

FAQ: Diagnosing Celiac Disease

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How is celiac disease (CD) diagnosed?

CD is diagnosed by a gastroenterologist. A patient who is suspected to have CD will first have a blood test to check for the celiac antibodies, either EMA or tTG, as well as a total IgA count. These first two tests will determine if there are specific antibodies in the blood that are only found in patients with CD (1). Sometimes DGP, a test similar to tTG, is used. Read below for details on these tests. Visit Blood Tests under Medical Management on www.celiacnow.org

If the blood test is positive, the patient will have an endoscopy and a biopsy of the small intestine performed by a gastroenterologist. During the procedure, the doctor uses a flexible device with a camera (endoscope) to remove a small amount of tissue from the small intestine usually from the first part of the small intestine called the duodenum (1). A doctor will look at the tissue under a microscope to determine whether there is damage to the intestine that is characteristic of CD. A biopsy is the gold standard for the diagnosis of CD and is a necessary part of diagnosis. Visit Endoscopy under Medical Management on www.celiacnow.org

It is important that all these tests be done BEFORE starting a gluten-free diet (GFD) (1). If testing is done AFTER a GFD is started, blood tests can normalize and the intestine may have had a chance to heal. In this case, your doctor will be unable to accurately diagnose CD. Starting a GFD without first confirming the diagnosis of CD using blood tests and endoscopy with biopsy of the small intestine is NOT recommended. However, if you have already initiated a GFD based on a **presumed** diagnosis of celiac disease then you will be advised to get a gene test (HLA-DQ2/HLA-DQ8) test to rule-out the possibility of celiac disease.

To rule IN the possibility of celiac disease you will need an endoscopy with a biopsy after a gluten challenge [see below: **What is a gluten challenge? Do I need one?**]

Taking the gluten challenge can be troublesome to some patients as this might cause a temporary worsening of symptoms(1). Hence it is best to first get a definitive diagnosis on a gluten containing diet with blood tests and biopsy before you start a GFD.

There is a second reason for not starting the GFD before a proper diagnosis. CD is a lifelong illness, not only requiring a life-long GFD, but also involving multiple parts of the body. It is possible that other illnesses responsible for symptoms may be missed if you are diagnosed incorrectly with CD based on resolution of symptoms alone. An important diagnosis may be missed and/or you may be following a difficult diet that is not improving your health.

Depending on the patient's particular symptoms and medical history, a number of physical examinations and lab studies may be carried out to help identify nutritional deficiencies, electrolyte abnormalities or other health concerns.

Physical Exam findings could include:

- Examination of the abdomen may reveal a bloated stomach due to swelling of intestinal loops with fluids and gas
- Signs of weight loss such as muscle atrophy (loss of muscle mass) or loose skin folds
- Orthostatic hypotension (a decrease in blood pressure when going from a seated or lying position to standing)
- Peripheral edema (a collection of fluids in the arms and legs)
- Bruising
- Dermatitis Herpetiformis (DH) (see section on DH)
- Cheilosis (severely reddened and cracked lips; most commonly seen at the corners of the mouth)
- Glossitis (inflammation of the tongue with formation of ulcers in the mouth)
- Peripheral neuropathy (decreased sensation or numbness in the fingers and toes)
- Physical exam findings related to hypocalcemia
 - Chvostek's sign: tapping on a specific area of the face results in twitching of the facial muscle
 - Trousseau's sign: inflation of a blood pressure cuff on either arm results in a "carpal spasm," seen as flexing of the wrist

Blood tests:

- Low iron levels are common (1).
 - Ferritin is generally the best test to measure iron stores.
 - Iron
- B12 and folate: Anemia due to deficiency in iron, folate and, in rare cases, vitamin B12 may be present(1).
- Vitamin D (25-OHD) (1)
- Zinc (1)

Other tests that clinicians may order depending on your condition include:

- Parathyroid hormone
- TSH (thyroid stimulating hormone)

- Potassium
- Serum calcium
- Magnesium
- Fat soluble vitamins (with diarrhea)
- Carnitine
- Albumin (protein stores) if malnutrition is suspected
- Cholesterol panel

Stool examination:

- Looking for bulky, greasy appearance and foul-smelling stools that can suggest improper absorption of fat
- Tests that actually measure the amount of fat in the stool can also help to determine if this condition is present.

Immunologic testing/serology:

- Measurement of antibody levels to:
 - Tissue Transglutaminase (IgA-tTG)
 - Endomysium (EMA)
 - Gliadin – deamidated gliadin peptide (DGP)

Imaging studies:

Imaging studies including x-rays, CT scans, and a variety of other tests are rarely necessary in the diagnosis of celiac disease. However, they may be needed to rule out other disorders in cases where the diagnosis is uncertain or to assess for complications of celiac disease.

- X-rays of the small bowel can be taken after the patient swallows a substance known as barium. On the X-ray, the doctor may observe dilatation of the small intestine or an absence of the normal pattern of the small intestine due to destruction of the villi. Similarly, abdominal ultrasound has also been used to suggest the diagnosis of celiac disease but at this time imaging studies are not routinely recommended in the diagnosis and follow up of celiac disease.
- Bone density studies (also referred to as a DEXA scan) should be performed in those recently diagnosed with celiac disease. DEXA scans are usually recommended after 12 months of strictly following a gluten-free diet.

Procedures:

In the initial workup of celiac disease, an endoscopic biopsy of the small intestine is usually performed. A small tube with a video camera on the tip is placed down the throat and into the stomach and small intestine while the patient is sedated. The gastroenterologist takes samples of tissue from the small intestine, which can then be looked at under the microscope for evidence of celiac disease. Visit Endoscopy under Medical Management on www.celiacnow.org.

The tests and procedures listed above are not to be taken as all-inclusive. Depending on the extent of disease, further testing or referral to other specialists may be necessary. Nonetheless, these are some of the common tests and results you might find carried out in an individual suspected of having celiac disease. Finally, improvement of symptoms upon the removal of gluten from the diet provides further clinical evidence of celiac disease.

What are the recommended blood tests to determine whether or not someone has celiac disease (CD)?

IgA-tTG and total IgA (immunoglobulin A): Currently, the most frequently used test is IgA anti-tTG, or tissue transglutaminase.

The tTG IgA test will be positive (>19) in about 98% of patients with CD that have been on a gluten containing diet. We call this number the test's sensitivity. The same test will come back negative (<20) in about 95% of healthy people without CD. We call this the test's specificity.

Total IgA: Your doctor may additionally check your total IgA level to determine if you have an IgA deficiency, which is a harmless condition that is present in 2-3% of patients with CD. If someone is IgA deficient, they may have a false negative result to their EMA or tTG tests. In this case, your doctor can order a DGP test. He/she could also order an IgG tTG (immunoglobulin G-tTG) test instead, although this is slightly less accurate than IgA tTG.

DGP: (deamidated gliadin peptide) There are occasional individuals whose IgA-tTG results may be misleading. In this case, we recommend using a newer test, anti-DGP (IgG and IgA antibodies to deamidated gliadin peptide)(1). It is similarly accurate to IgA-tTG and is useful for patients with IgA deficiency.

EMA: Another blood test that your doctor may order is an EMA, or endomysial antibody test. This test is used less frequently than the IgA anti-tTG, but since it detects the same target antigen on a tissue section it can be just as accurate.

AGA: Anti-gliadin antibodies, or AGA, were used in the past, but are typically not routinely checked now because they are much less accurate than tTG or EMA.

Gene Testing: If your doctor is still uncertain as to whether or not you have CD, s/he may order an HLA-DQ2 or HLA-DQ8 blood test. This is a genetic test that will help her/him determine whether or not you have CD. Again, this can only rule out the disease but will not definitively confirm the disease.

Visit Blood Tests, Endoscopy and Genetics under Medical Management on www.celiacnow.org.

How accurate are the blood tests?

These blood tests are very accurate, especially when the tTG and EMA levels are elevated, as in patients with celiac disease (CD). In a small number of cases, though, a patient with CD may have a negative blood test.

Visit Blood Tests under Medical Management on www.celiacnow.org.

How long does it take for the tTG blood test for celiac disease to be normal?

It depends on the test. One of the tests used most often, tissue transglutaminase (tTG), has a half-life of six months. In other words, it should drop by a half-fold in six months. Hence, if you started off at a tTG level in the thousands, it might take several years to normalize. However, most tTG levels normalize within several months to one year in adults on the gluten-free diet. Evidence suggests that after 6 – 12 months of adherence to a GFD, 80 % of patients will test negative by bloodwork and in about 90 % of those adhering to the GFD for 5 years (1).

Many times it is tricky to predict when the test should become normal since some tTG tests don't report values beyond a certain value. For example, one test reports values up to 120 mg/dl after which all values whether, in the hundreds or thousands, are reported in the same manner, i.e. >120.

Is it important to have repeat blood tests or biopsies to confirm that I have celiac disease?

It is important to be accurately diagnosed with blood tests and a biopsy before going on a gluten-free diet. After starting the diet, follow-up tests are individualized based on age, symptoms, and other health problems. Routine follow-up with a dietitian skilled in celiac disease and a gastroenterologist is strongly recommended (1). In most cases, blood tests are performed on a regular basis, while repeat biopsies are not usually necessary. A doctor will determine which specific tests are needed.

I think I have celiac disease (CD), but I had a negative blood test. How do I know if I have it?

If you are on a gluten-containing diet, and had a negative blood test for CD, you can elect to have a biopsy taken. Approximately up to 5-16% of patients with CD have a negative blood test (1). If your blood tests and your duodenal biopsy are both negative on a gluten containing diet, you can conclude that you do not have CD. If any new symptoms develop over time, you can always be rechecked.

Visit Screening and Blood Tests under Medical Management on www.celiacnow.org.

Some patients without CD may experience discomfort after ingesting gluten. These patients may feel better on a gluten-reduced diet. This condition is called non-celiac gluten sensitivity and is not the same as celiac disease. Visit Non-Celiac Gluten Sensitivity on www.celiacnow.org.

My doctor told me I have celiac disease (CD), but I feel fine. Should I start the gluten-free diet?

There is no evidence that strongly supports recommending a gluten-free diet if you had a positive blood test for CD and/or biopsy findings of celiac disease, but no symptoms of the disease. However, the answer remains controversial and the experts are undecided. If you have no symptoms but you have positive bloodwork with evidence of small intestine damage in addition to evidence of other organ involvement or nutritional deficiencies then you have a condition called “silent celiac” disease and may benefit from a GFD. However if your intestinal biopsies are normal and you have no evidence of other organ involvement or nutritional deficiencies then you have a condition called “potential celiac disease”. This may be especially true in children with high risk relatives who are frequently tested (2). If an individual has no symptoms at all, some doctors will wait and watch. Your doctor will check other lab values, though, to determine whether CD has had other effects on your body. You should be aware of symptoms of CD that do not affect your gastrointestinal system that you may be experiencing. Visit FAQs Associated Conditions on www.celiacnow.org.

Other doctors are more aggressive and will recommend that their patients start a gluten-free diet, especially if they are concerned about a possible cancer risk. Due to the lack of clear guidelines it is best to talk to a celiac disease doctor about the pros and cons of treatment for CD.

Why are people sometimes diagnosed so late in life? Could a person have had it for years and not known it?

The typical age of celiac diagnosis among adults is sometime in their forties. It is very common for people to have had it for a while before being diagnosed. The average time from onset of gastrointestinal symptoms until diagnosis is 11 years. This lag time might be significantly higher in people who have celiac disease but do not have symptoms.

How often should a patient or family member of a patient have a repeat blood test if his/her test was negative?

If your doctor has a strong suspicion that you have celiac disease (CD), even with a negative blood test s/he may perform an endoscopy with biopsy, as up to 5-16 % of patients with CD may have a falsely negative blood test (1). If the blood test and biopsy are normal then you do not have CD and there is no need for repeat testing unless your symptoms change. For an adult relative of a person with CD, there is no need to repeat a blood test unless the relative starts to develop symptoms of CD. Children, however, may need to be tested regularly, and should see a pediatric gastroenterologist. Visit Screening, Blood Tests and Endoscopy under Medical Management on www.celiacnow.org.

If a child has a sibling and a parent who have been diagnosed with celiac disease (CD) by both blood test and biopsy, do you recommend that the child have genetic testing even though his blood test was negative? The child in question has no obvious symptoms.

This is a choice parents need to make for themselves and their children. However, children of parents with CD or with siblings with CD should consider the genetic test. If negative, CD can essentially be ruled

out for life, while the standard blood tests could turn positive in the future and so require repeated testing.

What is the meaning of HLA-DQ2 and HLA-DQ8?

HLA-DQ2 and HLA-DQ8 are the names of two genetic markers which are part of the immune system and are able to stick to the gluten proteins. Every person with celiac disease (CD) has at least one of these genetic markers. If your doctor is unsure as to whether or not you have CD, s/he can perform a simple blood test to determine whether or not you have one or both of these genes. If you do not have one of these two genetic markers, your doctor can rule out CD. If you DO have one of these genetic markers, it is possible that you have or may develop CD. Your doctor will need to perform more tests. You do not need to eat gluten in order to have the gene testing.

Do people with celiac disease (CD) have one or both of the genes, HLA-DQ2 and HLA-DQ8, passed down from their parents? How do you inherit these genes? Can a parent have gluten sensitivity and the son or daughter have CD?

The Human Leukocyte Antigen (HLA) genes are linked to many autoimmune diseases such as CD. Everyone has a copy from the mother and a copy from the father. These copies can come in different versions called alleles. The HLA gene alleles that predispose to CD are called DQ2 and DQ8. One may have DQ2 or DQ8 in one of the copies or in both. People who have only one copy of DQ2 or DQ8 have a risk of about 3% of having CD, whereas people who have two copies of either have a risk around 10%.

HLA types are actually combinations of genes so it is possible to be DQ2 positive even if neither of your parents has this gene. Overall though, at least 50% of children of parents carrying DQ2 or DQ8 will also have one of these. Almost all people with CD have at least one DQ2 or DQ8 copy. This is why genetic testing is so useful to rule out CD. Nevertheless, since 30-40% of the general population has at least one copy of DQ2 or DQ8, the gene test is not a good test to confirm CD (1).

To date, it is not clear whether non-celiac gluten sensitivity is associated with the same genes linked to CD or any other genes. While it is not uncommon to see families with different members being either celiac or non-celiac gluten sensitive, we do not know at this point whether this is caused by chance or not.

What is a gluten challenge? Do I need one?

A gluten challenge is recommended when a person is on a gluten-free diet, but his/her doctor is unsure of whether or not the patient has celiac disease (CD). Genetic testing can resolve this question if celiac genes (HLA DQ2 and DQ8) are absent. If celiac genes are present a gluten challenge may be needed (1). In this case, gluten is reintroduced into the diet starting with ¼ slice of gluten containing bread and increasing to 2 slices of bread for, ideally, 6-8 weeks (if the challenge can be tolerated for that long). Blood tests and an intestinal biopsy are performed. If the gluten challenge is not tolerable for the full 8-week period blood tests and biopsy can be performed sooner (3). People with confirmed CD do not need to have a gluten challenge.

Note that patients should ONLY undergo a gluten challenge if instructed to do so by their doctor. Patients who have been following a gluten-free diet should not reintroduce gluten into their diet without talking to their doctor.

Is there a stool test to determine whether or not I have celiac disease (CD)?

Stool tests have not been proven to be effective in screening for CD. Blood tests remain the most effective and reliable way of screening for CD.

How does having a problem with candida affect celiac disease (CD)?

Candida albicans is a yeast that is part of our normal digestive and skin flora. In certain cases when the immune system or the normal flora is altered (such as antibiotic use, malnutrition, diabetes, etc.), this usually harmless yeast can cause inflammation of the skin as well as digestive and genital mucous surfaces. It may even get into the bloodstream. Although there is some cross reactivity that has been evidenced between gluten peptide and proteins on candida, actual causation is difficult to establish at this time(4). Hence this theory is not widely accepted.

Are high eosinophil levels connected to celiac disease (CD) and/or allergies (such as pollen, mold, mildew and dust mites) or asthma?

Asthma, allergic rhinitis (hay fever) and atopic dermatitis are all part of a common spectrum of diseases called atopic diseases. A common finding in the blood work of people with this spectrum of diseases is a high eosinophil count. Some researchers have found that asthma and CD tend to happen together often. Nevertheless, based on our current knowledge, CD and atopic diseases are separate diseases with different biologic mechanisms.

What is the difference between being sensitive to gluten and having celiac disease (CD)?

In non-celiac gluten sensitivity (NCGS), a person has gastrointestinal symptoms from gluten exposure but does not have significant rise in tTG level (the blood test for CD) or any damage to the small intestine. NCGS is not believed to be triggered by a T-cell mediated immune response to gluten, as is the case with CD. In CD, gluten activates one's immune system to attack the cells of the small intestine and cause damage. That is why tTG or other celiac-specific markers rise.

Often, it is not easy to distinguish between these two entities based on the clinical picture alone. Genetic testing, blood work and endoscopy might be needed. However, our group at BIDMC recently found that people who report symptoms with gluten exposure and who have negative blood markers, no family history of CD, no personal history of autoimmune diseases (such as type I diabetes), and no diarrhea associated with weight loss are extremely unlikely to have CD and do not need endoscopy(4). Visit Non-Celiac Gluten Sensitivity on www.celiacnow.org.

Does non-celiac gluten sensitivity cause visible damage in an endoscopy/biopsy?

Non-celiac gluten sensitivity (NCGS) does not cause visible damage of the small intestine in endoscopy. But occasionally, the biopsy may show some inflammatory cells only. The presence of normal villous architecture is the characteristic feature of NCGS, unlike in celiac disease.

Is it possible that non-celiac gluten sensitivity (NCGS) is a precursor to celiac disease (CD)?

Current knowledge about NCGS is still very limited. So far, most research has failed to prove a common biology in both conditions. People with NCGS often have symptoms that may be more similar to Irritable Bowel Syndrome (IBS) than with CD but there is considerable overlap in symptoms. Some research has shown that patients with diarrhea-predominant Irritable Bowel Syndrome (IBS-D) may have gluten sensitivity. Also, according to guidelines, all patients with IBS-D should get screened for CD. The true relationship between CD, NCGS and IBS remains unknown. At this point, we believe that the risk of NCGS progressing to CD is very low. We await further studies of this issue.

Shouldn't every citizen in the U.S. be tested for celiac disease (CD)?

Screening every person in the US for CD might not be cost-effective given that it is estimated to affect only about 1% of the general population(1). Nonetheless, most of the subjects who have CD are not aware of their diagnosis. This is due to insufficient screening in high risk individuals and low disease awareness in the community. To improve diagnosis rates, we recommend screening adults and second degree relatives of people with CD as well as people with autoimmune diseases who have suggestive symptoms. It is also recommended that children of individuals with CD get screened once even if they are not symptomatic.

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