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LABORATORY DIAGNOSIS OF AUTOIMMUNE HEPATITIS

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Autoimmune liver diseases include autoimmune hepatitis (AIH), primary biliary cirrhosis (PBC), and primary sclerosing cholangitis (PSC).

There is no specific diagnostic test for AIH. Diagnosis is based on careful exclusion of other causes of chronic liver disease, together with the finding of several suggestive features, such as the morphological changes. 70–80% of patients present with high titres of antinuclear (ANA), smooth-muscle (SMA), or type 1 liver-kidney microsomal antibodies (anti-LKM1), but diagnosis can be difficult in the 20–30% who do not have these markers. Many such patients have other autoantibodies, including those showing perinuclear staining on neutrophils (pANCA) and antibodies reacting with the hepatocyte-specific asialoglycoprotein receptor (ASGPR). Several other autoantibodies that seem to be more specific for autoimune hepatitis have been described, including antibodies against "soluble liver antigen" (SLA) and another recognises a cytosolic liver-pancreas antigen (LP).These two antibodies have been reported in only about 30% of patients, and some of these patients do not have ANA, SMA, or anti-LKM1. There is some evidence that anti-SLA and anti-LP are one and the same autoantibody. Investigators claim that anti-SLA/LP has 100% specificity (with 30% sensitivity) for autoimmune hepatitis.

Primary sclerosing cholangitis (PSC) is a chronic and progressive cholestatic liver disease, which is characterized by inflammation and fibrosis of mainly the large bile ducts leading to biliary cirrhosis in a high percentage of patients. In PSC multiple non-specific autoantibodies, which are rather an epiphenomena to chronic inflammation, can be found including antinuclear antibodies (ANA) in 7–77%, anticardiolipin antibodies in 4–66%, anti-smooth muscle antibodies in 13–20%, anti-thyroid peroxidase (TPO) antibodies in 16% and rheumatoid factor in 15%. Atypical perinuclear-staining, antineutrophil cytoplasmic antibodies (p-ANCA) can be found in 60–93% of patients with PSC, but also in patients with AIH.

Primary biliary cirrhosis (PBC) is a chronic liver disease characterised by cholestasis, antimitochondrial antibody (AMA) and lymphocyte-predominant portal inflammation with a variable degree of fibrosis. The targets of the AMA response are enzymatic members of

the family of the 2-oxo-acid dehydrogenase complexes. Approximately 90–95% of PBC sera react against the pyruvate dehydrogenase E2 complex. Although AMA is considered the humoral hallmark of PBC, antibodies against various mitochondrial enzymes can be frequently detected in patients with infectious liver. Depending on the assay used, up to 15% of PBC patients have been found to be AMA-negative. Sera from a subgroup of patients, including some AMA-negative patients, are positive for antibodies to nuclear components including Sp100, promyelocytic leukemia proteins, and two components of the nuclear pore complex. Antinuclear antibodies (ANA) are also detectable in approximately 50% of subjects with PBC. Most clinical laboratories use indirect immunofluorescence microscopy to detect ANA and two labeling patterns that predominate in PBC are punctate nuclear rim and multiple nuclear dots. Antibodies giving these patterns most often recognize nuclear pore membrane protein gp210 and nuclear body protein sp100, respectively. These ANA are highly specific for PBC and detected in approximately 25% of patients. Less frequently, ANA apparently unique to PBC recognize other proteins of the nuclear envelope and nuclear bodies. While antibodies against gp210, sp100 and some other nuclear proteins are very specific to PBC and may therefore be useful diagnostic markers. The clinical significance of ANA in PBC has been widely investigated and data indicate that, unlike AMA, they are not associated with disease severity and may be present many years before other clinical, biochemical, or histological manifestations do occur.

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DIAGNOSTYKA LABORATORYJNA ZAPALENIA WATROBY O PODŁOŻU AUTOIMMUNOLOGICZNYM

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