



GASTROENTEROLOGY

# Celiac disease testing services



Labcorp features a full-service offering to support physicians in the evaluation for and management of patients with Celiac Disease (CD). Labcorp's leading services include:

- Antibody profile testing
- HLA-DQA/DQB genotyping to detect DQ2 and DQ8, with genetic risk assessment, including an option to reflex to antibody testing if HLA results are positive
- Testing for gluten in stool
- CD pathology (small bowel biopsy)
- Expert genetic consultation
- Broad network of managed care health plans
- Nationwide network of patient service centers
- Standardized methods across all Labcorp regional laboratories that assure comparability of test results performed in any location

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CD is estimated to affect one out of every 100 people, yet fewer than 17% of affected patients have been diagnosed. CD is an autoimmune disorder that involves an immune response to gluten in genetically susceptible individuals.<sup>1</sup> Early diagnosis and lifelong treatment with a gluten-free diet are critical to relieve symptoms and reduce risk of complications such as secondary autoimmune disorders, identifying patients who have celiac disease can be challenging, due to variable, nonspecific symptoms and varying age of onset. Celiac antibody testing can be used to support a diagnosis of CD. A positive small bowel biopsy provides a definitive diagnosis. Celiac HLA testing can be used to rule out CD.



# Celiac disease antibody testing

CD antibody tests can be used to screen patients with suspected disease or to monitor adherence and response to a gluten-free diet.<sup>1</sup> Celiac-specific antibodies include tissue transglutaminase (tTG) IgA, deamidated gliadin peptide (DGP) IgA and IgG, and endomysial antibody (EMA) IgA.<sup>1,5,6</sup>

Individuals with active celiac disease will have elevated levels of one or more of these specific CD antibodies. tTG IgA is the recommended single test for detection of CD in individuals >2 years.<sup>4</sup>

IgA class antibodies are commonly used for CD testing; however, IgG antibodies may be used as an alternative for patients who are IgA deficient.<sup>1,4</sup>

Testing total IgA is recommended along with tTG IgA when there is a high probability of CD.<sup>4</sup> Combining several tests

for CD rather than using tTG IgA alone may increase the sensitivity for CD but reduces specificity and therefore is not recommended in low-risk populations.<sup>4</sup> According to the 2019 AGA Clinical Practice Update on Diagnosis and Monitoring of Celiac Disease, tTG IgA antibody levels greater than 10 times the upper limit of normal (or greater than 100 units/mL for the Labcorp test) is an accurate and reliable test for diagnosing active CD.<sup>7</sup>

When screening children younger than 2 years of age for CD, it is recommended to combine the IgA tTG test with DGP (IgA and IgG). For children under 2 years, tTG and EMA are less sensitive than later in life.<sup>4</sup>

It is important for patients to be on a gluten-containing diet when tested for celiac antibodies.<sup>4</sup> Antibody testing may fail to detect CD due to a gluten-free diet or to IgA deficiency.<sup>1</sup>



## Symptoms

CD may present with a wide variety of gastrointestinal and/or non-gastrointestinal symptoms.

**Gastrointestinal:** e.g. diarrhea, abdominal pain, bloating, or constipation.

- More than 20% of patients with CD fulfill criteria for irritable bowel syndrome<sup>4</sup>
- Diarrhea is a presenting symptom in fewer than 50% of patients<sup>1</sup>

**Non-gastrointestinal:** e.g. dermatitis herpetiformis, chronic fatigue, joint pain, osteoporosis, failure to thrive, delayed puberty, unexplained infertility, dental enamel defects, neurologic symptoms, migraines, attention deficit, or secondary autoimmune diseases such as diabetes and thyroiditis.<sup>1,6</sup>

- Iron deficiency anemia is the main symptom in 8% of patients<sup>1</sup>

Silent CD can be present, with positive celiac antibodies and small bowel inflammation without symptoms<sup>1</sup>

# Recommendations for celiac testing<sup>4</sup>

- Test patients with symptoms or laboratory evidence suggestive of malabsorption. Consider testing in those with other symptoms or laboratory evidence suggestive of CD
- Test patients with a first-degree family member with CD and with possible symptoms or laboratory evidence of CD
- Consider testing asymptomatic relatives with a first-degree family member with CD
- Test patients with elevated serum aminotransferase levels when no other etiology is found
- Test patients with Type I diabetes mellitus and any digestive symptoms or laboratory evidence of CD

## Benefits of celiac disease antibody testing



Cost effective and noninvasive method to evaluate patients suspected of CD<sup>4</sup>



Helps identify individuals for whom endoscopic biopsy confirmation would be useful<sup>1</sup>



A positive antibody result is highly suggestive of CD<sup>1,2</sup>

tTG IgA antibodies levels greater than 10 times the upper limit of normal (or greater than 100 units/mL for Labcorp test) is an accurate and reliable test for diagnosing active CD, according to the 2019 AGA Clinical Practice guideline, and may alleviate the need for a biopsy.<sup>7</sup>

- Can detect silent celiac in relatives of patients with CD<sup>1</sup>

# Celiac disease genetic testing

HLA-DQA/DQB genetic testing is an important tool in evaluating patients for CD. HLA-DQ2 is found in more than 90% of celiac cases, HLA-DQ8 in ~ 5%, and half DQ2 in almost all remaining cases.<sup>1</sup> A negative HLA-DQA/DQB test result essentially excludes CD as a diagnosis.<sup>1,4</sup> Although a positive HLA result is not diagnostic, it identifies predisposition for CD.<sup>1,2</sup> The HLA DQ Association test provides a genetic risk assessment for CD.<sup>1,2</sup>

## Estimated celiac risk from associated HLA genotypes<sup>2,3</sup>

HLA DQ2/DQ8 Genotype	Risk
DQ2+DQ8	1:7 (14.3%)
DQ2+DQ2 or DQ2 Homozygous DQB1*02	1:10 (10%)
DQ8+DQ8	1:12 (8.4%)
DQ8+DQB1*02	1:24 (4.2%)
Homozygous DQB1*02	1:26 (3.8%)
DQ2 alone	1:35 (2.9%)
DQ8 alone	1:89 (1.1%)
General population risk (genotype unknown)	1:100 (1%) <sup>1,3</sup>
½ DQ2: DQB1*02	1:210 (0.5%)
½ DQ2: DQA1*05	1:1842 (0.05%)
No HLA-DQA/DQB susceptibility alleles	1:2518 (<0.04%)

**NOTE:** Actual risk for celiac disease may be greater than shown above when there are symptoms of celiac disease, positive results from celiac antibody tests, positive intestinal biopsy, or if there is a family history of celiac disease.



## Benefits of celiac disease genetic testing

- Can effectively rule out CD<sup>4,5</sup>
- Accurate when patient is on a gluten-free diet<sup>1</sup>
- Useful when diagnosis of CD is unclear
  - Ambiguous antibody or small bowel biopsy results<sup>1,3,4</sup>
  - Discrepancy between antibody and biopsy findings<sup>4,5</sup>
- Can help assess CD risk in first-degree relatives of affected patients<sup>1,4</sup>
- Recommended to rule out CD in individuals with Down's Syndrome<sup>4</sup>
- Only needs to be performed once in a lifetime because the HLA genetic test results do not change with time

## Celiac HLA DQ association with reflex to antibody testing

Labcorp's celiac reflex test option assesses genetic risk and excludes celiac diagnosis or screens for antibodies in a single test order.<sup>8</sup>

## Gluten in stool testing

Strict compliance with a gluten-free diet is challenging. Many patients on a gluten-free diet have persistent symptoms and damage to the gastrointestinal tract, along with detectable levels of gluten in their stool samples. It is useful for patients with CD or with non-celiac gluten-sensitivity.<sup>8,9</sup>

This test may be used for the following applications:<sup>9</sup>

- Monitoring CD and NCGS patients for adherence to a GFD
- Monitoring accidental gluten consumption due to mislabeling or food/product contamination
- Assisting in the diagnosis of a true "refractory" CD that is not related to accidental gluten consumption

## Celiac consultation

Labcorp's celiac expertise extends beyond tests to include consultative services. Labcorp's scientific staff—including Dr. Annette Taylor, a geneticist and recognized leader in the celiac field—can provide client consultations and are readily accessible to answer questions about test selection and results.

# Celiac disease test profiles

Test Name	Test No.
<b>For individuals with symptoms suggestive of celiac disease and who are on a gluten-containing diet.</b>	
Tissue Transglutaminase (tTG), IgA (Recommendation to combine with Total IgA when there is a high probability of CD. See test 164047 below.)	<b>164640</b>
Celiac Antibodies tTG IgA and Total IgA with Reflex to tTG IgG and DGP IgG	<b>164047</b>
Celiac HLA DQ Association with Reflex to Celiac Antibodies tTG IgA, tTG IgG, DGP IgA, DGP IgG and Total IgA <i>Genotyping for detection of HLA-DQ2 (DQA1*05:01 or 05:05 and DQB1*02:01 or 02:02) and HLA-DQ8 (DQB1*03:02), genetic risk assessment. A negative Celiac HLA DQ Association result essentially rules out CD. A positive result reflexes to celiac antibody testing.</i>	<b>164019</b>
<b>Suggested profile for children &lt;2 years old</b>	
Celiac Antibodies Profile tTG IgA, tTG IgG, DGP IgA, DGP IgG, and Total IgA	<b>164010</b>
<b>Alternative profiles including EMA IgA</b>	
Celiac Antibodies Profile tTG IgA, tTG IgG, DGP IgA, DGP IgG, EMA IgA, and Total IgA	<b>165126</b>
Celiac Antibodies tTG IgA, EMA IgA, Total IgA With Reflex to tTG IgG	<b>165142</b>
<b>For individuals on a gluten-free diet at risk for CD, asymptomatic relatives of patient with CD, or patients with ambiguous antibody or biopsy results</b>	
Celiac HLA DQ Association <i>Genotyping for detection of HLA-DQ2 (DQA1*05:01 or 05:05 and DQB1*02:01 or 02:02) and HLA-DQ8 (DQB1*03:02); complete DQA and DQB genotypes; homozygosity for DQB1*02; genetic risk assessment.</i>	<b>167082</b>
<b>For individuals on a gluten-free diet to monitor adherence to the diet, to detect unintentional gluten consumption, or to help in the assessment of patients suspected to have refractory celiac disease by ruling out gluten exposure as a cause of prolonged symptoms.</b>	
Gluten, Fecal, Quantitative	<b>123027</b>

Individual celiac-associated antibody tests—see test menu at [Labcorp.com](http://Labcorp.com).

Celiac Disease Pathology (small bowel biopsy)—Dianon Pathology is Labcorp's specialty testing laboratory for anatomic pathology.

## References

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