Gluten-free diet adherence assessment by testing for gluten in stool samples

Introduction

Celiac Disease (CD) is a serious, underdiagnosed autoimmune condition that is caused by an immune response to dietary gluten-containing products in individuals with a genetic predisposition to CD.[1,2] Celiac disease affects approximately 1% of people in the United States, and the prevalence is rising.[2,3] The only available treatment for CD is complete, lifelong avoidance of gluten consumption (known as a gluten-free diet, or GFD).[1,2,4] However, strict compliance with a GFD is very challenging, and a significant subset of patients who are trying their best to adhere to a GFD are not relieved from symptoms and have persistent biopsy-detectable damage of the mucosal layer in their gastrointestinal tract.[1,4] One study found that among patients on a strict GFD, 38% of biopsied patients still had intestinal damage.[5] An analysis of data from a large registry of patients diagnosed with celiac disease revealed that 47% reported symptoms even with adherence to a strict GFD.[6]

More common than celiac disease, non-celiac gluten sensitivity (NCGS) is another condition involving an intolerance to gluten that improves on a GFD. NCGS is gaining attention among clinicians, but because there is no biomarker specific for NCGS, it is implicated when celiac disease, wheat allergy, and other causes of symptoms have been ruled out.[2,4,7] In a survey of the general population, 13% of participants self-reported as sensitive to gluten.[7]

One of the main reasons for GFD non-compliance is that there are many sources for gluten contamination that may cause accidental gluten consumption. While CD patients may be able to tightly control and avoid consumption of gluten-containing foods in the kitchen at home or in restaurants that use only gluten-free labeled foods, it is nearly impossible to control products that are mislabeled as "gluten-free."[8] There is currently no widely available method to accurately detect and measure the amount of gluten present in consumable products such as food, medications, and supplements, and many products labeled as gluten-free may in fact contain gluten in amounts that are sufficient to trigger symptoms and mucosal damage in CD patients.[9,10]

An alternate approach

While the intestinal biopsy is the gold standard for the detection of villous atrophy—mucosal damage that is the hallmark of CD—it is more practical and cost-effective to be able to monitor patients for adherence to a GFD using non-invasive methods. However, currently utilized serological markers such as tTG IgA and EMA IgA are reported to have a sensitivity below 50% for the detection of persistent villous atrophy in patients on a GFD, and there is a need for a more accurate way of monitoring the non-response to a GFD.[5,11] The detection of gluten in stool samples is reported to be a reliable alternate approach to monitoring adherence to a GFD, thus allowing for the direct measurement of the disease-triggering source in these patients.[11] In a study of celiac patients on a GFD, among patients with persistent symptoms, 67% had detectable levels of gluten in their stools.[11] Gluten in stool remains detectable for up to 4 days after consumption.[11] In another study of patients endeavoring to adhere to a strict GFD, two-thirds were shown to have been exposed to gluten during the 10-day study period.[12]

The benefits of testing for gluten in stool samples

- Monitors celiac disease and non-celiac gluten sensitivity patients for adherence to gluten-free diet
- Monitors accidental gluten consumption due to mislabeling or food/product contamination
- Assists in the assessment for true "refractory" celiac disease that is not related to accidental gluten exposure[2,4]

labcorp

Labcorp's solution

Labcorp is proud to be the first clinical reference laboratory in the US to introduce quantitative testing for gluten in stool samples in order to detect exposure to gluten consumption within the four previous days. The test, **Gluten, Fecal, Quantitative [123027],** would be useful for patients who are attempting to adhere to a GFD, in order for them to determine if they have had recent unintended exposure to gluten. The test is validated to be sensitive enough to detect the presence of gluten down to a concentration of 12 ng/mL in a stool sample about the size of a teaspoon.

This test may be used for the following applications:

- Monitoring CD and NCGS patients for adherence to a GFD;
- Monitoring accidental gluten consumption due to mislabeling or food/product contamination;
- Assisting in the assessment for true "refractory" CD that is not related to accidental gluten exposure.[2,4]

Labcorp offers:

Test Name	Test No.
Gluten, Fecal, Quantitative	**123027**

*For the most current information regarding test options, including specimen requirements and CPT codes, please consult the online Test Menu at www.Labcorp.com.

References

1. Guandalini S, Assiri A. Celiac disease: a review. *JAMA Pediatr.* 2014 Mar;168(3):272-278.
2. Taylor AK, Lebwohl B, Snyder CL, Green PHR. Adam MP, Ardinger HH, Pagon RA, et al, editors. Celiac Disease. In: GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2021. 2008 Jul 3 [updated 2019 Jan 31].
3. Lebwohl B, Sanders DS, Green PHR. Coeliac disease. *Lancet.* 2018 Jan 6;391(10115):70-81.
4. Rubin JE and Crowe SE. Celiac Disease. *Ann Intern Med.* 2020 Jan. 7;172(1):ITC1-ITC16.
5. Silvester JA, Kurada S, Szwajcer A, Kelly CP, Leffler DA, Duerksen DR. Tests for Serum Transglutaminase and Endomysial Antibodies Do Not Detect Most Patients With Celiac Disease and Persistent Villous Atrophy on Gluten-free Diets: a Meta-analysis. *Gastroenterology.* 2017 Sep;153(3):689-701.e1.
6. Chen K, Geller M, Leffler D, et al. Disease burden and quality of life impacts in patients with celiac disease on a gluten-free diet: an analysis of the iCureCeliac® registry. Poster presented at the American College of Gastroenterology (ACG) Virtual Meeting 2020, October 23-28, 2020.
7. Balistreri WF. Should We All Go Gluten-Free? Medscape Web site. https://www.medscape.com/viewarticle/857971. Feb 4, 2016. Accessed December 2021.
8. Forbes GM. Celiac Disease Patients Should No Longer Be Consuming Measurable Amounts of Gluten. *Gastroenterology.* 2020 Sep;159(3):1189.
9. Bruins Slot ID, Bremer MGEG, van der Fels-Klerx I, Hamer RJ. Evaluating the Performance of Gluten ELISA Test Kits: The Numbers Do Not Tell the Tale. *Cereal Chem.* 2015;92(5):513-521.
10. The Celiac Disease Foundation Submits Comment to FDA on Draft Guidance Regarding Gluten in Medications. Celiac Disease Foundation Web site. https://celiac.org/about-the-foundation/featured-news/2018/02/celiac-disease-foundation-submits-comment-fda-draft-guidance-regarding-gluten-medications/. February 15, 2018. Accessed December 2021.
11. Comino I, Fernández-Bañares F, Esteve M, et al. Fecal Gluten Peptides Reveal Limitations of Serological Tests and Food Questionnaires for Monitoring Gluten-Free Diet in Celiac Disease Patients. *Am J Gastroenterol.* 2016 Oct;111(10):1456-1465.
12. Silvester JA, Comino I, Kelly CP, Sousa C, Duerksen DR, Doggie Bag Study Group. Most Patients with Celiac Disease on Gluten-free Diets Consume Measurable Amounts of Gluten. *Gastroenterology.* 2020 Apr;158(5):1497-1499.e1.