Background Information

Liver Disease Diagnostics

The term “liver disease” applies to many diseases and disorders that cause the liver to function improperly or to stop functioning. Abdominal pain, jaundice, or abnormal results of liver function test are indicative of liver disease.

There are many kinds of liver diseases. Viruses cause some of them, like hepatitis A, hepatitis B and hepatitis C. Others can be the result of drugs, poisons or alcohol abuse. In autoimmune liver diseases such as autoimmune hepatitis and primary biliary cirrhosis, cells from the immune system attack the liver tissue.

If the liver forms scar tissue because of an illness, it is called cirrhosis. Jaundice can be one sign of liver disease.

The autoimmune liver disease panel:

The autoimmune liver disease panel is a series of tests that is done when a person is thought to have autoimmune liver disease. An autoimmune liver disease means that the body’s immune system attacks the liver.

These tests include:

- ➔ anti-liver kidney microsome antibodies (LKM-1 antibodies)
- ➔ antimitochondrial antibodies (AMA-M2)
- ➔ antinuclear antibodies (ANA)
- ➔ anti-smooth muscle antibodies (ASMA)

Sometimes the panel may also include other tests. Often immune protein levels (serum IgG and immunoglobuline) in the blood are also checked.

Why the tests are performed:

In autoimmune disorders, cells from the immune system attack tissue or organs. The most common autoimmune liver disease are autoimmune hepatitis (AIH) and primary biliary cirrhosis (PBC).

What the test results mean:

Blood tests for autoimmune diseases are not completely accurate. The can have false negative results and false positive results. Therefore these tests are only an diagnostic aid.

Please note:

- A weakly positive or low titre positive test for autoimmune disease is often not due to any disease.
- A positive test on the panel may be a sign of autoimmune hepatitis or other autoimmune liver disease.
- A positive test result for antimitochondrial antibodies (especially for AMA-M2) is indicative of primary biliary cirrhosis (PBC).
- If the immune protein level is high but albumin is low, the patient may suffer from liver cirrhosis or chronic active hepatitis.

Primary biliary cirrhosis

Primary biliary cirrhosis (PBC) is an autoimmune disease of the liver that causes scarring, fibrosis and finally cirrhosis. PBC is found most frequently in women between the ages of 35 and 70. Disease clusters in families.

Laboratory tests:

If PBC is suspected, liver function tests and laboratory tests to measure serum IgM (increased in PBC!) and AMA (especially AMA-M2!) should be done. ELISA tests for **AMA-M2** are 95% sensitive and 98% specific for PBC. False-positive results can occur in autoimmune hepatitis type 1.

Other autoantibodies, such as **ANA**, anti-smooth muscle antibodies (**ASMA**), and **rheumatoid factor** may be present. PBC diagnosis is often supported by detection of **anti-centromere antibodies**, **anti-Sp100 antibodies** and **anti-gp210 antibodies**, particularly when AMA-M2 test is negative.

Liver biopsy may be necessary for diagnosis and staging.

	AIH	**PBC**	**PSC**
age	all ages	35-70 years	children, 25-50 years
sex	female > male	female >>male	male > female
gamma globuline	yes	no	yes
immunoglobuline	IgG elevated	IgM elevated	IgM elevated (30-50%)
“classical” antibodies	**AIH type 1:** ANA, ASMA, anti-SLA (“AIH type 3”) **AIH type 2:** anti-LC-1, anti-LKM-1	AMA, AMA-M2, anti-Sp100 (“nuclear dots”), *(ANA, ASMA, RF, anti-CENP, anti-Sp100, anti-gp210)*	atyp. pANCA (“xANCA”)

Table 1: Differentiation of various autoimmune liver diseases.

Autoimmune hepatitis

Autoimmune hepatitis (AIH) is an inflammatory liver disease caused by the immune system mistakenly attacking the cells of the liver. It can be found in anyone at any age, but about 80% of those affected are women.

The diagnosis of autoimmune hepatitis is best achieved with a combination of clinical, laboratory and histological findings. The disease is characterised by interface hepatitis, elevated transaminase levels, and serologically by the presence of autoantibodies and increased levels of immunoglobulin G.

Overlapping presentation with primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC) has been observed. AIH responds to immunosuppressive treatment, which should be instituted as soon as the diagnosis is made.

There are several subtypes of AIH recognised, but the clinical utility of distinguishing subtypes is limited. AIH type 1 affects predominantly adults while 80% of patients with AIH type 2 are children.

Seropositivity for **ANA** and/or **ASMA** defines AIH type 1, positivity for **anti-LKM-1 antibodies** (*liver kidney microsome type 1* antibody) and/or **LC-1 antibodies** (LC-1 = *liver cytosol type 1*) indicate AIH type 2. AIH type 2 patients with anti-LC-1 antibodies have histologically more severe disease compared to those without anti-LC-1 antibodies.

Anti-SLA antibodies are proposed as specific markers of a type of severe AIH seronegative for the conventional AIH type 1 autoantibodies (this type is formerly known as “AIH type 3”). Anti-SLA antibodies denote AIH type 1 patients with a more severe course of disease and a propensity for relapse after corticosteroid withdrawal compared to their negative counterparts.

Primary sclerosing cholangitis

Primary sclerosing cholangitis (PSC) is the most common form of sclerosing cholangitis. Most of patients with PSC are men (70%), with mean age at diagnosis 40 years. PSC has no known cause.

PSC is suspected in patients with unexplained abnormalities in liver biochemical tests, particularly in those with inflammatory bowel disease (IBD). A cholestatic pattern showing elevated alkaline phosphatase and gamma-glutamyltransferase (GGT) rather than aminotransferases is typical. Gamma globulin and IgM levels tend to be increased.

The only and nonspecific serological reactivity is an atypical perinuclear antineutrophil cytoplasmic antibody (“**xANCA**”). Characteristically, **AMA** typically positive in primary biliary cirrhosis (PBC), are negative in PSC sera.

References:

Bogdanos DP, Invernizzi P, Mackay IR, Vergani D. Autoimmune liver serology: Current diagnostic and clinical challenges. *World J Gastroenterol* 2008 June 7; 14(21): 3374-3387 – DOI: 10.3748/wjg.14.3374. ➔ *free full text article*

Bogdanos DP, Liaskos C, Pares A, Norman G, Rigopoulou EI, Caballeria L, Dalekos GN, Rodes J, Vergani D. Anti-gp210 antibody mirrors disease severity in primary biliary cirrhosis. *Hepatology* 45 (6):1583-1584, 2007. ➔ *free full text article*

Crosignani A, Battezzati PM, Invernizzi P, Selmi C, Prina E, Podda M. Clinical features and management of primary biliary cirrhosis. *World J Gastroenterol* 2008 June 7; 14(21): 3313-3327 – DOI:10.3748/wjg.14.3368. ➔ *free full text article*

Granito A, Muratori L, Muratori P, Pappas G, Guidi M, Cassani F, Volta U, Ferri A, Lenzi M, Bianchi FB. Antibodies to filamentous actin (F-actin) in type 1 autoimmune hepatitis. *J Clin.Pathol.* 59 (3):280-284, 2006. ➔ *free full text article*

Muratori P, Granito A, Pappas G, Pendino GM, Quarneti C, Cicola R, Menichella R, Ferri S, Cassani F, Bianchi FB, Lenzi M, and Muratori L. The serological profile of the autoimmune hepatitis/primary biliary cirrhosis overlap syndrome *Am J Gastroenterol.* 104 (6):1420-1425, 2009. ➔ *free full text article*

Rigopoulou EI, Mytilinaiou M, Romanidou O, Liaskos C, and Dalekos GN. Autoimmune hepatitis-specific antibodies against soluble liver antigen and liver cytosol type 1 in patients with chronic viral hepatitis. *J Autoimmune.Dis* 4:2, 2007. ➔ *free full text article*

Rust C, Beuers U. Overlap syndromes among autoimmune liver diseases. *World J Gastroenterol* 2008 June 7; 14(21): 3368-3373 – DOI:10.3748/wjg.14.3368. ➔ *free full text article*

You will find more references on the ORGENTEC website >> Literature Service

updated: 08/02/2012