CELIAC DISEASE
TESTING SERVICES

LabCorp

CELIAC DISEASE

LabCorp features a full-service offering to support physicians in the evaluation of patients for celiac disease. LabCorp's leading services include

- Antibody profile testing
- HLA-DQA/DQB genotyping with relative risk assessment, including an option to reflex to antibody testing if HLA results are positive
- Celiac disease pathology (small bowel biopsy)
- Expert genetic consultation
- Broad network of managed care health plans
- Nationwide network of patient service centers

Celiac Disease Antibody Testing

Celiac disease antibody tests can be used to screen patients with suspected disease or to monitor adherence and response to a gluten-free diet.[1] Celiac disease antibody screening tests most commonly used include tissue transglutaminase (tTG) IgA, endomysial (EMA) IgA, and deamidated gliadin peptide (DGP) IgA and IgG.[5,6]

Individuals with active celiac disease will have elevated levels of one or more specific CD antibodies. tTG IgA is the preferred single test for detection of celiac disease in individuals >2 years.[4]

No single antibody offers 100% sensitivity and specificity. Sensitivities and specificities are 98% for tTG IgA, 95% and 99% for EMA and 97% and 95% for combined DGP.[7] IgA class antibodies are commonly used for celiac disease testing; however, IgG antibodies may be used as an alternative for patients who are IgA deficient.[1,4] Combining several tests for celiac disease rather than using tTG IgA alone may somewhat increase the sensitivity for CD but reduces specificity and therefore is not recommended in low-risk populations.[4]

When screening children younger than 2 years of age for celiac disease, it is preferrable 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.[4] Antibody testing may fail to detect celiac disease due to a gluten-free diet or to IgA deficiency.[1]

Symptoms

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

Gastrointestinal: eg. diarrhea, abdominal pain, bloating, or constipation

- Over 20% of patients with celiac disease fulfill criteria for irritable bowel syndrome[4]
- Diarrhea is a presenting symptom in fewer than 50% of patients[1]

Non-gastrointestinal: eg. 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.[1,6]

- Iron deficiency anemia is the main symptom in 8% of patients[1]

Silent celiac disease can be present, with positive celiac antibodies and small bowel inflammation without symptoms[1]

Recommendations for Celiac Testing[4]

- Test patients with symptoms or laboratory evidence suggestive of malabsorption. Consider testing in those with other symptoms or laboratory evidence suggestive of celiac disease
- Test patients with a first-degree family member with celiac disease and with possible symptoms or laboratory evidence of celiac disease
- Consider testing asymptomatic relatives with a first-degree family member with celiac disease
- 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 suggestive of celiac disease

Celiac disease (CD) is estimated to affect 1 out of every 100 people, yet fewer than 17% of affected patients are diagnosed as having the disease.[1-3] 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.[1,4-6] Identifying those patients who have true celiac gluten sensitivity can be challenging, due to variable, nonspecific symptoms and varying age of onset.[1,6] Antibody and HLA genetic testing can be used to support a diagnosis of CD. A positive small bowel biopsy provides a definitive diagnosis[1]

Benefits of Celiac Disease Antibody Testing

- Cost effective and noninvasive method to evaluate patients suspected of celiac disease[4]
- Helps identify individuals for whom endoscopic biopsy confirmation would be useful[1]
- A positive antibody result is highly suggestive of celiac disease[1,2]
- Can detect silent celiac in relatives of patients with celiac disease[1]

Celiac Disease Genetic Testing

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

Estimated Celiac Risk from Associated HLA Genotypes[2,3]

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%)[1,3]
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

- Accurate when patient is on a gluten-free diet[1]
- Can effectively rule out celiac disease[4,5]
- Useful when diagnosis of celiac disease is unclear
  - Ambiguous antibody or small bowel biopsy results[1,3,4]
  - Discrepancy between antibody and biopsy findings[4,5]
- Can help assess celiac disease risk in first-degree relatives of affected patients[1,4]
- Only needs to be performed once in a lifetime because the HLA genetic test results do not change over 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. This test option differentiates celiac disease from non-celiac sensitivity.

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.

For more information about our HLA testing or for a celiac genetic consultation, **call 800-533-1037.**

Celiac Disease Test Profiles	Test No
Suspicion of celiac disease in patients consuming gluten and evaluation of asymptomatic relatives	
Celiac HLA DQ Association with Reflex to Celiac Antibodies tTG IgA, tTG IgG, DGP IgA, DGP IgG and Total IgA 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. A negative Celiac HLA DQ Association result essentially rules out celiac disease. A positive result reflexes to celiac antibody testing.	164019
Celiac HLA DQ Association With Reflex to Celiac Antibodies tTG IgA/IgG With DGP IgA/IgG Pos/Neg Combination Screen 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. A negative Celiac HLA DQ Association result essentially rules out celiac disease. A positive result reflexes to celiac antibody testing. This test option does not discriminate between the antibody types tested. A positive result indicates positivity for any individual or combination of the antibodies tTG IgA, tTG IgG, DGP IgA, DGP IgG.	164031
For individuals on a gluten free diet, asymptomatic relatives or patients with ambiguous antibody or biopsy results	
Celiac HLA DQ Association 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.	167082
For individuals with symptoms suggestive of celiac disease and who are on a gluten-containing diet	
Celiac Antibodies tTG IgA and Total IgA with Reflex to tTG IgG and DGP IgG	164047
Celiac Antibodies tTG IgA, DGP IgA, Total IgA with Reflex to tTG IgG and DGP IgG	164002
Celiac Antibodies Profile tTG IgA, tTG IgG, DGP IgA, DGP IgG, and Total IgA Suggested profile for children <2 years old.	164010
Alternative profiles including EMA IgA	
Celiac Antibodies Profile tTG IgA, tTG IgG, DGP IgA, DGP IgG, EMA IgA, and Total IgA	165126
Celiac Antibodies tTG IgA, EMA IgA, Total IgA With Reflex to tTG IgG	165142
Also available	
Gluten Sensitivity Antibodies Cascade IgA and IgG antibodies to deamidated gliadin peptide and tissue transglutaminase (tTG/DGP screen), IgG antibodies to gliadin (AGA), wheat allergen-specific IgE (wheat IgE). Profile starts with tTG/DGP screen test. If positive, testing stops. If negative, testing reflexes to the AGA test. If positive, testing stops. If negative, it reflexes to the wheat IgE test.	164125
Bowel Disorders Evaluation Rule-out Cascade Celiac disease screen (simultaneous detection of tTG and DGP IgG and IgA); atypical perinuclear antineutrophil cytoplasmic antibody (pANCA); anti-Saccharomyces cerevisiae antibodies (ASCA) IgG; antigliadin antibodies IgG. Aid in diagnosis of celiac disease, IBD, differential diagnosis of Crohn's disease (CD) and ulcerative colitis (UC), nonceliac gluten sensitivity, and IBS.	164085
Individual celiac-associated antibody tests - see test menu at www.labcorp.com.	

Celiac Disease Pathology (small bowel biopsy) - Dianon Pathology is LabCorp's specialty testing laboratory for anatomic pathology. **Please contact your local account representative for information on establishing services.**

References

1. Taylor AK, Lebwohl B, Snyder C, and Green PHR. Celiac disease. In: Pagon RA et al. editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. 2008 Jul 3 [updated 2015 Sep 17]. Available at: http://www.ncbi.nlm.nih.gov/books/NBK1727/.
2. Megiorni F, Mora B, Bonamico M, et al. HLA-DQ and risk gradient for celiac disease. *Hum Immunol* 2009;70: 55-59.
3. Pietzak MM, Schofield TC, McGinnis MF, and Nakamura RM. Stratifying risk for celiac disease in a large at-risk United States population by using HLA alleles. *Clin Gastroenterol Hepatol* 2009;7: 966-971.
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6. Guandalini S, Assiri A. Celiac disease: a review. *JAMA Pediatr* 2014;168:272-278.
7. Leffler DA and Schuppan D. Update on serologic testing in celiac disease. *Am J Gastroenterol* 2010;105:2520-2524.
8. Sapone A, Bai JC, Ciacci C, et al. Spectrum of gluten-related disorders: Consensus on new nomenclature and classification. *BMC Med* 2012;10(13):1-12.

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Visit the online Test Menu at **www.LabCorp.com** for full test information, including CPT codes and specimen collection requirements.