

Gastroenterology

Celiac Disease: Myths and Facts

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Celiac disease is a genetically inherited autoimmune disorder triggered by dietary gluten that damages the intestinal villi in the proximal small intestine. Once tall and slender, the damaged villi become blunted or completely flattened. As a result, the available absorptive area is reduced considerably, which causes malabsorption. This condition affects both children and adults. In young children, celiac disease most commonly is detected some time (typically months) after cereals have been introduced to the diet. In older children and adults, frequently it is diagnosed following various challenges to the immune system. These types of challenges include infections, pregnancy and childbirth, and surgery. Once diagnosed, the disease is treated with a lifelong adherence to a gluten-free diet, which requires the patient to avoid dietary gluten found in wheat, rye, and barley and products derived from these sources. Consultation with a knowledgeable dietitian can help a patient and family adopt the diet and avoid learning that a product contains gluten after the fact.

DISPELLING THE MYTHS OF CELIAC DISEASE

Unfortunately, many myths still abound about celiac disease, and these misunderstandings on the part of physicians result in critical delays in diagnosis. In the United States, an adult typically receives a diagnosis of celiac disease more than 10 years after symptoms are first noted.¹ This delay in diagnosis is considerably shorter in children, who tend to experience less subtle symptoms including short stature, diarrhea, stomach pain, and behavior changes. Commonly, adult patients may suffer for years with anemia, fatigue, and mild or vague abdominal symptoms such as bloating, pain, loose stools, or constipation. Many receive a diagnosis of irritable bowel syndrome and may be referred to psychiatric counseling after therapies are unsuccessful. Even many of those who finally undergo an upper-digestive endoscopy may not be fortunate enough to receive an accurate diagnosis; when results of an endoscopic examination of the duodenum are normal, physicians often do not obtain duodenal biopsies. Unfortunately, this is the rule, not the exception, for patients with celiac disease.

These delays increase the amount of time a person with celiac disease is exposed to gluten and may result in the development of other autoimmune disorders. There is now solid evidence that the risk of developing associated autoimmune disorders increases with increased diagnostic delay.² Furthermore, celiac disease may present a wide variety of complications. Among them, neurological and psychiatric conditions such as epilepsy, ataxia, depression



and/or anxiety, and learning and behavioral difficulties; gynecological problems such as adverse effects on pregnancy, repeated miscarriages, and infertility³; skeletal problems, including osteopenia, osteoporosis, and related fractures; and liver disease.

Thus, a common myth that must be dispelled is that celiac disease is simply a gastrointestinal disease that causes chronic diarrhea. Gastrointestinal symptoms (still a common manifestation in infancy and early childhood) may indeed be totally lacking in a patient with celiac disease and can be quite common. Table 1 lists the main forms of extraintestinal celiac disease. It is imperative that physicians understand that behind each of these disorders, a hidden celiac disease may be the real and only culprit.

THE FACTS ABOUT CELIAC DISEASE

FACT: The prevalence of celiac disease in the United States is more than 1 in 200 healthy individuals. The likelihood that a primary care physician will encounter patients with undetected celiac disease in his or her practice is very high. In addition, specialists in many fields, including obstetrics and gynecology, developmental pediatrics, endocrinology, neurology, immunology, and gastroenterology have a significant number of patients in their practices who may have celiac disease.

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In 1998, Alessio Fasano and colleagues⁴ tested blood samples from a blood bank to develop a reference point for the prevalence of celiac disease in the United States. They found that of 2,000 samples, 1 in 250 exhibited celiac-specific antibodies. In a much larger,

Table 1. — Main Presentations of Extraintestinal (or ‘Atypical’) Celiac Disease

- Dermatitis herpetiformis
- Permanent enamel hypoplasia
- Iron deficiency anemia that is resistant to oral iron therapy
- Short stature, delayed puberty
- Chronic hepatitis with hypertransaminasemia
- Primary biliary cirrhosis
- Arthritis
- Osteopenia/Osteoporosis
- Epilepsy with occipital calcifications
- Primary ataxia
- Psychiatric disorders
- Infertility

nationwide prevalence study also led by Fasano⁶ (in which we participated), it was determined that of 13,000 participants, the rate of celiac disease in the healthy population exceeded 1 in 200. According to these projections, about 0.7 percent of the US population has celiac disease. At this time, it is estimated that only a small fraction of these individuals have received a diagnosis.

FACT: There are 256 symptoms and related conditions that indicate a patient may have celiac disease. However, a significant percentage of people with celiac disease, possibly the majority, exhibit no symptoms at all; these individuals are considered to have silent celiac disease and often are relatives of patients diagnosed with celiac disease. Since they also appear to be at risk of complications, screening is indicated in first-degree family members of people with celiac disease, as well as for people who have a related condition or series of symptoms. Table 2 lists the prevalence of some conditions known to be associated with celiac disease.

FACT: Screening for celiac disease requires correct use of the available serological

markers. While frequently physicians ask for a “celiac panel,” this is understood differently by different laboratories, and often includes antibodies such as anti gliadin, which now is obsolete, owing to its lack of sensitivity and specificity. An appropriate blood screening should include antiendomysial antibody (EMA) or anti-tissue transglutaminase (tTG) and the determination of total serum IgA level.

The EMA and tTG tests are designed to measure the presence of the same antibody using two different methods. At this time, the EMA test is slightly more sensitive and specific than the tTG test. Provided the total serum IgA level is normal, these tests have a very high negative predictive value for patients who range in age from 2 through 50 years. A positive test result is not enough evidence to diagnose celiac disease; however, it is strong enough to indicate that a small-bowel biopsy is warranted.

FACT: The gold standard for diagnosing celiac disease is an EGD with multiple biopsies of the duodenum and jejunum. It is a common misperception that damage from celiac disease will be visible to the physician who performs the esophagogastroduodenoscopy (EGD). In most

Table 2. — Prevalence of Conditions Associated With Celiac Disease	
Condition	Approximate Prevalence of Celiac Disease, %
Insulin-dependent diabetes mellitus	6
Thyroiditis	4
Sjögren syndrome and other connective-tissue diseases	5
Primary biliary cirrhosis	3
Down syndrome	12
Turner syndrome	3
Williams syndrome	3

cases, intestinal damage is detected only through pathology. It is also commonly thought that celiac disease involves all of the duodenum. In fact, the microscopic lesion of celiac disease often is patchy. But that's not all: The flat mucosa originally described as the landmark of this condition is indeed nothing but the tip of the iceberg of the pathological changes. More subtle signs of celiac disease, including the presence of intraepithelial lymphocytes, precede that profound alteration,⁶ and in many cases may be the only changes seen ("minimal enteropathy"). For instance, the Figure shows a microscopic view of a tall, slender villus that few pathologists would recognize as abnormal. There is a subtle, but significant, increase in intraepithelial lymphocytes.

In the early 1990s, a select panel of experts (including Dr. Guandalini, co-author of this article) from the European Society for Pediatric



FIGURE. — Microscopic view of a tall, slender villus. Few pathologists would recognize it as abnormal. There is a subtle, but significant, increase in intraepithelial lymphocytes.

Gastroenterology and Nutrition⁷ formulated diagnostic guidelines for celiac disease that currently are accepted worldwide. In light of the new research developments, it is apparent that these guidelines should be wisely and expertly implemented. These guidelines stipulate that obtaining an intestinal biopsy is mandatory to finalize the diagnosis.⁸ In other words, despite the recent improvements in serological testing, the biopsy is still required for diagnosis. In some

doubtful cases, testing the subject for the HLA DR3, DR5/7, or DR4 genes (which are known to be linked to celiac disease) also may be necessary. We routinely perform this analysis in selected cases.

FACT: A gluten-free diet is the only treatment for celiac disease, and it is a lifelong treatment. Zero tolerance is the only acceptable

approach to a condition triggered and maintained by unknown, possibly minimal, amounts of gluten. As a result, considering the widespread, insidious presence of gluten in thousands of available products, it is mandatory that the expert professionals who counsel these patients ensure that they understand the diet and its subtleties and comprehend how important it is to maintain strict adherence to the diet. Effective patient counseling at the time of diagnosis helps ensure that patients do not act on the urge to "cheat" and will adapt to the social and emotional changes that the diet requires.

CONCLUSION

At the University of Chicago Celiac Disease Program (UCCDP), we understand the patients' needs and address them using a multi-disciplinary, team-based approach that includes clinicians with a sound expertise in the area, experienced pathologists, specially trained dietitians, and nurses. Referring physicians receive frequent, regular updates from our team. After the diagnosis, the team provides support for the patient's new diet and follow-up care to monitor the remission of symptoms and dietary compliance. In short, our patients receive the kind of excellent care that is the constant aim at the University of Chicago. But the UCCDP mission goes beyond excellence in care: We strive to increase the diagnosis rate of this condition; coordinate advocacy on key consumer issues; work to improve medical education; and conduct direct research on the basic and clinical aspects of the disease.

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A SIGNIFICANT PERCENTAGE OF PEOPLE WITH CELIAC DISEASE EXHIBIT NO SYMPTOMS AT ALL.

The recent recruitment of Bana Jabri, MD, PhD, represents another major step forward as we strengthen our research efforts. Dr. Jabri is a world-renowned investigator in gut immunology with a long-standing specific interest in the intimate mechanisms of the pathogenesis of celiac disease. Our goal is to understand and ultimately, prevent or even cure this disease, which is one of the most common, yet underdiagnosed chronic diseases of Caucasians. In sum, we are working so that celiac disease may no longer be called, in the words of Susanna Lohiniemi, director of the Finnish Society for Celiac Disease, “Tricky to find, hard to treat, impossible to cure.”⁹

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