

**A GUIDE TO INTERPRETATION
IN
AUTOIMMUNE LIVER DISEASES**

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 I Autoimmune Hepatitis:

a. ANA.

- ANA is the major antibody seen in autoimmune hepatitis.
- It has extensive heterogeneity (anti-double-strand DNA, anti-single-strand DNA, antichromatin, anti-histone, anti-nuclear lamins and anti-RNP).

b. Anti-Smooth Muscle.

- Is detected by immunofluorescence but not specific unless the 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 antibody.
- 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 1.
- 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 1 patients.

e. Atypical P-ANCA.

- Seen in 65 – 95% of Type 1 patients, usually in high titers.
- Also seen in sclerosing cholangitis.
- It is not seen in Type 2 autoimmune hepatitis.

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- II. Type 2 Autoimmune Hepatitis:
 - a. Anti-Liver/Kidney Microsome I (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:
 - a. Anti-Mitochondrial Antibody (AMA)
 - AMA is the marker antibody for Primary Biliary Cirrhosis (PBC) and is seen in 90% of cases.
 - 10% of PBC are therefore AMA negative.
 - The antigenic target is the E2 subunit common to several mitochondrial enzyme systems.
 - Anti-centromere antibodies are present in 10-15% of cases.
 - Antinuclear pore antibodies (antibodies against nuclear envelope proteins) can be seen in AMA-negative PBC detected by the staining pattern on hep 2 substrate (nuclear lamins staining pattern).
 - Clinically similar to AMA positive patients.
 - An additional nuclear dot staining pattern can be seen on hep 2 substrate.
 - The IgM isotype is frequently increased in PBC.

- IV. Sclerosing Cholangitis:
 - 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.
 - 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. Anti-cardiolipin 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.