Celiac Center

Beth Israel Lahey Health
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Blood Tests in Celiac Disease

Key Point

- Blood tests can be useful in helping to diagnose celiac disease, as well as in providing a general idea of how patients with CD are healing once diagnosed.

Blood Tests for Diagnosis

What blood tests are used to diagnose celiac disease?

There are basically four tests doctors use nowadays.

- **Tissue Transglutaminase IgA Antibody (commonly referred to as tTG-IgA) and Total IgA Antibody:** This is the main and most recommended initial test for anyone over the age of two who is not on a gluten-free diet.[1] It is highly accurate in detecting signs of celiac disease in your blood. These signs, called antibodies, are proteins that your immune system produces to fight off things it perceives as harmful.
- A positive antibody test alone is not always sufficient for a definitive diagnosis. Although uncommon, a person can have celiac disease even if their blood tests are negative. A seronegative celiac disease is the most frequent reason why adults with intestinal damage (called villous atrophy) have negative celiac blood tests.[2]
- Also, a small number of people with celiac disease (about 2-3%) don't make enough of a substance called IgA. This is a condition called IgA deficiency and is generally asymptomatic (meaning it has no symptoms) but may be associated with increased risk of some infections. If your total IgA is low, the tTG-IgA test can result in a false negative. To ensure the results are reliable, doctors often also test for serum total IgA.[3]
- Therefore, your doctor will recommend a follow-up procedure called an endoscopy with a biopsy to confirm the diagnosis. This is performed using a tiny camera to examine the small intestine and take a small tissue sample to check for the damage characteristic of celiac disease.

- **Deamidated Gliadin Peptide IgA/IgG Antibodies (commonly referred to as DGP) and Tissue Transglutaminase IgG Antibody (commonly referred to as tTG-IgG):** If the Total IgA test shows you have an IgA deficiency, your doctor will use these tests instead. They look for a different type of antibody (called IgG) to check for celiac disease.

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- There is also an IgG tTG test but it is less accurate than the IgG DGP test. Conversely, IgA tTG is more accurate than IgA DGP.

What about other tests?

- **Endomysial Antibody (commonly referred to as EMA):** A positive result is a powerful indicator that a person has celiac disease. However, a negative result can occur even when celiac disease is present. Because it is expensive and can miss cases, it is no longer used as a first-step test, serving more as a confirmation test in some situations. Particularly when children have a positive EMA test and tTG-IgA levels 10 times higher than the upper normal limit, a biopsy may not be necessary.[4,5]

- **Anti-Gliadin Antibody (commonly referred to as AGA):** These are old tests that are no longer recommended. They are not very accurate, and because modern tests are much better they were removed from guidelines.[6]

Potential Celiac Disease

- Your doctor might mention 'potential celiac disease' in case you have positive celiac antibody blood tests, but your intestinal mucosa appears normal in a biopsy. Some may or may not go on to develop the intestinal damage seen in active celiac disease. Keeping a regular follow-up with your doctor will guide further actions according to symptoms and risk factors. [7,8]

Is there a blood test that can detect celiac disease in a person on a gluten-free diet?

- Currently, there is no routine blood test that can accurately diagnose celiac disease if you are already on a gluten-free diet. This is because avoiding gluten allows your antibody levels to return to normal, although this may not mean the intestinal lining has healed.[9,10] To get an accurate diagnosis, your doctor might suggest one of the following paths.

- **Human Leukocyte Antigen (commonly referred to as HLA-DQ2/DQ8):** This blood test checks for the main genes associated with celiac disease. It cannot diagnose celiac disease. About 30% of the general population has these genes, but most will never develop the condition.[11,12]
- It is excellent for ruling out celiac disease. If you test negative for both genes, it is more than 99% certain that you do not have and will not develop celiac disease. This is very helpful if you are already gluten-free, because a negative result means you can avoid a gluten challenge that might cause bothersome symptoms.[13]
- **The Gluten Challenge**: If celiac disease cannot be ruled out and you are on a gluten-free diet, your doctor may recommend a gluten challenge. This means you will need to reintroduce gluten into your diet for a period so the tests can become accurate again. This should always be done under a doctor's supervision.
- The challenge involves eating 3 to 6 grams of gluten per day (about 1.5 to 3 slices of bread). For the best accuracy, the challenge should last for at least 8 weeks (about 2 months), and ideally

12 weeks (about 3 months). If symptoms become too difficult, a biopsy after just two weeks may still show damage. In these cases, a negative result from a short challenge cannot definitively rule out celiac disease as some people take months of gluten exposure to develop diagnostic changes in blood tests or biopsy. [9,14]

The Future in Diagnosis

- Researchers are working on exciting new tests to shorten or even avoid a gluten challenge if you are on a gluten-free diet.
- Activated gut-homing CD8 T cells test has shown the potential to confirm a diagnosis after a very short gluten challenge of three days instead of the traditional several weeks.[15]
- Another blood test measures a substance called Interleukin-2 (commonly referred to as IL-2). It appears to be the earliest and most sensitive marker of acute gluten exposure. In these studies, a person on a gluten-free diet consumes a small, single dose of gluten protein from vital wheat flour mixed with water. A less invasive but still confident assessment, because IL-2 does not rise in people without the condition. [9,16]

Blood Tests for Health Maintenance

- Once you are diagnosed with celiac disease, the goal of treatment is not just to feel better, but to achieve complete intestinal healing. An intestine that has not fully healed can lead to long-term health risks, even if you don't have symptoms.[17] Your doctor will use follow-up tests to monitor your health in two key areas.

Can blood tests check if my intestine is healing and if I'm following the diet correctly?

Yes, but the best approach still relies in being evaluated by a gluten-expert dietitian.[18]

- **Antibody Tests (tTG/DGP):** Your doctor will check your antibody levels 3 to 6 months after you start a gluten-free diet, and then about once a year. A life-long gluten free diet is a key component of your treatment. Hence, a significant drop in these levels is a good sign that the diet is working.
- **Biopsy:** Normal antibody levels do not guarantee that your intestine has fully healed. Because of this, your doctor may order follow-up intestinal biopsy about two years after diagnosis to confirm that the intestinal lining has recovered.[19]
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- **The Future in Follow-up**: A new type of test can detect Gluten Immunogenic Peptides in urine or stool samples (commonly referred to as GIP). These tests directly find tiny pieces of gluten that your body has not fully digested, which shows if you have eaten gluten recently.
- Either can be performed easily at home. Stool GIP tests are highly sensitive, able to detect gluten intake of ≥250 mg with 100% sensitivity and can remain positive for up to 5-7 days. Urine GIP tests are faster, detecting gluten within 4-6 hours, but for a shorter window of 1-2 days. Although

some studies have shown that positive result is also strongly linked to ongoing intestinal damage, its clinical utility is still being investigated. [20,21]

What tests are used to check for other health issues related to celiac disease?

Because celiac disease can affect your whole body, your doctor will monitor for other conditions.

- Thyroid Disease: There is a strong link between celiac disease and autoimmune thyroid conditions. Your doctor should regularly check your thyroid function with a blood test called TSH. [22]

Liver Disease: It's common to have elevated liver enzymes (a sign of liver stress) at diagnosis, which usually return to normal with a gluten-free diet. New research shows that people with celiac disease have a doubled long-term risk of developing chronic liver disease, and this risk can last for decades. Because of this, your doctor should continue to monitor your liver enzymes as part of your regular care. 23

Examples:

Disease	Blood Tests
Thyroid disease	• Thyroid Stimulating Hormone (TSH) • Thyroid Hormones (T3, T4) • Thyroid antibodies (anti-TPO, anti-TSHR, anti-microsomal)
Liver Disease	• ALT • AST • Alkaline Phosphatase • Bilirubin

What tests are commonly used to help better understand the nutritional status of a person with celiac disease?

- When your intestine is damaged, it's hard for your body to absorb all the nutrients it needs from food. Your doctor will test you for common nutritional deficiencies, including iron, B vitamins (such as folate and B12), vitamin D, calcium, and zinc. These levels should be checked again 3 to 6 months after starting the diet and then periodically. Even with a healthy gluten-free diet, some deficiencies can continue while your intestine is healing, so supplements may be needed. [24]
- Patients with celiac disease have an increased risk for weak and brittle bones (a condition called osteoporosis). A bone density scan (commonly referred to as DXA) can be used to evaluate this risk alongside blood tests. It is often recommended for women in post menopause, adults above 45 in general, or with severe endoscopy findings at the time of diagnosis. [19,25]

Examples:

System involved / Common Symptoms	Tests

Blood cells (Red)
– Fatigue
– Shortness of Breath
	• Iron stores
	  ○ Ferritin
	  ○ Iron Binding Capacity
	  ○ Serum iron
	• Complete blood count (CBC)
	  ○ Red cell morphology
	• Folic acid
	• Vitamin B12

Bones – Higher risk of fractures	• Vitamin D • Calcium • Parathyroid Hormone (PTH)
Brain and nerves – Fatigue – "Brain fog" – Limb tingling – Abnormal gait	• Vitamin B6 • Vitamin B12 • Carnitine
General health – Frequent respiratory infections – Frequent digestive infections	• Copper • Zinc

Take Home Messages

- The tTG and DGP antibody tests are the main blood tests to diagnose and monitor celiac disease.
- Seeking evaluation while on a gluten-containing diet can improve your chances of an accurate diagnosis.
- Many other tests are useful for detection of disorders related to celiac disease and monitoring of nutritional deficiencies. These should be considered on a case-by-case basis with your clinician.

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