Intestinal biopsy is the gold standard for diagnosing celiac disease, but serologic tests provide an effective first step in identifying biopsy candidates. In addition, genetic tests that confirm the presence or absence of specific genes associated with celiac disease may be useful in some circumstances. However, serologic and genetic tests are adjuncts to, not replacements for, biopsies. If serologic or genetic tests indicate the possibility of celiac disease, a biopsy should be done promptly and before initiating any change in the patient’s diet.

**SEROLOGIC TESTS**

Serologic tests look for three antibodies common in celiac disease:

- anti-tissue transglutaminase (tTG) antibodies
- endomysial antibodies (EMA)
- antigliadin antibodies (AGA)

The most sensitive antibody tests are of the immunoglobulin A (IgA) class, but immunoglobulin G (IgG) tests may be used in patients with IgA deficiency. Because no one serologic test is ideal, panels are often used. However, the tests included in a celiac panel vary by lab and may include one or more that are unwarranted. The American Gastroenterological Association recommends beginning with tTG in the clinical setting.1 For accurate diagnostic test results, patients must be on a gluten-containing diet.

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**tTG ANTIBODY**

The tTG test is an enzyme-linked immunosorbent assay (ELISA) test. The tTG test has a sensitivity of more than 90 percent, yielding few false positive results. The test also has a specificity of more than 95 percent, meaning it yields few false negative results.1 Point-of-care tTG tests have been developed but are not yet approved for use by clinicians in the United States.

**EMA**

The test for EMA is slightly less sensitive than tTG but is highly specific for celiac disease, approaching 100 percent accuracy.2 EMA is measured by indirect immunofluorescent assay, a more expensive and time-consuming process than ELISA testing. In addition, the EMA test is subject to operator interpretation, making the results more subjective than those for tTG.

Some studies show the titers, or relative concentrations, of tTG and EMA are correlated with the degree of intestinal damage, making these tests less sensitive among patients with milder celiac disease.3

**AGA**

Tests for AGA are not sensitive or specific enough for routine use. However, they may be useful for screening children less than 18 months old in whom tTG and EMA tests may yield false negative results.2

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A new generation of tests that use deaminated gliadin peptides (DGP) have sensitivity and specificity that are substantially better than the older gliadin tests. DGP tests are more accurate than tTG and AGA and may be the most reliable tests to detect celiac disease in people with IgA deficiency.

IGA DEFICIENCY

Between 2 and 3 percent of celiac patients have selective IgA deficiency—a rate about 10 times higher than in the general population. If IgA tTG or IgA EMA are negative but celiac disease is still suspected, total IgA should be measured to identify selective IgA deficiency. In cases of IgA deficiency, IgG tTG or DGP-IgG should be measured.

GENETIC SCREENING TESTS

Nearly all people with celiac disease have gene pairs that encode for at least one of the human leukocyte antigen (HLA) gene variants, or alleles, designated HLA-DQ2 or HLA-DQ8. However, these alleles are common. They are found in about 40 percent of the general U.S. population, and most people with these alleles do not have celiac disease. Negative findings for HLA-DQ2 and HLA-DQ8 can essentially rule out current or future celiac disease in patients for whom other tests, including biopsy, do not provide a clear diagnostic result.

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