Legacy LabAdvisor



Quarterly laboratory and pathology update from Legacy Laboratory Services in collaboration with Cascade Pathology

Edition 4

Inside this issue

Testing for celiac disease2

New testing developments.....3

Defining and determining celiac disease through serological testing

By Mitchell Ryan, M.D. — Cascade Pathology Services

Celiac disease is an immune-mediated enteropathy caused by permanent gluten sensitivity in genetically susceptible individuals. Its presentation is highly variable and diagnosis ultimately requires histologic confirmation

by small bowel biopsy. Serology aids in determining whether biopsy is indicated. Serologic screening tests for celiac disease include antitissue transglutaminase, anti-endomysial and antigliadin antibody tests, all of which are performed at Legacy Laboratory Services.

The best serologic screening tests for celiac disease are IgA anti-tissue transglutaminase (tTG) and IgA anti-endomysial (EMA) antibody tests.¹ These tests are preferred over anti-gliadin antibody tests, which are no longer routinely recommended, but still play a role in testing children under the age of two.² Serologic screening with IgA anti-tTG is recommended for patients with gastrointestinal symptoms, including chronic diarrhea, malabsorption, weight loss and abdominal distention, or who have other signs and symptoms of celiac disease.

• A systematic analysis (Rostom et al.) examining published studies for the diagnostic accuracy of celiac tests found specificities for current generation IgA tTG assays are uniformly high, with pooled specificities of 98 and 99 percent for adults and children, respectively. Sensitivities vary more, but pooled sensitivities are still high at 98 percent for adults and 96 percent for children. In contrast, both specificities and sensitivities for anti-gliadin antibodies are about 80 percent or less in adults and between 80 to 90 percent in children. Recently developed gliadin antibody tests using deamidated gliadin peptides yield increased sensitivity and specificity values compared to standard gliadin antibody tests. Anti-gliadin antibody tests performed at Legacy Laboratory Services use synthetic, deamidated gliadin-derived peptides.

IgG-class anti-tTG and EMA tests, like the IgA-class tests, are quite specific, but in general are poorly sensitive with sensitivities being around 40 percent. IgG-class tTG and EMA celiac tests therefore have limited utility, and serve primarily for celiac screening in IgA deficient individuals. Approximately 5 to 10 percent of celiac patients are IgA deficient, and of course, will yield negative results for IgA-class antibody tests.

Please refer to the table for celiac tests available at Legacy Laboratory Services, as well as for ordering information and pertinent comments.



Clinical laboratory tests for celiac disease

Test	Method	Comments						
Best tests for serologic celiac disease screening								
Tissue Transglutaminase IgA	ELISA	Primary serologic screen for celiac disease						
Tissue Transglutaminase IgA, Reflex	ELISA and IFA	Screens for IgA anti-tTG by ELISA; if positive, reflexes to IgA anti-EMA titer, performed by IFA. Titer may be useful for tracking therapeutic response. Anti-tTG titer is not available						
Supplemental and alterna	tive laboratory tests for celiac	disease screening						
IgA, Serum	Nephelome-try	Identifies IgA deficiency, a possibility for nega- tive IgA anti-tTG results in otherwise clinically suspicious cases						
Tissue Transglutaminase, IgG	ELISA	Specific but insensitive relative to IgA anti-tTG. Generally useful for celiac screening in IgA defi- cient patients only						
Gliadin Peptide Antibodies, IgA and IgG	ELISA	In general, gliadin tests have lower sensitivi- ties and specificities than tTG and EMA tests. Remains an alternative for celiac testing in children under the age of two						
Panel								
Celiac Care Set	ELISA, IFA, Nephelome-try	Includes tTG IgA, EMA IgA (screen not titer), gliadin IgA, gliadin IgG, total IgA						

- 1. Tissue transglutaminase (tTG) is the major target antigen recognized by anti-endomysial antibodies, endomysium being the connective tissue stroma ensheathing muscle fibers. Current (second) generation anti-tTG tests use recombinant or purified human tTG in ELISA formats to detect anti-tTG. Anti-EMA tests are immunofluoresence assays using non-rodent esophageal tissue sections to visualize antibodies against endomysium. (NIH).
- 2. Because children under two years old may not make anti-EMA or anti-tTG antibodies, anti-gliadin antibody testing remains useful for this particular age group. (Farrell).

References:

- 1.) NIH consensus development conference on celiac disease, National Institutes of Health Consensus Development Conference Statement, June 28-30, 2004. Available at: http:// consensus.nih.gov/2004/2004/CeliacDisease188html.htm, accessed on 2/20/2006
- 2.) Farrell RJ and Kelly CP. Celiac Sprue. 2002. NEJM 346:180-8
- 3.) Hill, ID et al. Guideline for the Diagnosis and Treatment of Celiac Disease in Children: Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. 2005. J Pediatr Gastroenterol Nutrition 40:1-19
- 4.) American Gastroenterological Association medical position statement: celiac sprue. 2001. Gastroenterology. 120:1522-5
- 5.) Korponay-Szabo IR, et al. Deamidated gliadin peptides form epitopes the transglutaminase antibodies recognize. 2008 J Pediatr Gastroenterol Nutrition 46:253-61

6.) Rostom, A et al. Sensitivity and specificity of tests for CD. Evidence Report/Technology assessment, No. 104, Celiac Disease., pages 123-128 Available at: http://www.guideline.gov/ summary.aspx?ss=15&doc_id=5692&nbr=3830, accessed on 12/072006

7.) Van Meensel B, Hiele M, Hoffman I. Diagnostic accuracy of ten second-generation (human) tissue transglutaminase antibody assays in celiac disease. 2004. Clinical Chemistry 50

New testing developments at Legacy Laboratory

Direct acting antiviral drugs and hepatitis C viral load monitoring

The FDA recently approved VictrelisTM (boceprevir) and Incivek TM (teleprevir), both direct-acting antiviral (DAA) drugs, for treatment of the chronic hepatitis C genotype 1 infection. The method used by Legacy Laboratory Services for our Hepatitis C RNA, Quantitative by PCR test Roche COBAS AmpliPrep/COBAS TaqMan HCV assay will meet the needs of these patients and can be used as an aid in management of therapies.

New two-hour glucose tolerance test is available for diagnosing diabetes in pregnant women

Legacy Laboratory Services now offers a two-hour oral glucose tolerance test for pregnant women - the Glucose OB Tolerance 2-Hour — that complies with the new American Diabetes Association (ADA) guidelines. Per the guidelines, all pregnant women not known to have diabetes should undergo GDM testing at 24-28 weeks of gestation. The recommended test is the Glucose OB Tolerance 2-Hour. This should be performed in the morning after an overnight fast of at least eight hours. The diagnosis of GDM is made when any one of the following glucose values are met or exceeded. Fasting 92 g/dL, 1-Hour 180 g/dL, 2-Hour 153 g/dL. However, the guidelines also recommend that pregnant women with any of the following high-risk factors should be screened earlier, at the first prenatal visit, for undiagnosed type 2 diabetes:

- Severe obesity
- Prior history of gestational diabetes mellitus (GDM) or delivery of large-for-gestational-age infant
- Presence of glycosuria
- Diagnosis of polycystic ovarian syndrome
- Strong family history of type 2 diabetes

The recommended test is the Glucose Non-OB Challenge Test 2-Hour. Women found to be diabetic at this stage should receive the diagnosis of overt, not gestational, diabetes.

For additional information, please contact Danelle Beaudoin, Ph.D., scientific director for chemistry at Legacy Laboratory Services: 503-413-5024.

Introducing Fetal Lung Maturity by Lamellar Body Counts

Legacy Laboratory Services introduced Lamellar Body Counts (LBCs) in December of 2011. LBCs in amniotic fluid aid in the determination of fetal lung maturity. Lamellar bodies are concentrically layered packages of phospholipids that are produced by Type II alveolar cells, representing the storage form of surfactant. As gestational age increases, LBCs increase. Lamellar bodies are approximately the same size and density as platelets. Due to their similar size, lamellar bodies can be counted on most hematology cell counters providing a quick, accurate evaluation of fetal lung maturity.

LBCs perform at least as well as lecithin/sphingomyelin ratio (L/S ratio) and surfactant/albumin ratio (otherwise known as FLM). We will continue to offer L/S ratios on a limited basis (see www.legacyhealth.org/labservices for more information). However, surfactant/albumin ratio is being discontinued by the sole manufacturer and is no longer available.

For technical information, please contact Danelle Beaudoin, Ph.D., scientific director for chemistry at Legacy Laboratory Services: 503-413-5024.

Questions and Answers

During the introduction of Lamellar Body Counts (LBCs) testing, Dr. Beaudoin talked with many obstetric clinicians. The following Q&A is related to those conversations:

1.) Why was the FLM discontinued?

Answer: The sole manufacturer discontinued the reagent. The best alternative option was LBCs. LLS continues to evaluate additional options including the Amniostat, a rapid semi-quantitative test for phosphotidylglycerol.

2.) What is the preferred specimen when ordering Lamellar Body Counts?

Answer: Amniotic fluid is the only specimen type currently accepted.

3.) What test should be ordered for vaginal pools? Answer: The lecithin/sphingomyelin (L/S) ratio should be ordered for this specimen type.

4.) How should the specimen for LBCs be submitted?

Answer: Lamellar bodies are fragile. The specimen cannot be frozen. If received within 24 hours, the specimen may be transported at ambient (20–25 C) temperature. For longer stability, specimen may be refrigerated up to eight days. Do not allow specimen container to come into direct contact with cold packs. Wrap with packing material if shipped cold.



LabAdvisor

Go paperless

Are you receiving *Legacy LabAdvisor* on paper, but would like to go paperless? Or would you like to start an electronic subscription? Simply fill out the short form at www.legacyhealth.org/labadvisor to receive the next issue of *LabAdvisor* in your inbox.



EMANUEL Medical Center	GOOD SAMARITAN Medical Center	MERIDIAN PARK Medical Center		MOUNT HOOD Medical Center		SALMON CREEK Medical Center	
RANDALL CHILDREN'S HOSPITAL Legacy Emanuel		LEGACY MEDICAL GR	OUP	LEGACY LABORATORY	LEGACY RESEARCH	LEGACY HOSPICE	