid-phase immunoassays such as enzyme-linked immunosorbent assays with recombinant or purified antigens.(6) In PBC patients, AMA are directed against a highly specific epitope within the lipoyl domain of the E2 subunits of the OADC, with the PDC-E2 being the immunodominant mitochondrial antigen.(5,7)

AMA stain the cytoplasm of HEp-2 cells by indirect immunofluorescence assay with a diffuse, granular cytoplasmic pattern. However, this pattern may not be consistent with AMA detected on triple rodent tissue or solid-phase immunoassays, and therefore the sole use of HEp-2 cells for AMA detection is not recommended.(8)

Reference Values

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.

Interpretation

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

Cautions

Positive results 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.

Supportive Data

Testing performed in the Antibody Immunology Laboratory of the antimitochondrial antibody-M2 by EIA revealed a false-positive rate of less than 2% in 196 normal samples, and overall concordance compared with indirect immunofluorescence of 90% on sera from the Mayo primary biliary cholangitis (PBC) Serum Bank. Ten discordant results were obtained (negative by enzyme immunoassay and positive by immunofluorescence assay). Seven of the 10 patients had no histologic evidence of PBC on liver biopsy.

Clinical Reference

1. 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. doi: 10.1016/j.jhep.2017.03.0222. Colapietro F, Lleo A, Generali E: Antimitochondrial antibodies: From bench to bedside. Clin Rev Allergy Immunol. 2021 Sept:1–12. doi: 10.1007/s12016-021-08904-y

3. Efe C, Torgutalp M, Henriksson I, et al: Extrahepatic autoimmune diseases in primary biliary cholangitis: Prevalence and significance for clinical presentation and disease outcome. J Gastroenterol Hepatol. 2021 Apr;36(4):936-942. doi: 10.1111/jgh.15214

4. Albayda J, Khan A, Casciola-Rosen L, et al: Inflammatory myopathy associated with anti-mitochondrial antibodies: A distinct phenotype with cardiac involvement. Semin Arthritis Rheum. 2018 Feb;47(4):552-556. doi: 10.1016/j.semarthrit.2017.06.004

5. 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. Gershwin ME, Mackay IR, Sturgess A, Coppel RL: Identification and specificity of a cDNA encoding the 70 kd mitochondrial antigen recognized in primary biliary cirrhosis. J Immunol. 1987 May;138(10):3525-3531.

7. Leung PS, Choi J, Yang G, et al: 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

8. Vergani D, Alvarez F, Bianchi FB, et al: Liver autoimmune serology: A consensus statement from the committee for autoimmune serology of the International Autoimmune Hepatitis Group. J Hepatol. 2004 Oct;41(4):677-683. doi: 10.1016/j.jhep.2004.08.002

Performance

Method Description

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; 04/14)

PDF Report
No

Day(s) Performed
Monday through Saturday

Report Available
2 to 3 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 Regional Manager. 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
86381

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
AMA	Mitochondrial Ab, M2, S	51715-1

Result ID	Test Result Name	Result LOINC® Value
AMA	Mitochondrial Ab, M2, S	51715-1