Celiac Disease Comprehensive Panel With Gliadin Antibody (IgG)

Test Code: 36336(X)

Specimen Requirements: 5 mL refrigerated serum in a red-top tube (no gel); 1 mL minimum. Alternatively, submit 5 mL refrigerated serum in a serum separator tube; 1 mL minimum.

CPT Codes*: 83516; 82784

CLINICAL USE

- Diagnose celiac disease in patients over 5 years of age

CLINICAL BACKGROUND

Celiac disease (CD), caused by an immune response to gluten in genetically susceptible individuals, leads to defects in the mucosa of the small intestine (eg, villous atrophy and crypt hyperplasia). Overall, CD affects approximately 1 in 100 people in the United States.[1] However, the prevalence is even higher among individuals with insulin-dependent diabetes mellitus; autoimmune thyroiditis; Down, Turner, or Williams syndromes; selective IgA deficiency; or a family history of CD (first-degree relative).[1] Young children with CD often have gastrointestinal symptoms (eg, diarrhea, abdominal pain, vomiting, constipation, and abdominal distention), while less than half of adults experience diarrhea.[2] Older children, adolescents, and adults with CD often have extraintestinal manifestations (eg, short stature, delayed puberty, anemia, osteoporosis, dermatitis herpetiformis, and neurological symptoms). However, many people with CD have mild or no symptoms.[2]

Early diagnosis of CD and initiation of a gluten-free diet are necessary for mucosal healing, which is more rapid and more complete in children than in adults.[3] Diagnosis begins with serologic testing and is confirmed by biopsy of the small intestine. Levels of CD-specific antibodies decrease after initiating a gluten-free diet, so the American College of Gastroenterology recommends that patients undergoing serologic testing for CD should be on a gluten-containing diet.[4]

- **Tissue transglutaminase antibodies (tTG IgA and tTG IgG):** tTG IgA is recommended as a first-line marker for CD,[4] with a sensitivity of 95% to 98% and a specificity of 94% to 95%.[1] tTG IgG has a lower sensitivity (40%) for CD, but is also highly specific (95%).[1]
- **Endomysial IgA antibody (EMA IgA):** EMA IgA has a lower sensitivity (>90%) but higher specificity (>95%) than tTG IgA for CD,[1] and can be used to confirm positive tTG IgA test results.
- **Deamidated gliadin peptide IgG antibody (DGP IgG):** DGP IgG has a sensitivity of 80% and a specificity of 98% for CD.[1]

Total IgA is measured to identify selective IgA deficiency, which is more common among CD patients (2% to 3%) than the general population (<0.25%) and can affect interpretation of serologic test results.[1] Patients with IgA deficiency may have negative results on IgA antibody tests (tTG IgA and EMA IgA), but positive results on IgG antibody tests (tTG IgG and DGP IgG). Among IgA-deficient patients, tTG IgG has a sensitivity of 85.7% (95% CI, 67.9% to 94.9%) for CD; DGP IgG has a sensitivity of 92.9% (95% CI, 76.3% to 99.1%).[5] Thus, patients with suspected celiac disease who are IgA-deficient should also be tested for tTG IgG and DGP IgG.[4]

The Celiac Disease Comprehensive Panel With Gliadin Antibody (IgG) begins by testing for tTG IgA in addition to quantifying total IgA. A tTG IgA result above the reference range prompts reflex to an EMA IgA test cascade at an additional charge: EMA antibody screen (CPT code 86255), with a positive result reflexing to EMA titer for quantification at an additional charge (CPT code 86256). Total IgA below the lower limit of the reference range, based on age, prompts reflex to tTG IgG and DGP IgG testing at an additional charge (CPT code 83516 [x2]). Panel components may be ordered separately **(Table)**.

INDIVIDUALS SUITABLE FOR TESTING

- Individuals (>5 years old) with signs, symptoms, or laboratory evidence suggestive of celiac disease

METHOD

- All specimens are tested for tTG IgA by immunoassay and total IgA by immunoturbidimetry.
  - tTG IgA above the reference range prompts reflex to EMA screening, conducted using an immunofluorescence assay performed with monkey esophagus sections. Positive EMA screen results at the 1:5 dilution prompt reflex to EMA titer, determined by serial dilution of samples to a maximum of 1:10,240.
  - IgA below the lower limit of the reference range prompts reflex to tTG IgG and DGP IgG antibody testing, performed using immunoassays.

Table. Individual Tests Included in the Celiac Disease Comprehensive Panel With Gliadin Antibody (IgG)

Test Code	Test Name	CPT Code
15064	Endomysial Antibody (IgA) Screen with Reflex to Titer[a,b]	86255
11212	Gliadin (Deamidated Peptide) Antibody (IgG)[a]	83516
8821	Tissue Transglutaminase (tTG) Antibody (IgA)	83516
11070	Tissue Transglutaminase (tTG) Antibody (IgG)[a]	83516
539	IgA	82784

[a] These tests are reflexes in the Celiac Disease Comprehensive Panel With Gliadin Antibody (IgG).
[b] Reflex tests are performed at an additional charge and are associated with an additional CPT code(s).

REFERENCE RANGES

DGP IgG:	< 20 Units	
EMA screen:	Negative	
EMA titer:	< 1:5	
tTG IgA:	< 4 U/mL	
tTG IgG:	< 6 U/mL	
Total IgA:	Age Range	Concentration (mg/dL)
	6-8 years	31-180
	9-11 years	33-200
	12-16 years	36-220
	17-60 years	47-310
	≥61 years	20-320

INTERPRETIVE INFORMATION

Positive results from any CD-specific antibody test (tTG IgA, tTG IgG, or DGP IgG) are consistent with a diagnosis of CD. Following a positive tTG IgA result, a positive EMA screen increases the specificity of the diagnosis. Guidelines indicate that a serologic diagnosis of CD should be confirmed with biopsy of the small intestine.[4]

Among patients with normal IgA levels, a negative tTG IgA result indicates that CD is unlikely. Patients with IgA levels below the lower limit of the reference range, based on age, may be IgA-deficient. Among IgA-deficient patients, negative tTG IgA results may reflect a lack of IgA antibodies, but negative DGP IgG and tTG IgG results indicate that CD is unlikely. However, negative serology does not rule out CD: some patients with CD may be seronegative, and some may have false negative results if they initiated a gluten-free diet before testing.

If serologic tests are negative, but clinical suspicion of CD remains high, biopsy of the small intestine may be appropriate.[4] Testing for HLA-DQ2 and HLA-DQ8 (HLA Typing for Celiac Disease; test code 17135), which are present in almost all people with CD, can help rule out CD when clinical and laboratory findings are equivocal.[4]

References

1. Pelkowski TD, Viera AJ. Celiac disease: diagnosis and management. *Am Fam Physician*. 2014;89:99-105.
2. Scanlon SA, Murray JA. Update on celiac disease - etiology, differential diagnosis, drug targets, and management advances. *Clin Exp Gastroenterol*. 2011;4:297-311.
3. Hill ID, Fasano A, Guandalini S, et al. NASPGHAN clinical report on the diagnosis and treatment of gluten-related disorders. *J Pediatr Gastroenterol Nutr*. 2016;63:156-165.
4. Rubio-Tapia A, Hill ID, Kelly CP, et al. ACG clinical guidelines: diagnosis and management of celiac disease. *Am J Gastroenterol*. 2013;108:656-676; quiz 677.
5. Villalta D, Tonutti E, Prause C, et al. IgG antibodies against deamidated gliadin peptides for diagnosis of celiac disease in patients with IgA deficiency. *Clin Chem*. 2010;56:464-468.

* The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.