



▶ **SELECTED AUTOANTIBODIES IN AUTOIMMUNE LIVER DISEASE**

- ▶ **Type I Autoimmune Hepatitis**
 - Anti-Nuclear Ab (ANA)
 - Anti- Smooth Muscle Ab
 - Anti-Actin Ab
 - Anti-Soluble Liver Antigen
 - Atypical P-ANCA

- ▶ **Type 2 Autoimmune Hepatitis**
 - Anti-Liver/Kidney Microsomal Ab
 - Anti-Liver Cytosolic Protein

- ▶ **Primary Biliary Cirrhosis (PBC)**
 - sp100 Ab
 - gp210 Ab
 - Anti-Mitochondrial Abs
 - ANA

- ▶ **Sclerosing Cholangitis**
 - Atypical P-ANCA
 - ANA

- ▶ **Autoantibodies Associated with Hepatitis C**
 - Rheumatoid Factor (70%)
 - ANA (10-30%)
 - Anti-Smooth Muscle Ab (60-70%)
 - Anti-Liver/Kidney Microsomal Ab (reported)
 - Anticardiolipin Abs (22%)
 - ANCA (reported)
 - Anti-Thyroid Abs
 - Cryoglobulins
 - Presence of HLA-DR4 is associated with a five-fold increase in incidence of autoimmune diseases.

See reverse side for detailed information

► A GUIDE TO INTERPRETATION IN AUTOIMMUNE LIVER DISEASE

A. General Comments

- The major role of autoantibody detection is in facilitating classification of the known autoimmune liver diseases.
- Autoantibodies are not known to be pathogenic in these conditions.
- They are not helpful in monitoring disease activity or prognosis in general.
- Patients can be seronegative at the onset of their disease. Repeat testing is therefore suggested if clinical suspicion remains.
- Persistent seronegativity suggests cryptogenic hepatitis.
- Antibody titers can fluctuate and new antibodies may occur over time.

B. Specific Autoantibody Profiles in Autoimmune Liver Disease

I. Type 1 Autoimmune Hepatitis

a. ANA

- ANA is the major antibody seen in autoimmune hepatitis.
- It has extensive heterogeneity (anti-dsDNA, anti-ssDNA, anti-chromatin, anti-histone, anti-nuclear lamins and anti-RNP).

b. Anti-Smooth Muscle

- Is detected by immunofluorescence but not specific unless titers are 1:320 or greater.
- Can be seen in other liver diseases and non-liver diseases as well.

c. Anti-Actin

- Type of anti-smooth muscle antibody with much better specificity for autoimmune hepatitis than anti-smooth muscle ab.
- Sensitivity reported to be 75% in Type I autoimmune hepatitis.
- Can be seen in 3-15% of other types of chronic hepatitis.

d. Anti-Soluble Liver Antigen (Anti-SLA)

- 100% specific for autoimmune hepatitis, Type I.
- Seen in 30% of cases in conjunction with other autoantibodies.
- Importantly, it can be seen as the sole autoantibody response in 10-15% of patients.
- Some researchers use this antibody as a marker for autoimmune hepatitis Type, 3 but these patients are clinically similar to autoimmune hepatitis Type I patients.

e. Atypical P-ANCA

- Seen in 65-95% of Type I patients, usually in high titers.
- Also seen in sclerosing cholangitis.
- It is not seen in Type 2 autoimmune hepatitis.

II. Type 2 Autoimmune Hepatitis

a. Anti-Liver/Kidney Microsome 1 (anti-LKM1)

- Major serologic marker in Type 2 autoimmune hepatitis seen in 95-100% of cases.
- Directed against cytochrome P4502D6.
- Can be seen in hepatitis C but uncommon.

b. Anti-Liver Cytosolic Protein

- 50% of patients with anti-LKM1 antibodies have antibodies to liver cytosolic protein.
- Can be the only autoantibody seen in Type 2 autoimmune hepatitis.

III. Primary Biliary Cirrhosis (PBC)

a. ANA by IFA

- PBC patients frequently are positive for ANA, especially multiple (1-20) nuclear dots and nuclear rim patterns on HEp-2.
- Anti-centromere antibodies are present in 10-15% of cases.
- Antinuclear pore antibodies can be seen in AMA-negative PBC. Clinically similar to AMA positive patients.

b. Anti-Mitochondrial Antibody (AMA) by IFA on Kidney/Liver/Stomach Substrate

- The sensitivity of AMA was reported in up to 95% of cases.
- The antigenic target is the E2 subunit common to several mitochondrial enzyme systems.
- The AMA pattern shows coarse granular filamentous staining extending throughout the cytoplasm.

c. Anti-Mitochondrial M2 EP (MIT3) by ELISA

- M2 specific antigens were identified as the E2 subunits of the pyruvate dehydrogenase complex (PDC-E2).
- While 80-90% of histologically proven patients have anti-PDC-E2 antibodies, about 10% of PBC patients only react to branched-chain 2-oxo-acid dehydrogenase complex (BCOADC-E2) and/or 2-oxo glutarate dehydrogenase complex (OGDC-E2). Identification of these antigens permitted the development of the new M2 ELISA.
- Reactivity has the dominant specificity (95%) with high sensitivity (88%).

d. Anti-gp210 and Anti-sp100 by ELISA

- Are detected in approximately 25% of all PBC patients and 30% of AMA-negative PBC patients.
- These antibodies have relatively low sensitivity but the specificity is greater than 99%.
- These antibodies may identify a subgroup of patients with a more severe disease course.
- These antibodies may help in earlier identification, diagnosis and treatment of patients negative for conventional markers.
- Combined testing for M2, gp210 and sp100 identifies 92% of PBC patients.

IV. Sclerosing Cholangitis

a. Atypical P-ANCA

- Atypical P-ANCA is the marker antibody in this disorder occurring in 65-85% of cases with or without ulcerative colitis.
- Atypical P-ANCA can persist after liver transplantation.

b. Anti-Nuclear Ab (ANA)

- ANA can be seen occasionally

V. Autoantibodies Associated with Hepatitis C

- | | |
|-----------------------------------------------------------------------------------------------------|----------------------------------------------|
| a. Rheumatoid factor: 70% | b. Anti-nuclear ab: 10-30% |
| c. Anti-smooth muscle ab: 60-70% | d. Anti-liver/kidney microsomal ab: reported |
| e. Anticardiolipin abs: 22% | f. Antineutrophil cytoplasmic abs: reported |
| g. Anti-thyroid abs | h. Cryoglobulins |
| i. Presence of HLA-DR4 is associated with a five-fold increase in incidence of autoimmune diseases. | |