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INFORMATION ON CELIAC DISEASE

Introduction: What is celiac disease?

Celiac disease is a disease of the small bowel. It's a chronic immune mediated bowel disorder in which ingestion of the protein gluten leads to changes in the small intestine (i.e. villous atrophy) in genetically susceptible individuals. Gluten is a protein found in wheat, rye, and barley. The main underlying issue is an abnormal response of the affected person's immune system to gluten.

Celiac disease is an increasingly common condition in the population and 1 to 1.5 % of people are affected. Females are two times more likely to be affected than males. Between 1975 and 2000 the prevalence of celiac disease rose five fold. The exact reasons for this are not clear.

Celiac diseases can lead to a variety of "intestinal symptoms" and "extraintestinal" symptoms, along with a deficiency of macronutrients and micronutrients.

The diagnosis is definitively confirmed by a biopsy of the small bowel.

What are the symptoms of celiac disease?

Affected patient have a wide array of symptoms – although some have none at all. It has been estimated by Fasano and colleagues that 21 % of patient with CD have no symptoms, 27 % have the classic CD presentation including diarrhea, malabsorption and weight loss, and 51 % have non classic CD presentation with issues such as constipation, anemia, osteoporosis, skin rashes, neurological issues and elevated liver enzymes. The wide array of possible symptoms and presentations of celiac disease leads to a delay in diagnosis simply because the condition mimics so many other health conditions. Many patients go (on average) about 11 years from symptom start until actually getting a proper diagnosis. Although there is a strong genetic predisposition, the average age of diagnosis is not until 45.

Symptoms of celiac disease may affect the bowel. However, there is a wide array of other symptoms that can be present. The bowel symptoms may be absent or subtle and include bloating, abdominal pain, diarrhea and constipation. In many people with celiac disease, the bowel issues are first mistaken for irritable bowel syndrome (IBS).

Below is a list of symptoms that patients with celiac disease may experience

General Category of Body Area Affected	Specific Symptom
General symptoms	• Chronic fatigue • Swelling of the hands and feet • Failure to thrive (infants and children)
Abnormal Blood tests	• Anemia (low hemoglobin) • Low ferritin levels (test for iron) • Low B12, Low Folate, Low vitamin A, D, E, K levels.
Gastrointestinal symptoms	• Abdominal pain, Vomiting, Reflux • Bloating, Constipation, Gas, Lactose intolerance • GI lymphoma • Foul smelling stool • Elevation of liver enzymes • Weight loss or weight gain
Joint and Muscle symptoms	• Arthritis, Bone pain, Fibromyalgia • Numbness/ Neuropathy (pins and needles) • Osteopenia • Short stature (children)
Reproductive system issues	• Delayed puberty, late menarche, early menopause • Recurrent miscarriages (women) • Menstrual irregularities (women) • Infertility (both men and women)
Skin issues	• Itchy skin (elbows, knees), Eczema like rashes • Hair loss
Dental issues	• Mouth sores (cankers), Discolored teeth
Brain and Neurological issues	• Attention Deficit, Anxiety, Depression, Brain Fog • Headaches and Migraines, Seizures, Irritability • Developmental delay (children)
Autoimmune Diseases	• A very wide range of autoimmune diseases may be associated or present in patients with celiac diseases including type 1 diabetes, multiple sclerosis, Hashimoto's thyroiditis, autoimmune hepatitis, Addison's disease, arthritis, Sjogren's, idiopathic dilated cardiomyopathy, IgA deficiency and IgA nephropathy
Family History	• Celiac disease is present in 10 % of family members

What blood tests are helpful in diagnosing celiac disease?

When evaluating for possible celiac disease, several blood tests are important as a first screening test. These include IgA anti TTG (which is mainly the one to order) as well as anti-endomysial antibodies (ordered if the anti TTG titers are low such as less than 2 times the upper limit of normal). Serum IgA is ordered to ensure that the patient does not have IgA deficiency (which would cause the IgA TTG test result to come back negative).

If a patient is found to be positive for the anti-TTG antibody they are then referred to gastroenterology for consideration of a biopsy of the bowel to confirm the diagnosis of celiac disease. There are classic features seen on biopsies of the duodenum part of the bowel that enable confirmation of the diagnosis.

The most helpful blood test for screening celiac disease is an IgA anti -TTG test (short for anti-tissue transglutaminase). This is the most helpful starting test and most labs use this preferentially over anti-endomysial antibodies. The IgA anti TTG has 98 % sensitivity and 98 % specificity.

If a patient has a condition known as IgA deficiency, the IgG deaminated gliadin peptide (DGP) is used for diagnosis instead of anti IgA TTG. It is a newer test but no better than anti TTG for a screening test.

If TTG is negative but there is still suspicion for celiac disease, several steps may be taken. First, anti-endomysial antibody test (and possibly IgG DGP antibodies) may be ordered. If positive, referral is made to the gastroenterology team for bowel biopsy. Second, HLA DQ2 and HLD DQ8 genetic testing may be performed if antibody tests are negative (seen in 2-3 % of patients with celiac disease). Almost all patients with celiac disease are HLA DQ2 or HLA DQ8 positive (or both). However, lots of people without celiac disease are also HLA DQ8 and HLA DQ2 positive too. The key point here is that if a patient undergoes testing for HLA DQ2 and HLA DW8 and the results come back negative .. it's quite unlikely they have celiac disease and further testing and work up for celiac disease can usually stop. Finally, if there is still suspicion, a gastroenterologist will likely perform a biopsy of the small bowel looking for the classic features of celiac disease.

These blood tests mentioned above (anti-TTG, anti-endomysial, anti-DGP) are only likely to be positive in a patient with celiac disease who is regularly consuming gluten in their diet. If a patient actually has celiac disease, but is avoiding all gluten, these tests could be negative. It only takes 6-12 months of a gluten free diet to convert a patient from having positive tests to negative tests. It's often worth still testing for anti-TTG and anti-endomysial antibodies because prior studies have taught us many people who think they are consuming a gluten free diet actually are still taking in a good amount of gluten.

However, if tests are negative and a patient is already on a gluten free diet, the recommended next step is to order HLA DQ2 and HLD DQ8 genetic testing. Almost all patients with celiac disease are HLA DQ2 or HLA DQ8 positive (or both). However, lots of people without celiac disease are also HLA DQ8 and HLA DQ2 positive too. The key point here is that if a patient undergoes testing for HLA DQ2 and HLA DW8 and the results come back negative .. it's quite unlikely they have celiac disease and further testing and work up for celiac disease can usually stop.

If one of the DQ2 or DQ8 tests come back positive, it's possible that celiac disease could still be present. In these cases consultation with a gastroenterologist is recommended to decide whether or not to have the patient get back on consuming gluten in the diet for 2 to 8 weeks as a "challenge test" and then repeating the blood tests or repeating bowel biopsies. 2 weeks of a gluten containing diet "challenge" is not quite as helpful in diagnosing celiac disease as an 8 week 'challenge' but can still yield helpful information for the gastroenterologist.

Repeating the anti-TTG and anti-endomysial blood tests at the end of the 8 week gluten containing diet "challenge" is normally done and then the tests are repeated again a month later if needed. Typically the gastroenterologist also does another bowel biopsy as well at that 8 week time point. Patients who actually now show positive antibodies for anti-TTG or anti endomysial are said to have potential celiac disease. Patients with a positive bowel biopsy with the features of celiac disease are said to have a confirmed diagnosis.

Do children need small bowel biopsy to confirm the diagnosis of celiac disease?

We generally refers suspected cases of pediatric celiac disease to a pediatric gastroenterologists to make that decision. The European Society for Paediatric Gastroenterology, Hepatology and Nutrition proposed a non-biopsy approach to the diagnosis of CD in children. These guidelines state that before a small intestinal biopsy can be avoided, a symptomatic patient must fulfil the following criteria:

- have a positive TTG antibody test result more than 10 times the upper limit of normal,
- have a positive endomysial antibody test result, and
- have positive results for HLA-DQ2 or HLA-DQ8 testing.

In addition to the anti TTG test, what blood tests are considered?

In addition to the screening tests, other tests may be helpful. These include hemoglobin, ferritin, albumin, calcium, potassium, magnesium, phosphate, ALP, zinc, vitamin D

How is celiac disease treated and monitored?

Patients who are diagnosed with celiac disease are counselled on how to avoid gluten in their diet through a gluten free diet (GFD). Consultation with a dietician is often very helpful to help patients understand how best to avoid gluten and structure their eating in ways that allow them to avoid gluten. IgA TTG antibodies can be periodically measured to see if the patient's diet is truly gluten free. Repeat biopsies can evaluate the health of the colon mucosa.

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