

## ACG Releases Guideline on Diagnosis and Management of Celiac Disease

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There has been a substantial increase in the prevalence of celiac disease over the past 50 years, and in the rate of diagnosis over the past decade. Despite this, it remains underdiagnosed in the United States. The American College of Gastroenterology (ACG) has released clinical guidelines with recommendations for diagnosing and managing celiac disease.

### Screening

Celiac disease is one of the most common causes of chronic malabsorption. Patients with symptoms, signs, or laboratory evidence of malabsorption (e.g., chronic diarrhea with weight loss, steatorrhea, postprandial abdominal pain and bloating) should be tested for celiac disease. Because the prevalence of celiac disease in clinical scenarios varies from modest (e.g., in patients with irritable bowel syndrome) to substantial (e.g., in those with unexplained iron deficiency anemia), patients in whom celiac disease is a treatable cause should also be considered for testing.

The incidence of celiac disease is significantly increased among persons with a first-degree family member who has the disease. Persons with an immediate family member who has a confirmed diagnosis should be tested if they have signs, symptoms, or laboratory evidence of the disease. Test-

ing should be considered for asymptomatic immediate family members of persons with a confirmed diagnosis. Families in which more than one person has been diagnosed with celiac disease are considered high risk, and screening recommendations should extend to all other family members, including second-degree relatives.

Celiac disease should be considered as a potential explanation for elevated serum transaminase levels when no other etiology can be found. Hypertransaminasemia is a potential subclinical finding that is gluten dependent in patients with celiac disease.

There is evidence that celiac disease is significantly more common in persons with type 1 diabetes mellitus than in the general white population, and that it is associated with greater risk of retinopathy and nephropathy. However, testing for celiac disease in asymptomatic patients is controversial. Patients with type 1 diabetes should be tested for celiac disease only if they have digestive symptoms, signs, or laboratory evidence of the disease.

### Diagnostic Testing

All diagnostic serologic testing for celiac disease should be performed before a gluten-free diet is initiated. Antibodies directed against native gliadin are no longer recommended for primary detection. Immunoglobulin A (IgA) anti-tissue transglutaminase (TTG) antibody is the preferred test in persons older than two years. In younger children, TTG IgA testing should be combined with IgG- and IgA-deamidated gliadin peptides to improve sensitivity.

Combining several tests instead of TTG IgA testing alone may marginally increase sensitivity, but it reduces specificity and is not recommended in low-risk populations. Total IgA should be measured in persons with a

high probability of celiac disease and in whom the possibility of IgA deficiency is considered. Alternatively, IgA and IgG testing can be performed simultaneously. IgG-based testing should be performed in patients with low IgA levels or selective IgA deficiency.

If suspicion for celiac disease remains high even after negative results have been obtained on serologic testing, bowel biopsy should be pursued.

### Confirmatory Testing

Confirmation of a diagnosis of celiac disease should be based on a combination of findings from the medical history, physical examination, serology, and upper endoscopy with histologic analysis of multiple duodenal biopsies. Gastrointestinal symptoms alone cannot accurately differentiate celiac disease from other gastrointestinal disorders. Improvement of symptoms after initiation of a gluten-free diet or clinical exacerbation of symptoms after reintroduction of gluten has a very low positive predictive value for celiac disease, and should not be used in the diagnosis in the absence of other supportive evidence.

A diagnosis of celiac disease requires the demonstration of histologic changes associated with the disease. Upper endoscopy with small bowel biopsy is a critical component of the evaluation. Multiple duodenal biopsies (one or two of the bulb and at least four of the distal duodenum) are recommended to confirm the diagnosis.

Lymphocytic infiltration of the intestinal epithelium in the absence of villous atrophy is not specific for celiac disease. Most patients with lymphocytic duodenitis are not in the spectrum of celiac disease, and other causes (e.g., *Helicobacter pylori* infection, small bowel bacterial overgrowth, systemic autoimmune disorders) should be considered after a workup to rule out celiac disease.

### Ancillary Testing

The most significant genetic risk factor for celiac disease is the presence of *HLA-DQ* heterodimers DQ2 and DQ8; *HLA-DQ2* and *HLA-DQ8* are present in almost all patients with the disease (with a negative predictive value of more than 99% when both test results are negative). However,

because *HLA-DQ2* is present in 25% to 30% of the white population, testing for either heterodimer should not be performed routinely. Testing for *HLA-DQ2* and *HLA-DQ8* may be useful to rule out celiac disease in select patients, such as those with Down syndrome; those with equivocal small-bowel histologic findings; those following a gluten-free diet in whom testing for celiac disease was not performed before the diet initiation; those with discrepant celiac-specific serology and histology; and those for whom the original diagnosis of celiac disease is in question.

Capsule endoscopy allows for noninvasive visualization of the whole small-bowel mucosa. However, it should not be used for initial diagnosis of celiac disease except in patients with positive celiac-specific serology who are unable or unwilling to undergo upper endoscopy with biopsy. It may be considered for the evaluation of small-bowel mucosa in patients with complicated celiac disease.

Tests that are not recommended for the diagnosis of celiac disease include stool studies, small-bowel follow-through, intestinal permeability testing, D-xylose testing, and salivary testing.

### Differentiating Celiac Disease from Non-Celiac Gluten Sensitivity

Non-celiac gluten sensitivity is a condition in which the diagnostic features of celiac disease are not present, but patients nonetheless develop celiac-like symptoms when exposed to dietary gluten. Celiac disease should be differentiated from non-celiac gluten sensitivity to identify patients at risk of nutritional deficiency and complications of celiac disease, to determine the risk of celiac disease and associated disorders in family members, and to influence the degree and duration of adherence to a gluten-free diet. Symptoms alone or symptom response to a gluten-free diet cannot reliably differentiate the conditions, and there is often substantial overlap in symptoms. The diagnosis of non-celiac gluten sensitivity should be considered only after celiac disease has been ruled out by appropriate testing (e.g., celiac serology, small bowel histology in patients who are not following a gluten-free diet, *HLA-DQ* typing to rule out celiac disease).

### Diagnosis in Patients Following a Gluten-Free Diet

The specific serologic and histologic features of celiac disease do not normalize immediately after initiating a gluten-free diet. If a patient has been following the diet for less than one month, serologic and histologic findings are often still abnormal and can be used for diagnosis. Conversely, some findings will revert to normal soon after initiating the diet. Therefore, normal histologic and serologic findings cannot be used to exclude celiac disease in patients who are following a gluten-free diet.

Gluten challenge testing is the preferred diagnostic test in *HLA-DQ2*- and *HLA-DQ8*-positive patients who have normal serologic and histologic findings when following a gluten-free diet. Some patients will opt to continue a strict gluten-free diet without undergoing a formal gluten challenge test; these patients should be treated similarly to those with confirmed celiac disease.

### Management

A gluten-free diet is the only effective treatment for celiac disease. For the duration of their lives, persons with the disease should strictly avoid all products containing wheat, barley, and rye proteins. Although pure oats

seem to be safe for most persons with celiac disease, they should be introduced slowly, and patients should be monitored for adverse reactions.

Patients with celiac disease should be referred to a dietitian for a nutritional assessment and counseling about a gluten-free diet. Those with a new diagnosis should also undergo testing for micronutrient deficiencies (e.g., iron, folic acid, vitamin D, vitamin B<sub>12</sub>).

Patients with celiac disease should be monitored regularly for new or residual symptoms, adherence to the diet, and assessment for complications. In children, special attention is recommended to assure normal growth and development. Consultation with a dietitian is recommended if gluten contamination is suspected.

A combination of history and serology should be used to monitor adherence to a gluten-free diet. Monitoring should also include verification that clinical abnormalities detected on initial laboratory investigations have normalized. If symptoms relapse or if there is no clinical response, upper endoscopy with bowel biopsies is recommended.

CARRIE ARMSTRONG, *AFP* Senior Associate Editor ■