

## Primary Biliary Cirrhosis - PBC

### Clinical Background

Primary biliary cirrhosis (PBC) is an autoimmune liver disorder characterized by chronic, progressive cholestatic disease.

#### Epidemiology

- Incidence – 25-27/1,000,000 in U.S.
- Age – peak onset in 40s
- Sex – M<F, 1:9

#### Risk Factors

- Presence of another autoimmune disorder
- Family history of PBC
  - The risk for a first-degree relative of a PBC patient is 50- to 100-fold higher than the general population

#### Pathophysiology

- Etiology is unknown
- Pathogenesis of PBC is believed to be caused by:
  - Defect in immune tolerance resulting in the expansion of self-mitochondrial antigen specific for T and B lymphocytes
  - Inappropriate immune response following environmental or infectious agent causes modification of mitochondrial proteins or molecular mimicry
- PBC is characterized by T-cell mediated destruction of bile duct epithelial cells resulting in loss of ducts and persistent cholestasis, which may lead to end-stage liver failure without treatment

#### Clinical Presentation

- Large majority of patients initially diagnosed are asymptomatic or only mildly fatigued
- Fatigue, pruritus, jaundice
- Complications
  - Osteoporosis
  - Esophageal varices
  - Hepatocellular carcinoma
- Association with other autoimmune disorders
  - CREST syndrome (calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia)
  - Sicca syndrome
  - Autoimmune thyroid disease
  - IgA deficiency
  - Chronic autoimmune hepatitis (AIH)
    - PBC and AIH have many overlapping immunologic features
    - Some patients may have serologic tests and histologic findings suggestive of AIH in addition to PBC (may be continuum of a single disease entity)
  - Addison disease
  - Systemic lupus erythematosus (SLE)
  - Autoimmune thrombocytopenia or hemolytic anemia

- Rheumatoid arthritis
- Scleroderma

#### Treatment

- Medical therapy
  - Ursodeoxycholic acid does not reduce the risk for mortality or liver transplantation
  - Cholestyramine for pruritis
- Liver transplantation for endstage cirrhosis

## Diagnosis

- Indications for testing – chronic pruritis, jaundice; elevated liver enzymes with predominant cholestatic picture
- Laboratory testing
  - Initial testing – aminotransferases, alkaline phosphatase, bilirubin
  - Serologic testing should include other autoimmune liver antibodies to rule out AIH
    - Anti-nuclear antibodies (ANA)
    - Smooth muscle antibody (SMA)
    - Liver-kidney microsome-1 antibody (LKM1)
    - Perinuclear staining anti-neutrophil cytoplasmic antibody (pANCA)
  - PBC is strongly associated with antimitochondrial antibody (AMA), M2 type
    - However, M2 levels in PBC do not appear correlated with clinical activity or disease progression
    - Approximately 5-10% of PBC patients are AMA negative
      - In these patients, testing for anti-sp100 and anti-gp210 antibodies may be clinically useful
- Histology – biopsy is not always indicated and not necessary for diagnosis if patient has positive AMA and evidence of cholestasis on liver testing, but it does allow classification of disease severity
  - Pathological lesion is chronic non-suppurative destructive cholangitis
- Imaging studies
  - If AMA negative and PBC is suspected, endoscopic retrograde cholangiopancreatography (ERCP), cholangiography or magnetic resonance cholangiopancreatography should be performed

#### Prognosis

- AMA with IgG3 subclass may identify patients with more severe disease risk

#### Differential Diagnosis

- Autoimmune hepatitis
- Biliary carcinoma
- Cholelithiasis
- Chronic hepatitis
- Nonalcoholic fatty liver disease
- Primary sclerosing cholangitis (PSC)

## Monitoring

- Anti-gp210 is prognostic in PBC
  - Failure to see a decline with treatment increases risk of progression to end-stage hepatic failure

## Lab Tests

### Indications for Laboratory Testing

Tests generally appear in the order most useful for common clinical situations. For test-specific information, refer to the test number in the ARUP Laboratory Test Directory on the ARUP Web site at [www.aruplab.com](http://www.aruplab.com).

Test Name and Number	Recommended Use	Limitations	Follow Up
Alanine Aminotransferase, Serum or Plasma <b>0020008</b> Method: Enzymatic	Initial testing to evaluate liver dysfunction		
Bilirubin, Direct & Total, Serum or Plasma <b>0020426</b> Method: Spectrophotometry	Initial testing to evaluate liver dysfunction		
Alkaline Phosphatase Isoenzymes <b>0021020</b> Method: Heat Inactivation/Enzymatic	Initial testing to evaluate liver dysfunction		
Autoimmune Hepatitis Panel Plus with Reflex to Titers <b>0055351</b> Method: Enzyme-Linked Immunosorbent Assay/Indirect Fluorescent Antibody	Rule out autoimmune hepatitis		
Mitochondrial M2 Antibody, IgG (ELISA) <b>0050065</b> Method: Enzyme-Linked Immunosorbent Assay	Aid in the diagnosis of primary biliary cirrhosis (PBC)	A negative M2 antibody result does not rule out PBC; about 5-10% of these patients are seronegative	

gp210 & sp100 Antibodies, IgG <b>0051636</b> Method: Enzyme-Linked Immunosorbent Assay	Aid in the diagnosis of patients suspected of having PBC, especially for those who are anti-mitochondrial autoantibody negative (detects autoantibody against sp100 and gp210)	Negative likelihood ratio for sp100 and gp 210 is 1.3	
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**Additional Tests Available**

Test Name and Number	Comments
Anti-Nuclear Antibodies (ANA), IgG Screen with Reflex to IFA Titer <b>0050080</b> Method: Enzyme-Linked Immunosorbent Assay/Indirect Fluorescent Antibody	
F-Actin (Smooth Muscle) Antibody, IgG by ELISA with Reflex to Smooth Muscle Antibody, IgG Titer <b>0051174</b> Method: Enzyme-Linked Immunosorbent Assay/Indirect Fluorescent Antibody	
Liver-Kidney Microsome - 1 Antibody, IgG <b>0055241</b> Method: Enzyme-Linked Immunosorbent Assay	
Anti-Neutrophil Cytoplasmic Antibody, IgG <b>0050811</b> Method: Indirect Fluorescent Antibody	
sp100 Antibody, IgG <b>0051625</b> Method: Enzyme-Linked Immunosorbent Assay	
gp210 Antibody, IgG <b>0051621</b> Method: Enzyme-Linked Immunosorbent Assay	
Centromere Antibody, IgG <b>0050714</b> Method: Multi-Analyte Fluorescent Detection	

**General References**

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### References from the ARUP Institute for Clinical and Experimental Pathology®

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### Diagnostic Algorithm(s)

PDF algorithm(s) available at [www.arupconsult.com](http://www.arupconsult.com).

Liver Disease or Hepatitis of Unknown Etiology Testing Algorithm

### Related Content

Cirrhosis

Hepatitis, Acute

Hepatitis, Autoimmune - AIH

Hepatocellular Carcinoma

Liver Disease Evaluation

Scleroderma - Systemic Sclerosis

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