Test Definition: TTGG

Tissue Transglutaminase Antibody, IgG, Serum

Overview

Useful For

Individuals with IgA deficiency

Evaluating patients suspected of having celiac disease, including patients with compatible clinical symptoms, patients with atypical symptoms, and individuals at increased risk (family history, previous diagnosis with associated disorder, positivity for *HLA DQ2* and/or *DQ8*

Screening test for dermatitis herpetiformis, in conjunction with an endomysial antibody test

Monitoring response to gluten-free diet in patients with dermatitis herpetiformis and celiac disease

Testing Algorithm

The following algorithms are available:
-Celiac Disease Comprehensive Cascade Test Algorithm
-Celiac Disease Diagnostic Testing Algorithm
-Celiac Disease Gluten-Free Cascade Test Algorithm
-Celiac Disease Routine Treatment Monitoring Algorithm
-Celiac Disease Serology Cascade Test Algorithm

Special Instructions

- Celiac Disease Diagnostic Testing Algorithm
- Celiac Disease Comprehensive Cascade Test Algorithm
- Celiac Disease Gluten-Free Cascade Test Algorithm
- Celiac Disease Routine Treatment Monitoring Algorithm
- Celiac Disease Serology Cascade Test Algorithm

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available

No

Specimen

Specimen Type

Serum

Ordering Guidance

Cascade testing is recommended for celiac disease. Cascade testing ensures that testing proceeds in an algorithmic

fashion. The following cascades are available; select the appropriate one for your specific patient situation.
-CDCOM / Celiac Disease Comprehensive Cascade, Serum and Whole Blood: complete testing including HLA DQ
-CDSP / Celiac Disease Serology Cascade, Serum: complete serology testing excluding HLA DQ
-CDGF / Celiac Disease Gluten-Free Cascade, Serum and Whole Blood: for patients already adhering to a gluten-free diet
To order individual tests, see Celiac Disease Diagnostic Testing Algorithm.

Specimen Required

Supplies: Sarstedt Aliquot Tube 5 mL (T914)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 0.5 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send a Gastroenterology and Hepatology Test Request (T728) with the specimen.

Specimen Minimum Volume

0.4 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	21 days	
	Frozen	21 days	

Clinical & Interpretive

Clinical Information

Celiac disease (gluten-sensitive enteropathy, celiac sprue) results from an immune-mediated inflammatory process following ingestion of wheat, rye, or barley proteins that occurs in genetically susceptible individuals.(1) The inflammation in celiac disease occurs primarily in the mucosa of the small intestine, which leads to villous atrophy. Common clinical manifestations related to gastrointestinal inflammation include abdominal pain, malabsorption, diarrhea, and/or constipation. Clinical symptoms of celiac disease are not restricted to the gastrointestinal tract. Other common manifestations of celiac disease include failure to grow (delayed puberty and short stature), iron deficiency,

recurrent fetal loss, osteoporosis, chronic fatigue, recurrent aphthous stomatitis (canker sores), dental enamel hypoplasia, and dermatitis herpetiformis. Patients with celiac disease may also present with neuropsychiatric manifestations including ataxia and peripheral neuropathy and are at increased risk for development of non-Hodgkin lymphoma. The disease is also associated with other clinical disorders including thyroiditis, type I diabetes mellitus, Down syndrome, and IgA deficiency.

Individuals with family members who have celiac disease are at increased risk of developing the disease.(2) Genetic susceptibility is related to specific human leukocyte antigen (HLA)markers. More than 97% of individuals with celiac disease in the United States have *DQ2* and/or *DQ8* HLA markers, compared to approximately 40% of the general population. For this reason, *HLA-DQ2* and *HLA-DQ8* are considered genetic risk factors for celiac disease and are required, but not sufficient, for the disease process to occur. HLA testing is not required for diagnosis in all cases but can be useful in situations where histology and serology are discrepant, or for individuals who have started a gluten free diet before evaluation.(3)

A definitive diagnosis of celiac disease requires a duodenal biopsy demonstrating villous atrophy.(3) Given the invasive nature and cost of the biopsy, serologic and genetic laboratory tests may be used to identify individuals with a high probability of having celiac disease. Because no single laboratory test can be relied upon completely to establish a diagnosis of celiac disease, individuals with positive laboratory results may be referred for small intestinal biopsy, thereby decreasing the number of unnecessary invasive procedures (see Celiac Disease Diagnostic Testing Algorithm). In terms of serology, celiac disease is associated with a variety of autoantibodies, including endomysial antibody, tissue transglutaminase (tTG), and deamidated gliadin antibodies.(4) Although the IgA isotype of these antibodies usually predominates in celiac disease, individuals may also produce IgG isotypes, particularly if the individual is IgA deficient. The most sensitive and specific serologic test is tTG IgA isotype, in individuals who produce sufficient total IgA. For individuals who are IgA deficient, testing for tTG and deamidated gliadin IgG antibodies is required.

A recent multi-cohort international study found that a tTG IgA titer of greater than or equal to 10 times the upper limit of normal (ULN) had a positive predictive value of 95% in an adult population.(5) In addition, several prospective studies have shown that a biopsy free approach to celiac disease diagnosis may be possible in children with a tTG titer greater than or equal to 10 times the ULN who meet certain criteria.(6-9) Given this evidence, the American College of Gastroenterology now suggests that a positive tTG IgA result greater than 10 times the upper limit of normal with a positive endomysial antibody in a separate blood sample may be sufficient for a diagnosis celiac disease in children.(3)

The treatment for celiac disease is maintenance of a gluten-free diet. In most patients who adhere to this diet, concentrations of associated autoantibodies decline, which is sometimes accompanied by reconstitution of the small intestinal villi. In most patients, an improvement in clinical symptoms is observed. For evaluation purposes, all serologic tests ordered for the diagnosis of celiac disease should be performed while the patient is on a gluten-containing diet. Once a patient has initiated the gluten-free diet, serologic testing may be repeated to assess the response to treatment. In some patients, it may take up to 1 year for antibody titers to normalize. Persistently elevated results suggest poor adherence to the gluten-free diet or the possibility of refractory celiac disease.

See Celiac Disease Diagnostic Testing Algorithm for the recommended approach to a patient suspected of celiac disease.

An algorithm is available for monitoring the patient's response to treatment, see Celiac Disease Routine Treatment Monitoring Algorithm.

Reference Values

<6.0 U/mL (negative)
6.0-9.0 U/mL (weak positive)
>9.0 U/mL (positive)
Reference values apply to all ages.

Interpretation

Positive results for tissue transglutaminase (tTG) IgG antibodies are consistent with a diagnosis for celiac disease, particularly in individuals who are IgA deficient. For individuals with moderately to strongly positive results, a diagnosis of celiac disease is possible and a small intestinal biopsy should be considered to confirm the diagnosis.

Negative results for tTG IgG antibodies indicate a decreased likelihood of celiac disease.

A decrease in the concentration of tTG IgG may begin after initiation of a gluten-free diet and could indicate a response to therapy.

Cautions

Because IgA antibodies typically predominate in celiac disease, testing for tissue transglutaminase (tTG) IgA antibodies is preferred over tTG IgG antibodies, except in the presence of IgA deficiency.

This test should not be solely relied upon to establish a diagnosis of celiac disease. It should be used to identify patients who have an increased probability of having celiac disease and in whom a small intestinal biopsy is recommended.

Affected individuals who have been on a gluten-free diet prior to testing may have a negative result.

If serology is negative or there is substantial clinical doubt remaining, then further investigation should be performed with endoscopy and small intestinal biopsy. This is especially important in patients with frank malabsorptive symptoms since many syndromes can mimic celiac disease. For the patient with frank malabsorptive symptoms, small intestinal biopsy should be performed regardless of serologic test results.

The antibody pattern in dermatitis herpetiformis may be more variable than in celiac disease; therefore, both endomysial antibodies and tTG antibody determinations are recommended to maximize the sensitivity of the serologic tests.

Clinical Reference

1. Rubin JE, Crowe SE. Celiac disease. Ann Int Med. 2020;172(1):ITC1-ITC16
2. Lebwohl B, Rubio-Tapia A. Epidemiology, presentation, and diagnosis of celiac disease. Gastroenterology. 2021;160(1):63-75
3. Rubio-Tapia A, Hill ID, Semrad C, et al. American College of Gastroenterology guidelines update: Diagnosis and management of celiac disease. Am J Gastroenterol. 2023;118(1):59-76. doi:10.14309/ajg.0000000000002075
4. Penny HA, Raju SA, Sanders DS. Progress in the serology-based diagnosis and management of adult celiac disease. Expert Rev Gastroenterol Hepatol. 2020;14(3):147-154
5. Penny HA, Raju SA, Lau MS, et al. Accuracy of a no-biopsy approach for the diagnosis of coeliac disease across different adult cohorts. Gut. 2021;70(5):876-883. doi:10.1136/gutjnl-2020-320913
6. Ylonen V, Lindfors K, Repo M, et al. Non-biopsy serology-based diagnosis of celiac disease in adults is accurate with different commercial kits and pre-test probabilities. Nutrients. 2020;12(9):2736

7. Werkstetter KJ, Korponay-Szabo IR, Popp A, et al. Accuracy in diagnosis of celiac disease without biopsies in clinical practice. Gastroenterology. 2017;153(4):924-935. doi:10.1053/j.gastro.2017.06.002
8. Wolf J, Petroff D, Richter T, et al. Validation of antibody-based strategies for diagnosis of pediatric celiac disease without biopsy. Gastroenterology. 2017;153(2):410-419.e17. doi:10.1053/j.gastro.2017.04.023
9. Ho SS, Keenan JI, Day AS. Role of serological tests in the diagnosis of coeliac disease in children in New Zealand. J Paediatr Child Health. 2020;56(12):1906-1911. doi:10.1111/jpc.15076Celiac disease

Performance

Method Description

Microwells are precoated with recombinant human tissue transglutaminase (tTG) antigen expressed in Baculovirus cells using complementary DNA coding for the long-spliced isoform of human tTG.

Calibrators, controls, and diluted patient samples are added to the wells, and autoantibodies recognizing the tTG antigen bind during the first incubation. After washing the wells to remove all unbound proteins, purified peroxidase-labeled rabbit antihuman IgG (alpha chain specific) conjugate is added. The conjugate binds to the captured human autoantibody, and the excess unbound conjugate is removed by a further wash step.

Bound conjugate is visualized with 3,3',5,5'-tetramethylbenzidine substrate, which gives a blue reaction product, the intensity of which is proportional to the concentration of the autoantibody in the sample. Phosphoric acid is added to each well to stop the reaction. This produces a yellow end point color, which is read at 450nm.(Package insert: QUANTA Lite R h-tTG IgG. Inova Diagnostics, Inc; Rev. 8, 01/2020)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

Same day/1 to 4 days

Specimen Retention Time

14 days

Performing Laboratory Location

Mayo Clinic Jacksonville Clinical Lab

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.

- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

86364

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
TTGG	Tissue Transglutaminase Ab, IgG, S	56537-4

Result ID	Test Result Name	Result LOINC® Value
TTGG	Tissue Transglutaminase Ab, IgG, S	56537-4