Celiac Disease and Non-Celiac Gluten Sensitivity

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The gluten-free diet is everywhere! For the public, it has become a panacea for health woes, an answer to years of ongoing problems. In the food industry, it creates a twinkle in many a CEO's eye—one that looks strikingly similar to a dollar sign. The gluten-free community has taken on a life and personality of its own.

In this day and age of social media, confusion and misinformation about celiac disease and non-celiac gluten sensitivity are widespread. As physicians, particularly in primary care, we have the opportunity to correct misperceptions as well as identify patients with these common and underdiagnosed conditions. The media swirl surrounding gluten is vast, and we need to respond to patient questions with accurate information and a well-informed diagnostic plan.

I have a large number of patients in my practice with celiac disease (CD) or non-celiac gluten sensitivity (NCGS), and the disparity in diagnosis and treatment in patient histories is astounding. There is confusion on many fronts. Misinformation stems in part from Internet lore and well-meaning friends, variables that are difficult to control. But I also see many people whose physicians have given them misinformation, or no information, about CD and NCGS. This shortfall is accompanied by the more recent trend of physician recommendations to start a gluten-free diet to "see if it helps" without first doing appropriate testing for CD. While well intended, this approach can be detrimental to patients and their families.

I hope that by reading this article, our local medical community will gain a clear understanding of three key points:

- The difference between CD and NCGS.
- The importance of testing patients for CD before starting a gluten-free diet.
- Reliable resources on CD and NCGS for both you and your patients.

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Celiac Disease

Celiac disease is common. A landmark 2003 study found the incidence of CD in people who were donating blood or getting routine checkups to be 1/133.[1] If someone was symptomatic or had a celiac-related disorder such as anemia, diabetes, osteoporosis, short stature, infertility or Down's syndrome, the incidence of CD increased to 1/68 in adults and 1/25 in children. If there was a first-degree relative with CD, the incidence increased further to 1/22—irrespective of whether or not the relative had any symptoms.

CD is an autoimmune, genetic, lifelong condition that can present at any age. It causes damage to the villi of the intestinal mucosa because of an abnormal immune reaction to gluten, a protein found in wheat, barley and rye. With continued ingestion of gluten, a person with CD develops malabsorption and its subsequent complications, including anemia, vitamin deficiencies, osteoporosis, infertility and neurologic symptoms. CD is a multi-organ system disorder and can affect the thyroid, liver, heart and reproductive organs, as well as the musculoskeletal system and brain.

The face and presentation of CD have changed dramatically over the last decade. The disease is a chameleon whose presentation varies from one person to the next. Once thought to be a "wasting" disease, now up to 50% of CD patients are overweight or obese at diagnosis.[2] Another common misconception is the need for gastrointestinal symptoms to initiate a diagnostic evaluation, yet such symptoms are only present 30–40% of the time at diagnosis, and their absence should not preclude an assessment.[3] "Atypical" presentations for CD are now common, such as anemia, fatigue, osteopenia, rashes, dental enamel defects and aphthous ulcers. Also changed is the belief that CD is found primarily in Northern European Caucasians. The ethnic boundaries of CD are now blurred as the disease appears to be equally common in other ethnic groups.[4–6]

Who gets CD?

The following three factors must be present to have active CD:

Genetic predisposition. Patients must carry the HLA-DQ2 gene and/or the HLA-DQ8 gene. The presence of one or both of these genes is necessary for diagnosis of celiac disease, but their presence is not diagnostic. Thirty to forty percent of the population carries one of these two markers, yet only 5% develop celiac disease. The presence of either DQ-2 or DQ-8 only indicates a predisposition. If neither marker is present, celiac disease can be ruled out. Researchers are currently evaluating other genes for their involvement in celiac disease. Of note, there are currently no scientifically validated genes associated with NCGS.

Gluten. Patients must be consuming gluten for CD to be active.

Environmental trigger. Not all triggers are known, but identified triggers include early/repeated infections, pregnancy and GI infections.[7,8]

What are the appropriate screening tests for CD?

Patients must be consuming gluten for screening tests to be valid. Basic screening is a serum TTG IgA, which should be accompanied by total serum IgA to rule out IgA deficiency. (Some labs also include a DGP-IGA and EMA in their celiac screen/panel, or they do these tests as a reflex.) The confirmatory test is an endoscopic biopsy. Of note, many celiac centers and practitioners follow a more extensive evaluation process involving screening antibodies, genetic testing, clinical response to a gluten-free diet, and endoscopy. These protocols and other testing algorithms are beyond the scope of this article.

What is the treatment for CD?

The only known treatment for CD is a strict, lifelong gluten-free diet—100% of the time. Pharmaceutical treatments currently in clinical trial may aid in the digestion of gluten or in decreasing intestinal permeability. Current over-the-counter digestive enzymes for digesting gluten are not appropriate for people with CD. The treatments under development are meant for times when there is a risk of cross-contamination, such as when dining out. They will not be a cure, but their development will be helpful in addressing the social and psychological issues surrounding CD. One company is pursuing a vaccine, but it is only in the early stages of development.

Non-Celiac Gluten Sensitivity

In 2011 researchers began addressing the presence of reactions to gluten in patients who did not have CD.[9,10] Subsequently, a consensus panel developed the following definition of NCGS: "Non-celiac gluten sensitivity is a term that relates to one or more of a variety of immunological, morphological or symptomatic manifestations that are precipitated by gluten in individuals in whom celiac disease has been excluded." In short, patients who have been properly evaluated for CD with a negative result but experience symptoms when ingesting gluten are deemed to have NCGS.

The pathophysiology of NCGS is the subject of intense study. It appears as if NCGS may encompass several different entities rather than one discrete disorder. In some patients, their reaction may be due to the carbohydrate component of gluten, such as in fructose malabsorption; in other patients, the reaction may be due to proteins, such as amylase trypsin inhibitors.

NCGS pathophysiology is a rapidly evolving area of knowledge with many unknowns. The sensitivity does not appear to be autoimmune in nature, and it is unknown if there is a genetic component or an environmental trigger. What is known is that a gluten-free diet is beneficial to these patients and can bring on much-needed relief of their symptoms.

How do you diagnose NCGS?

There is no validated test to diagnose NCGS. Some online labs offer blood, saliva or stool tests for gluten sensitivity, but they are unvalidated and not recommended. It is impossible to develop a test when the mechanism of NCGS has not been determined. Diagnosis is made by ruling out CD while the patient is on a gluten-containing diet. Once CD is ruled out, a gluten elimination diet is prescribed. If symptoms improve, the patient is deemed to have NCGS. Using a response to initiation of a gluten-free diet as a prognostic indicator will give inaccurate results, as both celiac and NCGS can have similar responses to a gluten-free diet.

How do you treat NCGS?

At this point, a gluten-free diet is the starting point for NCGS patients. The diet may not provide complete relief, so further evaluation may be needed. Once studies clarify what NCGS truly is, more targeted and individualized therapies will be developed.

It is not clear how strict the gluten-free diet needs to be for patients with NCGS. Do they need to be as careful as patients with CD? Do they have the same risk of long-term complications if they do not adhere to the diet? The answers are unknown.

The Importance of Testing

The blood tests and biopsy used to test for CD require a patient to be consuming gluten to obtain valid results. If you start a patient on a gluten-free diet without first evaluating for CD, it becomes very difficult to get a proper diagnosis. Patients who experience clinical improvement on a gluten-free diet will rarely restart a gluten-containing diet to get an appropriate diagnosis. They finally feel well, and returning to being sick is just not an option.

The importance of testing cannot be overemphasized. Consider these factors:

CD is lifelong, but we don't know about NCGS. Why subject someone to a lifelong, strict gluten-free diet if they don't need it? The social and psychological implications can be vast.

CD requires a strict gluten-free diet. This may not be the case for all patients with NCGS. This difference can be life-changing to some patients.

CD is genetic. If you miss a diagno-

sis of CD, you may miss or delay a diagnosis in their child, sibling or parent.

CD has long-term risks and complications. These parameters may be different for NCGS. We simply don't know yet. Appropriate diagnosis is necessary for proper follow-up care.

Insurance reimbursement can be more challenging without a diagnosis. Currently, there is no reimbursement code for NCGS. You and your patients are more likely to get reimbursed for a diagnosis of CD that will be missed if it is never tested for.

Accommodations. Because of a 2012 settlement between Lesley University and the Department of Justice, schools may soon be legally required to accommodate students with documented food allergies and CD. In order to obtain ADA accommodations, students will need documentation stating they have a diagnosis of CD or food allergies. At this time, NCGS does not appear to be covered under the ADA.

I hope the information above has helped clarify the rapidly evolving topic of gluten-related disorders. Unfortunately, according to current estimates, only 15% of American patients with CD are diagnosed. By using this article and the resources in the sidebar, you should be able to identify more of these patients and get them on the road to a healthier and more vibrant life. ◇

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Reliable Resources

Beth Israel Deaconess Celiac Center: www.celiacnow.org

Celiac Community Foundation of Northern California: www.celiaccommunity.org

Columbia University Celiac Center: www.celiacdiseasecenter.columbia.edu

University of Chicago Celiac Disease Center: www.cureceliacdisease.org