Test Definition: CDGF

Celiac Disease Gluten-Free Cascade

Overview

Useful For

Evaluating patients suspected of having celiac disease who are currently (or were recently) on a gluten-free diet

Profile Information

Test ID	Reporting Name	Available Separately	Always Performed
CELI2	HLA-DQ Typing	Yes, (Order CELI)	Yes
CDGF1	Celiac Disease Interpretation	No	Yes

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
TTGA	Tissue Transglutaminase Ab, IgA, S	Yes	No
DAGL	Gliadin(Deamidated) Ab, IgA, S	Yes	No
DGGL	Gliadin(Deamidated) Ab, IgG, S	Yes	No
TTGG	Tissue Transglutaminase Ab, IgG, S	Yes	No
IGA	Immunoglobulin A (IgA), S	Yes	No

Testing Algorithm

If HLA-DQ typing is positive or equivocal for DQ2 or DQ8, then IgA, tissue transglutaminase (tTG) IgA and IgG, and deamidated gliadin IgA and IgG will be performed at an additional charge.

The following algorithms are available in Special Instructions:

-Celiac Disease Comprehensive Cascade

-Celiac Disease Diagnostic Testing Algorithm

-Celiac Disease Gluten-Free Cascade

-Celiac Disease Routine Treatment Monitoring Algorithm

-Celiac Disease Serology Cascade

Special Instructions

- Celiac Disease Diagnostic Testing Algorithm

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

Method Name

CELI2: Polymerase Chain Reaction (PCR)/Sequence-Specific Oligonucleotide Probe (SSO)

NY State Available

Yes

Specimen

Specimen Type

Serum
Whole Blood ACD-B

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: complete testing including HLA DQ

-CDSP / Celiac Disease Serology Cascade: complete testing excluding HLA DQ

-CDGF / Celiac Disease Gluten-Free Cascade: for patients already adhering to a gluten-free diet

To order individual tests, see Celiac Disease Diagnostic Testing Algorithm in Special Instructions.

Specimen Required

Both blood and serum are required.

Specimen Type: Blood

Container/Tube: Yellow top (ACD solution B)

Specimen Volume: 6 mL

Collection Instructions: Do not transfer blood to other containers.

Specimen Type: Serum

Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Specimen Volume: 2 mL

Forms

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

Specimen Minimum Volume

Blood: 3 mL
Serum 1.5 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	
Whole Blood ACD-B	Refrigerated (preferred)		
	Ambient		

Clinical and 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.(1) Common clinical manifestations related to gastrointestinal inflammation include abdominal pain, malabsorption, diarrhea, and constipation.(2) 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.(3) 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.(1,2) The disease is also associated with other clinical disorders including thyroiditis, type I diabetes mellitus, Down syndrome, and IgA deficiency.(1,3)

Celiac disease tends to occur in families; individuals with family members who have celiac disease are at increased risk of developing the disease. Genetic susceptibility is related to specific HLA markers. More than 97% of individuals with celiac disease in the United States have DQ2 and/or DQ8 HLA markers, compared with approximately 40% of the general population.(3)

A definitive diagnosis of celiac disease requires a jejunal biopsy demonstrating villous atrophy.(1-3) 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. Subsequently, those individuals with positive laboratory results should be referred for small intestinal biopsy, thereby decreasing the number of unnecessary invasive procedures. In terms of

serology, celiac disease is associated with a variety of autoantibodies, including endomysial, 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.(2) The most sensitive and specific serologic tests are tTG and deamidated gliadin antibodies.

The treatment for celiac disease is maintenance of a gluten-free diet.(1-3) In most patients who adhere to this diet, levels of associated autoantibodies decline and villous atrophy improves (see Celiac Disease Routine Treatment Monitoring Algorithm in Special Instructions). This is typically accompanied by an improvement in clinical symptoms.

It should be noted that HLA typing is not required to establish a diagnosis of celiac disease. Consider ordering CDSP / Celiac Disease Serology Cascade if HLA typing is not desired or has been previously performed.

Reference Values

HLA-DQ TYPING

Presence of DQ2 or DQ8 alleles associated with celiac disease

Interpretation

HLA-DQ Typing:

Approximately 90% to 95% of patients with celiac disease have the HLA-DQ2 allele; most of the remaining patients with celiac disease have the HLA-DQ8 allele. Individuals who do not carry either of these alleles are unlikely to have celiac disease. For these individuals, no further serologic testing is required. However, individuals with these alleles may not, during their lifetime, develop celiac disease. Therefore, the presence of DQ2 or DQ8 does not conclusively establish a diagnosis of celiac disease. For individuals with DQ2 and/or DQ8 alleles, in the context of positive serology and compatible clinical symptoms, small intestinal biopsy is recommended.

Immunoglobulin A (IgA):

Total IgA levels below the age-specific reference range suggest either a selective IgA deficiency or a more generalized immunodeficiency. For individuals with a low IgA level, additional clinical and laboratory evaluation is recommended. Some individuals may have a partial IgA deficiency in which the IgA levels are detectable, but fall below the age-adjusted reference range. For these individuals, both IgA and IgG isotypes for tTG and deamidated gliadin antibodies are recommended for the evaluation of celiac disease.

Tissue Transglutaminase (tTG) Antibody, IgA/IgG:

Individuals positive for tTG antibodies of the IgA and/or IgG isotype may have celiac disease and small intestinal biopsy is recommended. Negative tTG IgA and/or IgG antibody serology does not exclude a diagnosis of celiac disease, as antibody levels decrease over time in patients who have been following a gluten-free diet.

Gliadin (Deamidated) Antibody, IgA/IgG:

Positivity for deamidated gliadin antibodies of the IgA and/or IgG isotype is suggestive of celiac disease, and small intestinal biopsy is recommended. Negative deamidated gliadin IgA and/or IgG antibody serology does not exclude a diagnosis of celiac disease, as antibody levels decrease over time in patients who have been following a gluten-free diet.

Cautions

This cascade 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 for whom a small intestinal biopsy is recommended.

This cascade is designed for use in patients who have already instituted, or recently discontinued, a gluten-free diet. For patients who are not following a gluten-free diet, CDCOM / Celiac Disease Comprehensive Cascade is the preferred test.

This cascade should not be used in patients for whom HLA DQ2/DQ8 typing has already been performed. For individuals who are positive for either DQ2 and/or DQ8, CDSP / Celiac Disease Serology Cascade should be ordered to assess the levels of autoantibodies associated with celiac disease. For individuals who are negative for DQ2 and DQ8, no further testing is necessary as a diagnosis of celiac disease is unlikely.

Supportive Data

See individual test IDs

Clinical Reference

1. Green PHR, Cellier C: Medical progress: Celiac disease. N EngL J Med 2007;357:1731-1743

2. Green PHR, Jabri J: Celiac disease. Ann Rev Med 2006;57;207-221

3. Harrison MS, Wehbi M, Obideen K: Celiac disease: More common than you think. Cleve Clinic J Med 2007;74:209-215

4. Update on celiac disease: New standards and new tests. Mayo Communique (2008)

Performance

Method Description

HLA-DQ Typing:

LABType applies Luminex technology to the reverse sequence-specific oligonucleotide probe (SSO) DNA typing method. First, target DNA is PCR-amplified using a group-specific primer. The PCR product is biotinylated, which allows it to be detected using R-Phycoerythrin-conjugated streptavidin. The PCR product is denatured and allowed to rehybridize to complementary DNA probes conjugated to fluorescently coded microspheres. A flow analyzer identifies the fluorescent intensity of phycoerythrin on each microsphere. The HLA Class II allele or allele groups of the sample is determined by the positive and negative bead ID's using a computer software program. The assignment of the HLA typing is based on the reaction pattern compared to patterns associated with published HLA gene sequences.(Package insert: One Lambda, LABType SSO Typing. rev. 30, 12/2018)

Immunoglobulin A (IgA):

Total IgA levels are measured by immunonephelometry. Rabbit antisera that specifically recognizes human IgA is added to the patient sample. Immune complexes form between the human IgA and the rabbit immunoglobulins; the immune complexes scatter light that is passed through the sample. The intensity of the scattered light is related to the amount of human IgA in the sample. The concentration of IgA in the sample is calculated from a multipoint calibration curve.(Behring Nephelometer II Operations Instruction Manual. Dade Behring, Inc. Newark, DE 19714. 2008)

Tissue Transglutaminase (tTG) Antibody, IgA/IgG:

IgA and IgG antibodies to tTG are detected by enzyme-linked immunosorbent assay (ELISA). Recombinant human tTG antigen expressed in *Escherichia coli* is adsorbed to wells of a microtiter plate under conditions that preserve the native state of the antigen. Diluted patient sera are added to the microtiter plate wells under conditions that allow binding of the antibodies to the tTG antigen. Unbound sample constituents are washed away and horseradish

peroxidase (HRP)-labeled antihuman IgA or IgG antibody conjugate is added to each well. After a second incubation, unbound HRP-label is removed and bound conjugate is detected by adding tetramethylbenzidine (TMB) chromogenic substrate. After a final incubation, colored product is measured spectrophotometrically; the absorbance of the patient sample is compared to the positive calibrator. The absorbance is directly proportional to the level of IgA or IgG antibodies to tTG, which is expressed in arbitrary units.(QUANTA Lite R h-tTG IgA and IgG. Inova Diagnostics, Inc. San Diego, CA, 92131. rev. 7, 1/2015)

Gliadin (Deamidated) Antibody, IgA/IgG:

IgA and IgG antibodies to deamidated gliadin peptides are detected by ELISA. Purified peptides are adsorbed to wells of a microtiter plate under conditions that preserve the native state of the antigen. Diluted patient sera are added to the microtiter plate wells under conditions that allow binding of the antibodies to the deamidated gliadin peptides. Unbound sample constituents are washed away and HRP-labeled antihuman IgA or IgG antibody conjugate is added to each well. After a second incubation, unbound HRP-label is removed and bound conjugate is detected by adding TMB chromogenic substrate. After a final incubation, colored product is measured spectrophotometrically; the absorbance of the patient sample is compared to the positive calibrator. The absorbance is directly proportional to the level of IgA or IgG antibodies to deamidated gliadin peptides, which is expressed in arbitrary units.(QUANTA Lite Gliadin IgA II and IgG II. INOVA Diagnostics, Inc. San Diego, CA, 92131. rev. 1, 4/2015)

PDF Report

No

Day(s) Performed

IgA, tTG IgG, Gliadin IgG, Gliadin IgA, tTG IgA: Monday through Saturday

HLA-DQ Typing: Monday through Friday

Report Available

7 to 14 days

Performing Laboratory Location

Rochester

Fees and 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 Regional Manager. 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

81376 x 2

82784-IgA (if appropriate)

83516-Deamidated gliadin IgA (if appropriate)

83516-Deamidated gliadin IgG (if appropriate)

83516-tTG IgA (if appropriate)

83516-tTG IgG (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
CDGF	Celiac Disease Gluten-Free Cascade	94493-4

Result ID	Test Result Name	Result LOINC Value
DQA	DQ alpha 1	94495-9
28991	Celiac Disease Interpretation	69048-7
DQB	DQ beta 1	53938-7
CELIG	Celiac gene pairs present?	48767-8