A Reevaluation
Algorithmic Testing for Celiac Disease

By
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In 2004 the Laboratory introduced a testing algorithm for celiac disease (CD). Since that time new tests have become available. Over the past year the Laboratory has reviewed our testing for CD. This has been done with the help of the GI Section and with the approval of the Endocrinology Section, who are the biggest single users of this testing. During that review, we realized there were ways the Lab could be more user friendly in providing testing for this disease. Previous Pathology and Laboratory Medicine Newsletters (October 2004 and August 2007) have discussed the laboratory diagnosis of CD and the algorithm which is currently being used at CMH. This Newsletter will review celiac disease and present the “new and improved” algorithm.

Celiac disease is an enteropathy caused by sensitivity to gluten, the protein of wheat, rye and barley. CD is associated with chronic inflammation of the intestinal mucosa and flattening of the epithelium. CD is frequently associated with GI symptoms such as diarrhea, failure to thrive, pain, vomiting, and/or constipation but can be asymptomatic. There is an increased incidence in children with type 1 diabetes, autoimmune thyroiditis, Down syndrome, Turner syndrome, Williams’s syndrome and selective IgA deficiency. CD is genetically associated with HLA DQ8 and DQ2 and relatives of patients are at increased risk. The North American Society for Pediatric Gastroenterology, Hepatology and Nutrition states “The development of celiac disease is clearly multigenic, with the presence of DQ2 or DQ8 being an essential component. Thus the probes for DQ2 and DQ8 have high sensitivity but poor specificity.” This is because 25-40% of the population has these genes. The prevalence of CD in children is 3-13 per 1000.

Serological tests for CD provide a reliable screen but do not replace biopsy. There are three major target antigens: human tissue transglutaminase (TTG), endomysium and gliadin. TTG is the primary antigen recognized by endomysial antibodies (EMA). The endomysium is the connective tissue stroma of muscle fibers. Gliadin is a glycoprotein of gluten.

According to the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition: “Measure TTG (tissue transglutaminase) for initial blood testing. AGA (Anti-Gliadin Antibody) IgA and AGA IgG tests are no longer recommended as initial testing due to the inferior accuracy of antigliadin antibody tests.” (www.celiachealth.org, www.naspghan.org). This recommendation is compounded with the finding that 2-3% of individuals with CD have selective IgA deficiency. The ontogeny of IgA is highly variable. Levels can remain below detectable limits until ~ 9 months of age and may not reach adult levels until ~ 10 years of age. An IgA level of 7mg/dl is the lower limits of detectability in our Laboratory. IgG anti- TTG is less specific than IgA anti-TTG and use to be the best choice in children with low or undetectable IgA. False positive tests for TTG antibodies have been reported in patients with autoimmune liver disease and other inflammatory bowel diseases. Testing IgA anti-tTG and EMA are indicated in these patients. The Children’s Mercy Hospital has been testing for IgA anti tTG since 2004.
Our current testing when the Celiac Algorithm is ordered is:

**IgA Level Is Done**
- **Ig A < 7**
  - IgG anti tTG
- **IgA 7-10**
  - IgG anti tTG
  - Ig A anti tTG
- **IgA > 10**
  - Ig A anti tTG

**New Test and Algorithm**

Since our initial introduction of this algorithm, a new test – IgG anti deaminated gliadin has become available. This test is better for those patients who do not have IgA then IgG anti tTG. In addition, we discovered that clinicians were ordering the EMA assay on patients who proved to be deficient in IgA. The EMA assay is IgA based and a negative result in an IgA deficient patient could be misleading. Finally, we discovered that IgA levels were being done on patients already known to have IgA levels. We also discovered that there were very, very few children who had IgA levels between 7 and 10.

With this information we have developed a new algorithm shown below. This algorithm will be introduced when the computer system changes that are needed have been made. The Lab will check the patient’s history for a previous IgA level. If IgA has been detected in the past we do not need to retest for IgA. In addition, the Lab will retain the specimen and order the appropriate testing based on IgA level and the result of the IgA anti tTG test if done.
There will always be patients for whom the Celiac Algorithm is not appropriate. The clinician can order the individual tests as needed. Below you will find information on the sensitivity, specificity and accuracy of these individual tests.

<table>
<thead>
<tr>
<th>Test</th>
<th>Sen</th>
<th>Spec</th>
<th>Accuracy</th>
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</thead>
<tbody>
<tr>
<td>IgA-tTG</td>
<td>78</td>
<td>95</td>
<td>86</td>
</tr>
<tr>
<td>IgG-tTG</td>
<td>28</td>
<td>97</td>
<td>68</td>
</tr>
<tr>
<td>IgA DG</td>
<td>74</td>
<td>95</td>
<td>86</td>
</tr>
<tr>
<td>IgG DG</td>
<td>65</td>
<td>98</td>
<td>84</td>
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<tr>
<td>IgA EMA</td>
<td>75-98</td>
<td>88-100</td>
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DG: Deaminated gliadin

This new algorithm will be introduced when the computer system changes have been made to permit it – hopefully soon. The exact date of the change will be announced in the E – News.

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**CME Series**

**Sponsored by Department of Pathology & Laboratory Medicine**

**Date:**  October 20, 2008  
**Time:**  Noon – 13:00  
**Location:**  Lab Conference Room 2206.10 WT  
**Speaker:**  Doug Blowey, MD  
**Topic:**  “Childhood Hypertension”