Celiac Testing in Adolescents and Adults with Down Syndrome

Brian Chicoine, MD
Medical Director

The starting place for making the diagnosis of celiac disease is the history and physical exam. The symptoms of celiac disease can vary widely (see resource on the description of celiac disease). The physical exam may show evidence of weight loss, abdominal tenderness, or others but often there are limited findings.

The next step is blood testing. What is the best blood test? What does the American Gastroenterological Association (AGA) recommend?

There are several types of antibodies (proteins that mediate the immune system and are elevated when there is an infection or in autoimmune diseases). Immunoglobulins type A (IgA) tend to have greater concentration in the gastrointestinal tract and Immunoglobulins type G (IgG) are more diffusely distributed. There are many subtypes of IgA and IgG depending on the infection or auto-immune condition.

Tissue transglutaminase is an enzyme found normally in the body. In celiac disease, an antibody (anti-Tissue Transglutaminase antibody) that attacks that enzyme is one of the antibodies that is elevated. The American Gastroenterological Association recommends using anti-Tissue Transglutaminase antibody IgA (IgA tTGA) as the blood test of choice. In the primary care setting, the IgA tTGA is the most efficient single serologic test for the detection of celiac disease.

What if the individual is not able to make sufficient IgA?

There are some people that don’t make adequate amounts of IgA. That would include IgA tTGA but also includes any IgA. However, the prevalence of IgA deficiency in celiac disease is sufficiently low such that the routine measurement of serum IgA levels along with IgA tTGA is not warranted as a first step toward diagnosis unless IgA deficiency is strongly suspected. In people with Down syndrome, we have also not found IgA deficiency to be common enough to warrant checking total IgA in all individuals we are drawing IgA tTGA.

What should I do if the IgA tTGA is not elevated but celiac disease is still suspected?

Anti-tissue transglutaminase IgG (IgG tTGA) may also be measured. In cases of selective IgA deficiency, the IgG tTGA has excellent sensitivity and specificity, although those IgG-based tests are markedly less sensitive and specific than the IgA-based tests in those with normal levels of IgA.

Measurement of the serum IgA level is also an appropriate next step in individuals with a negative IgA tTGA in whom celiac disease is still suspected. A low total serum IgA in a person with a normal IgA tTGA would suggest that the person cannot make adequate amounts of IgA and, therefore, the IgA tTGA is not an accurate test in this individual and other tests should be measured.
What are some other blood tests?

_Gliadin IgA and IgG_
These are older tests that were measured in the past. However, evidence indicates that the additional inclusion of IgG antigliadin antibody and IgA antigliadin antibody is not warranted.

_Total globulin_
Total globulin is a measure of certain proteins in the blood. Included in the total globulin are antibodies including IgG and IgA. In our patients with Down syndrome we often find an elevated total globulin on a chemistry panel. We don’t use this as a screening test for celiac disease. However, if we find it, we will order a IgA tTGA. We have found a significant number of our patients with an elevated total globulin have an elevated IgA tTGA and many of them have celiac disease.

_Stool for IgA tTGA_
Some have also recommended stool testing for IgA tTGA. However, we have not used this test nor is it recommended by the AGA.

_Genetic testing_
Almost all patients with celiac disease have either the gene DQ2 (approximately 95% of patients with celiac disease) or DQ8 (approximately 5% of patients with celiac disease). Some have advocated doing genetic testing. This reveals whether the individual has the genetic predisposition to develop celiac disease. However, if positive, it doesn’t indicate whether the person has actually developed celiac disease or just has the predisposition. Assessing the history, physical exam, blood work, and endoscopy with biopsy are still required to assess for the actual presence of the disease.

However, if the genetic testing is negative for those two genes, our present understanding of the genetics of celiac disease indicates the individual should not be able to develop celiac disease. We have found that the genetic testing is generally not covered by insurance and can be costly. Therefore, we have not tested this frequently.

What if the blood test is abnormal?

Positive serologic test results are supportive of the diagnosis of celiac disease. However, the next recommended step is proceeding with a biopsy of the small intestine. This is done through endoscopy. Distal duodenal biopsy specimens demonstrating characteristic histologic changes in the small intestinal mucosa remain the gold standard for establishing the diagnosis of celiac disease. The findings include a spectrum of change from total to partial villous atrophy (sloughing off of the microscopic fingers in the small intestine that help us absorb calories, vitamins, and minerals), and other changes.

Reaching a definitive diagnosis can be difficult in those with minimal histologic findings, in those with a negative serologic test result, or if the disease is patchy or an insufficient number or poorly oriented biopsy specimens were taken. There are other disease entities that can resemble celiac disease histologically.
(microscopically). Most of these entities are either rare in the developed world, are suggested by the clinical history, or have distinguishing histologic findings on careful review of the biopsy samples.

We do have families that express concern about putting their family member with Down syndrome through an endoscopy for a small bowel biopsy. Many of our patients require general anesthesia (rather than milder sedation) to complete the test. That does add a higher risk. When there is an abnormal blood test, some families have decided to proceed with the diet without the biopsy based on the symptoms, the higher incidence of celiac disease in people with Down syndrome, and the possibility that the biopsy could miss an abnormal area due to the small intestine of some individuals having patchy disease.

Proceeding with treatment without a biopsy is not the usual standard and some people with a positive blood test don’t have celiac disease. Therefore, some may be treated who don’t actually have celiac. However, when that choice is selected by our patients and their families, we monitor them as we would any patient that had a biopsy to confirm the diagnosis. This includes monitoring symptoms and considering drawing the blood test that was initially abnormal (e.g. IgA tTGA) periodically to monitor for improvement. It is generally recommended to wait 6-12 months between blood tests (it may take that long for changes). However, we may test it sooner in a patient who didn’t have a biopsy to see if it is going higher and may give us a better value to compare the 6 or 12 month value.

**Should everyone get the blood testing?**

There are unanswered questions as far as doing blood testing as a screening test in all individuals with Down syndrome. The Down Syndrome Medical Interest Group (DSMIG) recommends testing all children with Down syndrome between the ages of two and three with a test such as Tissue Transglutaminase Antibody IgA and Total IgA. However, a person with DS may develop celiac disease at any age so the question remains if it is beneficial to test all people with DS periodically or whether it is better to monitor for symptoms and then do blood testing.

We have not adopted a universal policy of testing all patients but have a very low index of suspicion for testing. For example, patients who are thin, losing weight, have mood or other psychological changes, develop other autoimmune conditions, are fatigued, develop a skin rash consistent with dermatitis herpetiformis, or have an elevated total globulin level are all patients we would consider for blood testing.

**Summary – Assessment**

1. History and physical exam.
2. If symptoms or findings or considering screening in person with DS, do IgA tTGA.
3. (a) If positive, consider biopsy of small intestine (may consider repeating blood test to confirm abnormality).
   (b) If negative, suspect celiac, consider getting total IgA and/or IgG tTGA.
4. If positive blood testing, uncertain biopsy, and ongoing concern regarding celiac, consider genetic testing.
GUIDELINE TITLE
AGA Institute Medical Position Statement on the Diagnosis and Management of Celiac Disease

BIBLIOGRAPHIC SOURCE