Marshfield Labs™
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Laboratory News

VOL. 36, NO. 11 - SEPTEMBER 25, 2013

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CHANGES IN CARDIAC TROPONIN I REPORTING

Gene Shaw, MD, Annu Khajuria, PhD

Effective ***October 1, 2013***, changes will be made in the reporting units and reference value for cardiac troponin I (cTnI). These changes are made to conform with recommendations from European Society of Cardiology (ESC)/American College of Cardiology Foundation (ACCF)/American Heart Association (AHA)/World Heart Federation (WHF) consensus documents crafted by international experts in cardiology, emergency medicine, and laboratory medicine.

These changes reflect ongoing improvements in the analytic precision and detection limit of cardiac troponin assays that allow detection of clinically significant myocardial injury at lower levels.

An increased cTnI concentration is defined as a value exceeding the upper reference limit (URL) of the 99th percentile of a normal reference population and is designated as the decision limit for the diagnosis of acute myocardial infarction (AMI).

Detection of a rise and/or fall of cardiac troponin with at least one value above the 99th percentile upper reference limit in an appropriate clinical setting is essential to establish the diagnosis of AMI and distinguish it from the elevations of cTnI levels that are associated with chronic heart diseases. Besides ischemic injury, other causes of these low-level elevations of cTnI include myocarditis, congestive heart failure, arrhythmias, surgical cardiac procedures, pulmonary embolism, and renal failure.

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CURRENT REFERENCE VALUE

Current reference value for cTnI is 100 ηg/L (0.1 ηg/mL).

PROPOSED CHANGES

cTnI will now be reported in ηg/L as whole numbers. The new reference value will be 45 ηg/L which is approximately the URL of the 99th percentile of a normal reference population across all the current methods in the Marshfield Clinic system.

At this level, the cTnI assay at Marshfield Labs can achieve a coefficient of variation (CV) of less than 10%. The limit of detection is 15 ηg/L.

RESULT REPORTING

cTnI results will be reported in the following format:

- Values ≤15 ηg/L will be reported as <16 ηg/L.
- **Values >45 ηg/L are consistent with myocardial injury.**

Results will have the following comments: "The 99th percentile URL for troponin I in a normal reference population is approximately 45 ηg/L. Serial measurements may be necessary to confirm or exclude the diagnosis of acute coronary syndrome. Repeat testing in 3 to 6 hours if clinically indicated."

For appropriate utilization and interpretation of cTnI results in the acute setting, obtaining a baseline value and serial testing is strongly recommended.

These changes have been approved by the Marshfield Clinic Cardiology and Emergency Medicine departments. Acute myocardial infarction remains a clinical diagnosis that requires integration of clinical presentation (including interventional procedures) along with clinical information (e.g., EKG and imaging) and laboratory data.

For any questions please call Annu Khajuria, PhD at 1-6311 or 715-221-6311.

REFERENCES

Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD; Joint ESC/ACCF/AHA/WHF Task Force for Universal Definition of Myocardial Infarction. Third Universal Definition of Myocardial Infarction. J Am Coll Cardiol. 2012; 60(16): 1581-98.

Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD; Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction. Third Universal Definition of Myocardial Infarction. Circulation. 2012; 126(16): 2020-35.

Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD; Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial. Third Iniversal Definition of Myocardial Infarction. Eur Heart J. 2012; 33(20): 2551-67.

Jaffe AS. Third Universal Definition of Myocardial Infarction. Clin Biochem 2013, 46: 1-4.

Harvey DW, Thygesen K, Alpert JS & Jaffe AS. Clinical Implications of the Third Universal Definition of Myocardial Infarction. Heart 2013; 00: 1-9.

FOUR NEW SEROLOGY TESTS FOR AUTOIMMUNE LIVER DISEASES

Joyce L. Flanagan, PhD, DABCC, FACB; Jeffrey M. Resnick, MD

Starting on ***October 8, 2013***, Liver Kidney Microsomal-1 (LKM-1), Soluble Liver Antigen (SLA), Smooth Muscle Antibody (SMA/Actin), and Mitochondrial Antibody (AMA) by ELISA method will be performed at Marshfield Labs in Marshfield to aid in the diagnosis of autoimmune hepatitis (AIH) and primary biliary cirrhosis (PBC).

BACKGROUND

Autoimmune hepatitis is a chronic, immune-mediated hepatitis, the pathogenesis of which has yet to be fully elucidated. The diagnosis of AIH requires the presence of characteristic clinical and laboratory features. These antibody tests are helpful in the diagnosis of autoimmune liver disease (Table 1).

Table 1. Autoantibodies in the Diagnosis of Autoimmune Hepatitis[1]

Autoantibody	Value in AIH
ANA* (Antinuclear antibody)	Diagnosis of type 1 AIH, AMA-negative PBC, (PSC)**
SMA* (**Actin**) (Smooth muscle antibody)	Diagnosis of type 1 AIH, AMA-negative PBC, (PSC)**
LKM-1* (Liver-kidney microsomal-1)	Diagnosis of type 2 AIH
SLA/LP* (Soluble liver antigen/Liver pancreas)	Diagnosis of type 3 AIH
LC-1* (Liver cytosol type 1)	Diagnosis of type 2 AIH
pANCA (atypical) (Perinuclear anti neutrophil cytoplasmic antibody)	Diagnosis of type 1 AIH, (PSC)**
LKM-3	Diagnosis of type 2 AIH
ASGPR (Asialoglycoprotein receptor)	May be helpful in the diagnosis of AIH and monitoring disease activity.
LM (Liver microsomal antibody)	Diagnosis of APECED hepatitis
AMA (Antimitochondrial antibody)	PBC differential diagnosis

*Autoantibodies are used conventionally in the diagnosis of AIH. The other autoantibodies may be useful in patients who lack the conventional autoantibody markers.

** PSC, primary sclerosing cholangitis, parenthesis indicate may be helpful.

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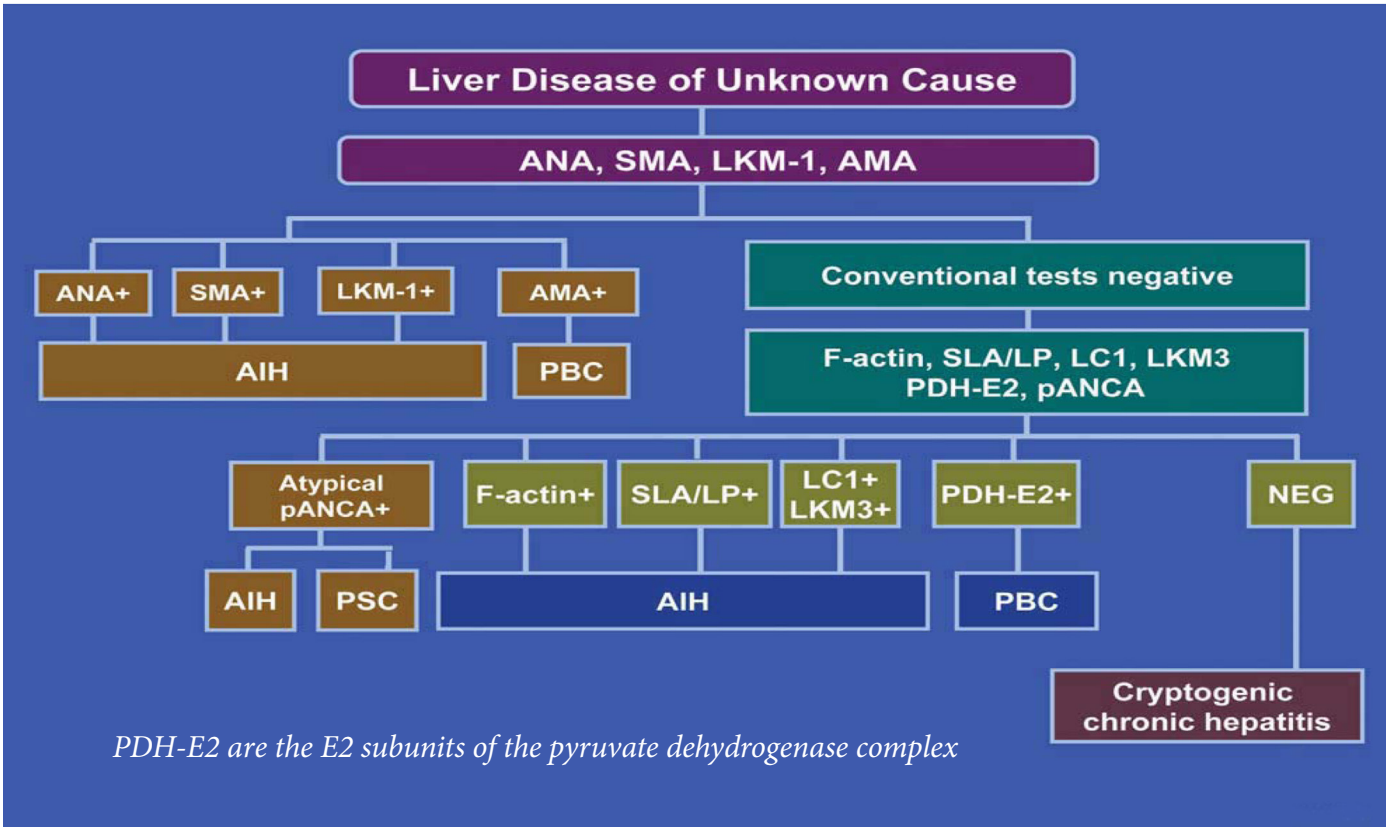
The algorithm for using serological tests to assist in the diagnosis of AIH[1]



There are three main types of AIH based on serological markers. Type 1 AIH is characterized by the presence of ANA, SMA, or both, and constitutes 80% of AIH cases[2]. Seventy percent of patients are female. Associations with other autoimmune diseases are common (15-34%). Type 2 AIH is characterized by the presence of anti-LKM-1[3] and/or anti-LC-1 and/or anti-LKM-3. Most patients with type 2 AIH are children. Anti-SLA/LP is highly specific for the diagnosis of type 3 autoimmune hepatitis[4] and has emerged as a possible prognostic marker of disease severity and risk of relapse after corticosteroid withdrawal.

A scoring system was published by the International Autoimmune Hepatitis Group (IAIHG) to aid in the diagnosis of AIH in 1993[5] and was revised in 1999[6]. A simplified scoring criteria[7] that claimed to have 88% sensitivity and 97% specificity (cutoff ≥6) and 81% sensitivity and 99% specificity (cutoff ≥7) is listed below (Table 2).

It should be emphasized that the diagnosis of autoimmune liver disease requires correlation of the laboratory test results with clinical, liver biopsy, and imaging assessment.

Table 2. Simplified Diagnostic Scoring Criteria for Autoimmune Hepatitis

Variable	Cutoff	Points
ANA or SMA(Actin)	≥ 1:40	1
ANA or SMA(Actin) or LKM or SLA	≥ 1:80 ≥ 1:40 Positive	2*

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IgG	> upper normal limit > 1.10 times upper normal limit	1 2
Liver histology (evidence of hepatitis is a necessary condition)	Compatible with AIH Typical AIH	1 2
Absence of viral hepatitis	Yes	2
	Total score	≥6 probable AIH ≥7 definite AIH

* Addition of points achieved for all autoantibodies (maximum, 2 points)

HOW TO ORDER THESE TESTS

Lab Test Code	Description	Clinic (Com)	Hospital (Centricity)
LKM1	Liver-Kidney Microsomal-1 Ab*	Liver-Kidney Microsomal-1 Ab	Liver-Kidney Microsomal-1 Ab
SLA	Soluble Liver Antigen Ab*, IgG	Soluble Liver Antigen Ab, IgG	Soluble Liver Antigen Ab, IgG
ACTIN	Smooth Muscle Ab*, Actin IgG	Smooth Muscle Ab, Actin IgG	Smooth Muscle Ab, Actin IgG
MITO	Mitochondrial Ab* (M2), IgG	Mitochondrial Ab (M2), IgG	Mitochondrial Ab (M2), IgG

*Ab = antibody

SPECIMEN REQUIREMENTS

Serum: 1.0 mL Red Top, SST acceptable
Minimum: 0.75 mL
Storage: refrigerate (2-8°C), frozen acceptable
Rejection criteria: grossly hemolyzed or lipemic samples

AVAILABLE

Tests are set up Tuesday and Thursday. Immunofluorescence assay (IFA) will be performed automatically on Wednesday and Friday for ELISA positive ACTIN (SMA) and LKM-1.

INTERPRETATION

Positive or Negative for ELISA result.
Titer for IFA.

CPT CODES

LKM1 = 86376
SLA = 83516
ACTIN (SMA) = 83516
MITO = 83516

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CONTACTS

Interpretive questions: Jeffrey M. Resnick, MD at ext. 1-6112 or 715-221-6112; Joyce Flanagan, PhD at ext. 1-6310 or 715-221-6310.
Technical questions: Greg Simon at ext. 1-6343 or 715-221-6343; Joyce Flanagan, PhD at ext. 1-6310 or 715-221-6310.

REFERENCES

1. Manns MP, Czaja AJ, Gorman JD, Krawit EL, Mieli-Vergani G, Vergani D, Vierling JM. AASLS practice guidelines: Diagnosis and management of autoimmune hepatitis. Hepatology 2010;51:1-31.
2. Czaja AJ, Manns MP. The validity and importance of subtypes in autoimmune hepatitis: a point of view. AM J Gastroenterol 1995;90:1206-1211.
3. Homberg JC, Abuaf N, Bernard O, Islam S, Alvarez F, Khalil SH, et al. Chronic active hepatitis associated with antiliver/kidney microsome type 1:a second type of "autoimmune" hepatitis. Hepatology 1987;7:1333-1339.
4. Baeres M, Herkel J, Czaja AJ, Wise I, Kindler S, Cacadu EL, et al. Establishment of standardized SLA/LP immunoassays: specificity for autoimmune hepatitis, worldwide occurrence, and clinical characteristics. Gut 2002; 51:259-264.
5. Johnson PJ, McFarlane IG. Meeting report: International autoimmune hepatitis group. Hematology 1993; 18:998-1005.
6. Alvarez F, Berg PA, Bianchi Fete al. International Autoimmune Hepatitis Group Report: Review of criteria for diagnosis of autoimmune hepatitis. J Hepatic. 1999; 31:929-938.
7. Hennas EM, Zeneca M, Cana AJ, Pares A, et al. Simplified criteria for the diagnosis of autoimmune hepatitis. Hematology 2008; 48:169-176.

INSULIN LIKE GROWTH FACTOR-1 (IGF-1) METHOD CHANGES.

Annu Khajuria, PhD, FCACB, FACB

Effective ***October 1, 2013,*** IGF-1 method changes on Immulite 2000 will be implemented due to the introduction of a new antibody pool for the method by Siemens USA.

Laboratory method re-evaluation studies have been performed and the changes observed are consistent with the manufacturer's data. Patient comparison studies with new antibody pool show a shift of 5 ηg/mL (0.5%) from the current assay. The reference intervals have therefore been revised.

EXPECTED CHANGES

Patient values will be lower than the current method by an average of 5 ηg/mL.

For any queries and additional information, call 1-800-222-5835 and ask for Annu Khajuria, PhD and/or Bryan Robeson.