

Autoimmune Liver Disease

Tools to Aid in the Accurate Diagnosis of
Autoimmune Liver Disease



**Inova
Diagnostics**

A Werfen Company

Liver Disease

Experts in autoimmunity

Inova Diagnostics provides a comprehensive menu of products to aid in the diagnosis of autoimmune liver disease and discriminate between the distinct subtypes and overlap syndromes⁴ as shown in the testing algorithm to the right.

The **NOVA Lite® IFA** slide kits have been recognized for quality and consistency when it comes to immunofluorescence assay (IFA) testing. The new addition of barcoding and automated digital archiving systems increase efficiency and provide positive patient identification. The **QUANTA Lite® ELISA** tests are high quality reagents which are compatible with a variety of automation solutions offered through Inova Diagnostics. **QUANTA Flash®** assays offer precise quantification and a broad analytical measuring range using chemiluminescent technology with results in as little as 30 minutes.

As a global leader in the area of autoimmune liver disease, Inova offers a variety of unique assays to increase confidence in the diagnosis of autoimmune liver disease. Proprietary assays such as the **QUANTA Lite® PBC Screen** which combines M2EP (MIT3), gp210 and sp100 in a dual specificity conjugate (IgG and IgA) allow for greater sensitivity to aid in the diagnosis of PBC.⁵ The **QUANTA Lite® F-Actin ELISA** for AIH, unique to Inova, shows good correlation with IFA and can be automated. Inova provides both assays and instrumentation with unmatched quality, reliability, and service for all of your autoimmune testing needs.

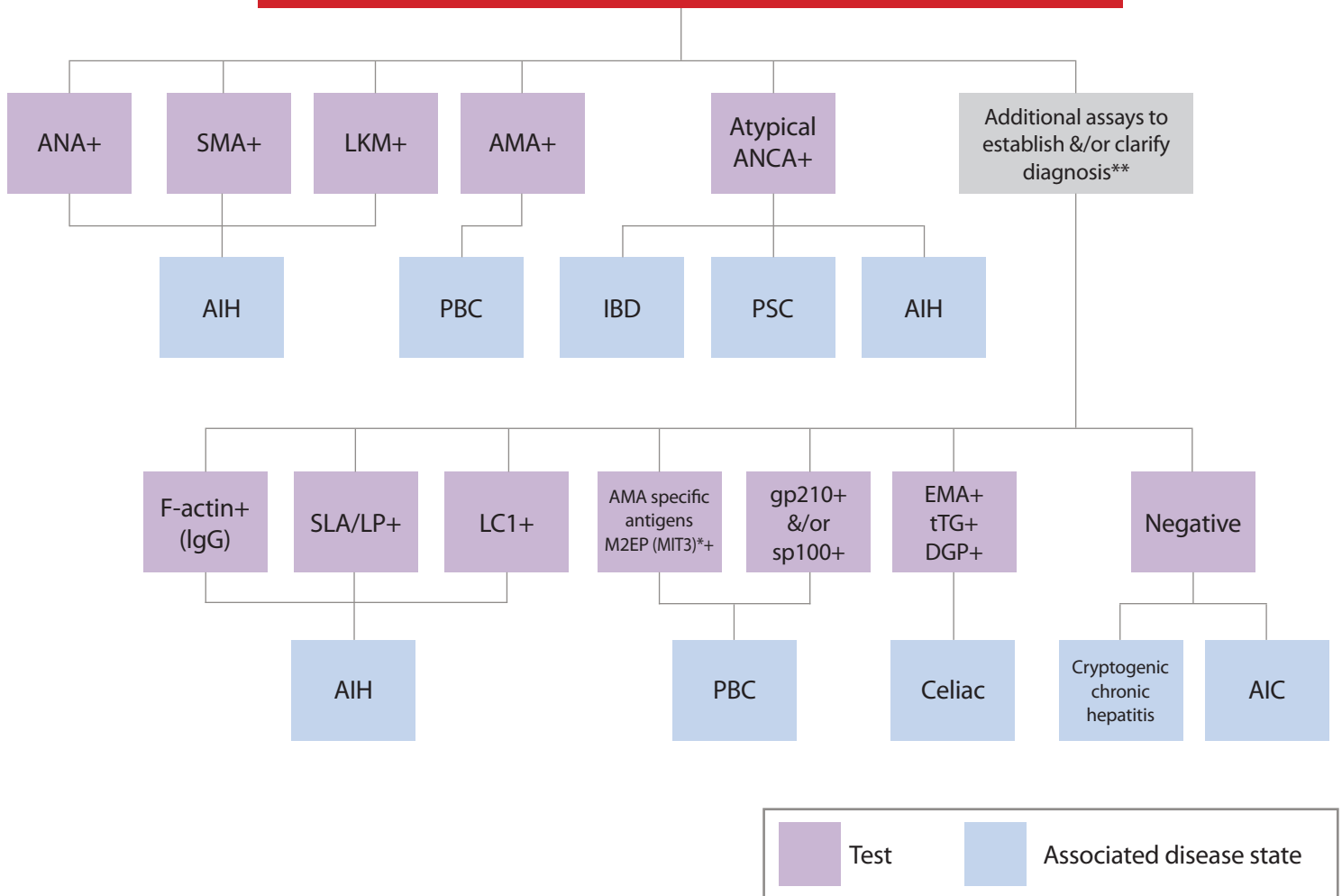
Summary of Autoantibody Prevalance in Analyzed Groups⁸

Diagnosis/number of patients	AMA M2 Conventional n (%)	AMA M2 (MIT3) IgG n (%)	AMA M2 (MIT3) IgA n (%)	gp210 n (%)	sp100 n (%)	SLA ⁵ n (%)	Centromere ⁶ n (%)	Chromatin ⁷ n (%)
AIH (AMA+) (n=10)	10 (100%)	10 (100%)	6 (60%)	1 (10%)	4 (40%)	2 (20%)	2 (20%)	3 (30%)
PBC (AMA+) (n=157)	143 (91%)	151 (96%)	117 (75%)	26 (17%)	35 (22%)	1 (1%)	16 (10%)	11 (7%)
PBC (AMA-) (n=57)	7 (12%)	14 (25%)	8 (14%)	6 (10%)	6 (11%)	0 (0%)	11 (19%)	8 (14%)
PSC (n=46)	0 (0%)	1 (2%)	1 (2%) low titer	0 (0%)	0 (0%)	1 (2%)	1 (2%)	8 (17%)
Unknown Cholangiopathy (n=11)	2 (18%)	3 (27%)	2 (18%)	0 (0%)	0 (0%)	0 (0%)	1 (9%)	3 (27%)

	≤10%
	11-30%
	31-50%
	>50%

DIAGNOSTIC ALGORITHM

Liver Disease of Unknown Cause



Abbreviations

AIC	autoimmune cholangitis	IBD	inflammatory bowel disease
AIH	autoimmune hepatitis	LKM	liver-kidney microsomal antibody
AMA	anti-mitochondrial antibodies	PBC	primary biliary cholangitis
ANA	anti-nuclear antibodies	PSC	primary sclerosing cholangitis
ANCA	anti-neutrophil cytoplasmic antibodies	SLA	soluble liver antigen
DGP	deamidated gliadin peptide	SMA	smooth muscle antibody
EMA	endomysial antibody	tTG	tissue transglutaminase

Testing strategies provided for informational purposes only.
Testing and diagnosis should be determined by a licensed clinician.

* M2 EP (MIT3) ELISA contains immunodominant epitope of PDC-E2, OGDC-E2 & BCOADC-E2

** Other assays with possible prognostic value: chromatin and dsDNA

Important assays you should know about

Get clear answers to solve your most difficult cases

Autoimmune Hepatitis (AIH) Tests

In a cohort of AIH-2 patients, **QUANTA Flash® LKM-1** demonstrated a sensitivity of 50.0% with a specificity of 93.0% including patients with HCV and a specificity of 100.0% when HCV patients were excluded.*¹⁰

The **NOVA Lite® IgG F-Actin*** kit utilizes a unique substrate comprised of a proprietary preparation of rat intestine epithelial cells for a distinct pattern and unmistakable results. The **QUANTA Lite® F-Actin ELISA** is a simple and more objective tool than IFA with a sensitivity of 74% vs 34% detecting smooth muscle antibodies. At a cutoff of 20 units, the ELISA detected all SMA positive AIH patients and >60 units suggests high probability for AIH.¹

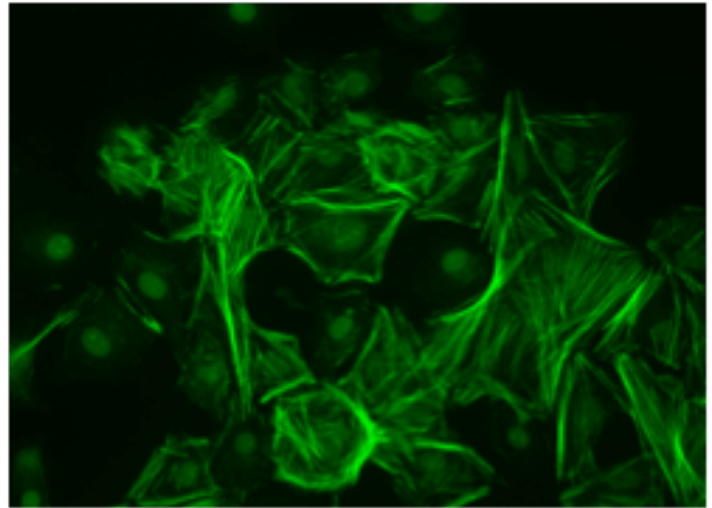
Approximately 15-25% of AIH patients have SLA antibodies and are negative for other antibodies.⁶ The accurate recognition of AIH is essential since treatment differs dramatically for AIH, PBC and viral hepatitis. Although often under-utilized, **SLA is recommended in the International Hepatitis revised scoring system.** The presence of SLA has almost 100% specificity for AIH.⁵

Primary Biliary Cholangitis (PBC) Tests

QUANTA Lite® M2EP (MIT3), the EP stands for enhanced performance resulting from a triple hybrid recombinant antigen that incorporates 3 immunodominant epitopes to PBC in one molecule. **M2EP (MIT3) provides higher sensitivity and specificity compared to conventional M2.** Over 1/4 of PBC patients negative for AMA by conventional M2 ELISA were positive with the QUANTA Lite M2EP (MIT3) ELISA.⁸

In the PBC patient population, **QUANTA Flash® M2 (MIT3)** CIA demonstrated excellent sensitivity and specificity with an odds ratio of 1530.7.¹¹

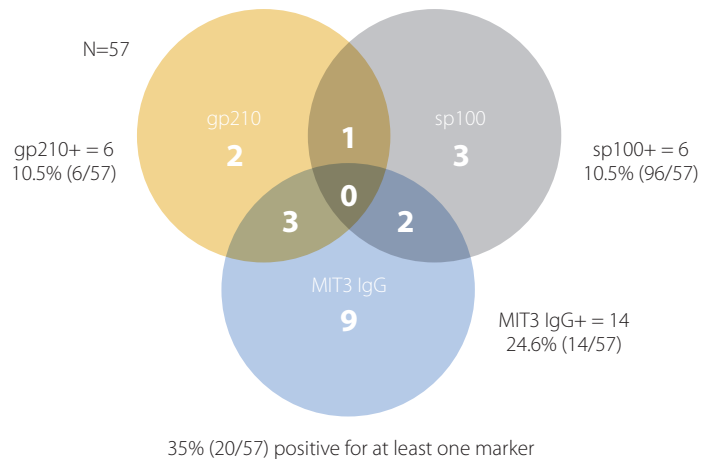
QUANTA Lite® PBC Screen includes M2EP (MIT3), gp210 and sp100, and is an appropriate first-line test to aid in the diagnosis of PBC including patients negative for markers assessed using conventional methods.⁹ Confirmation of a positive PBC screen result by the individual assays is recommended. The presence of gp210 and sp100 is highly specific for PBC.



Distinct patterns for clear results with NOVA Lite® IgG F-Actin slides

QUANTA Lite liver disease tests on AMA-negative PBC Specimens⁸

Overlap of specificities in 57 specimens from PBC patients negative for AMA by conventional M2 ELISA



* Available outside the USA only

Liver Disease

Serology assays can help guide accurate diagnosis

For individuals affected by autoimmune liver disease, the body's immune system attacks the cells of the liver causing inflammation and damage resulting in symptoms which may include jaundice, skin rashes, joint pain, discoloration of stool and urine, fatigue and itching of the skin. In the most advanced form, autoimmune liver disease can progress to cirrhosis. Therefore, early and accurate diagnosis is critical in order to initiate treatment and prevent disease progression.¹

The two main immune mediated liver diseases are autoimmune hepatitis (AIH) and primary biliary cholangitis (PBC). AIH results in chronic inflammation of the liver hepatocytes, while PBC is a disease that slowly destroys the bile ducts resulting in cholestasis. Both diseases are of unknown etiology and are more common in females than males. The prevalence of AIH and PBC are similar and estimated to be up to 1.2 cases per 100,000 individuals in the US and Europe, with fewer cases reported in Asia. Primary sclerosing cholangitis (PSC) and autoimmune cholangitis (AIC) are additional classifications of autoimmune liver disease with prevalence data estimated to be half of AIH and PBC. All together, **autoimmune liver disease accounts for 6% of liver transplantations in the US and 3% in Europe.**²

The accurate diagnosis of patients suffering from autoimmune liver disease is often difficult to determine. Therapy differs significantly based on disease classification. Patients with PBC are typically treated with ursodeoxycholic acid (UDCA) while patients with AIH are frequently treated with corticosteroids.³ To aid in the diagnosis, clinicians often utilize clinical, histologic and serologic findings.

Conventional autoantibodies used in the categorization of AIH are antinuclear antibodies (ANA), anti-smooth muscle antibodies (ASMA), and antibodies to liver/kidney microsomal type 1 (LKM-1). **The revised scoring system of the International Hepatitis Group includes often under-utilized markers such as anti-soluble liver antigen (SLA), anti-actin, anti-liver cytosol type1 (LC1) and perinuclear anti-neutrophil cytoplasmic antibodies (pANCA).**⁴ In contrast, the classic diagnostic markers for PBC are anti-mitochondrial antibodies (AMA). Other autoantibodies in PBC include gp210, sp100 and the mitochondrial subunit E2 (M2EP or MIT3).

The different classifications for autoimmune liver disease and associated autoantibodies are listed below:

Autoimmune Liver Disease Classifications	Description	Associated Autoantibodies
Primary Biliary Cholangitis (PBC)	<ul style="list-style-type: none">Irritation and inflammation of the liver bile ducts, which block the flow of bileThis obstruction damages liver cells and leads to scarring called cirrhosis	<ul style="list-style-type: none">AMAM2EP (MIT3)gp210sp100
Autoimmune Hepatitis (AIH)	<ul style="list-style-type: none">Chronic inflammation of the liver with no known cause nor cure70% of those with autoimmune hepatitis are femaleTimely diagnosis and treatment is important as mortality rates in severe AIH can be as high as 40% within 6 months if untreatedThere are two types of AIH:<ul style="list-style-type: none">Type 1 accounting for the majority of casesType 2 distinguished by the unique presence of anti-LKM1	<ul style="list-style-type: none">ANApANCAF-Actin (IgG)SLALC1LKM-1
Autoimmune Cholangitis (AIC)	<ul style="list-style-type: none">Clinical features of PBC, but AMA negative	<ul style="list-style-type: none">ANAASMA
Primary Sclerosing Cholangitis (PSC)	<ul style="list-style-type: none">Inflammation and fibrosis of intra & extra hepatic bile ducts	<ul style="list-style-type: none">pANCA
Overlap Syndromes	<ul style="list-style-type: none">Overlap Syndromes – Combination of features from AIH, PBC and/or PSC	

Liver Disease Tests

Product ordering information

Method	Name	Package	Part#
CIA	QUANTA Flash M2 (MIT3)	50 Test	701303
	QUANTA Flash LKM-1	50 Test	701298
ELISA	QUANTA Lite Actin IgG	1 X 96 wells	708785
	QUANTA Lite M2 EP (MIT3)	1 X 96 wells	704540
	QUANTA Lite gp210	1 X 96 wells	708995
	QUANTA Lite sp100	1 X 96 wells	708990
	QUANTA Lite PBC Screen IgG/IgA	1 X 96 wells	704560
	QUANTA Lite SLA	1 X 96 wells	708775
	QUANTA Lite LKM-1	1 X 96 wells	708745
IFA	NOVA Lite IgG F-Actin*	5 X 6 wells	708255
	NOVA Lite ANCA (Ethanol-Fixed)	10 x 6 wells	708299
		20 x 12 wells	708298
		DAPI conjugate	708301
	NOVA Lite ANCA (Formalin-Fixed)	10 x 6 wells	708295
		20 x 12 wells	708297
		DAPI conjugate	708300
	NOVA Lite ANA KSL Mouse Kidney, Stomach, Liver	10 x 4 wells	708390
		25 x 8	708380
	NOVA Lite Rat Liver, Kidney, Stomach	10 x 5 wells	704170
		25 x 10 wells	704180
	NOVA Lite HEp-2 IgG (Fc specific)	5 x 12 wells	708101
20 x 12 wells		708100	
DAPI conjugate		704320	

* Available outside the USA only

For more information contact your Inova representative, call customer service at +1-858-586-9900, or visit our website at www.inovadx.com

References

1. Czaja, A. J., D. K. Freese, et al. (2002). "Diagnosis and treatment of autoimmune hepatitis." *Hepatology* 36(2): 479-497.
2. Czaja A.J. Autoimmune hepatitis. In: Sleisenger and Fordtran's Gastrointestinal and Liver Disease. 6th ed. Philadelphia, Pa: WB Saunders Company; 1998:1265-1274.
3. European Association for the Study of the Liver. (2009). "EASL Clinical Practice Guidelines: management of cholestatic liver diseases." *J Hepatol* 51(2): 237-267.
4. Hennes, E. M., M. Zeniya, et al. (2008). "Simplified criteria for the diagnosis of autoimmune hepatitis." *Hepatology* 48(1): 169-176.
5. Czaja, A. J., Z. Shums, et al. (2004). "Nonstandard antibodies as prognostic markers in autoimmune hepatitis." *Autoimmunity* 37(3): 195-201.
6. Nakamura, M., H. Kondo, et al. (2007). "Anti-gp210 and anti-centromere antibodies are different risk factors for the progression of primary biliary cirrhosis." *Hepatology* 45(1): 118-127.
7. Czaja, A. J., Z. Shums, et al. (2003). "Frequency and significance of antibodies to chromatin in autoimmune hepatitis." *Dig Dis Sci* 48(8): 1658-1664.
8. P. Milkiewicz et al. Value of Autoantibody Analysis in the Differential Diagnosis of Chronic Cholestatic Liver Disease. *Clinical Gastroenterology and Hepatology* 2009;7:1355-1360.
9. Bizzaro, N., G. Covini, et al. (2012). "Overcoming a "probable" diagnosis in antimitochondrial antibody negative primary biliary cirrhosis: study of 100 sera and review of the literature." *Clin Rev Allergy Immunol* 42(3): 288-297.
10. Garcia, M. et al. LKM-1 Chemiluminescent immunoassay demonstrates reliable clinical performance in autoimmune hepatitis. 10th International Congress on Autoimmunity; 2016 Apr 6-10; Leipzig, Germany.
11. Garcia, M. et al. M2 (MIT3) Chemiluminescent immunoassay demonstrates reliable clinical performance in primary biliary cholangitis. 10th International Congress on Autoimmunity; 2016 Apr 6-10; Leipzig, Germany.

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