# Celiac disease

CE 2.1 CONTACT HOURS

# Helping patients live gluten-free

*Abstract: Celiac disease affects approximately 1% of the U.S. population, and many cases go undiagnosed until later in life. A wide range of symptoms, illnesses, and disorders may accompany undiagnosed celiac disease. This article reviews screening, diagnosis, and treatment of celiac disease for the NP.*

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Celiac disease, an autoimmune disease of the small intestine that occurs in genetically predisposed individuals, affects approximately 1% of the population, and is one of the most common lifelong conditions in the United States.[1,2] Recent studies show that the prevalence of celiac disease has increased over the last 3 decades. While the reason for this is unclear, researchers have also found that the condition is still underdiagnosed.[3] Serious clinical disease and early mortality are the consequences of undiagnosed and untreated celiac disease.[2,4]

NPs in both primary and chronic care are in a unique and essential position to screen for and monitor celiac disease. Clinical recognition of the full range of signs, symptoms, complications, and associated disorders of celiac disease will help NPs diagnose, treat, and manage the disease.

## Prevalence

Celiac disease affects both children and adults and can present at any age.[1,2,4,5] The final statement from the 2004 National Institutes of Health Consensus Development Conference on Celiac Disease revealed a prevalence rate for celiac disease between 0.5% and 1%.[6] A study utilizing blood samples from a participants of CLUE I and CLUE II cohort studies in Washington County, Maryland in both 1974 and 1989 revealed that celiac disease autoimmunity can develop at any age, and the prevalence of celiac disease has increased five-fold during the last 3 decades.[3]

## Pathophysiology

Celiac disease is caused by a complex interaction between the immune system, derivatives of dietary grains, and an individual's genetic makeup.[1,5] The immune-mediated response to gluten—a protein complex found in wheat, barley, and rye—causes damage to the jejunum.[1,2] The consumption of gluten causes the production of antibodies that attack the intestinal villi, causing inflammation and damage. This inflammation and damage leads to illnesses associated with malabsorption.[5,6] (See *Microscopic findings in celiac disease.*)

There is a vast amount of literature on the genetic makeup of individuals with celiac disease. Almost all patients with celiac disease carry gene pairs that encode for at least one of the human leukocyte antigen (HLA) gene variants, or alleles, HLA-DQ2 or HLA-DQ8.[1-4] These alleles are common, appearing in about 40% of the U.S. population.[5] It is unlikely that individuals who do not carry these alleles will ever develop celiac disease.[1] Although the antigen responsible for causing celiac disease is known, the trigger is not.

Symptoms of celiac disease are varied; however, the most well-known symptoms are chronic diarrhea, foul-smelling voluminous stools, and weight loss (see *Symptoms of celiac disease*).



**Key words: autoimmune disease, celiac disease, gluten intolerance, nutritional deficiencies**

## Microscopic findings in celiac disease

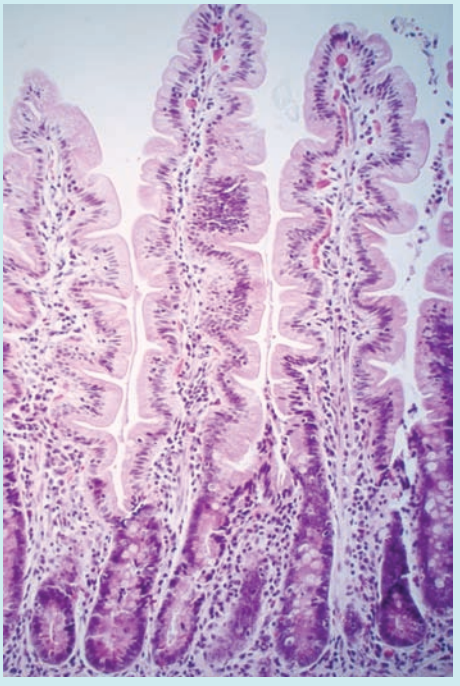

Figure 1 (left) shows a normal proximal small intestine with tall slender villi with crypts at the base.

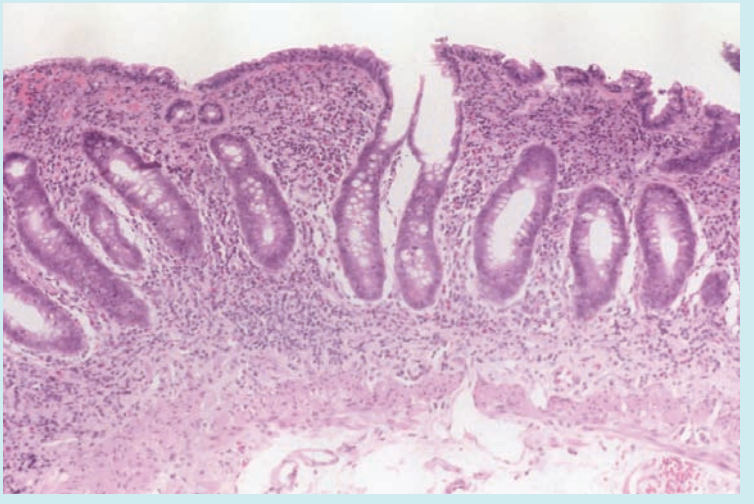

Figure 2 (above) represents a mucosal biopsy from a patient with advanced celiac disease showing complete loss of the villi with infiltration of the lamina propria by lymphocytes and plasma cells.

Source: Rubin R, Strayer D, eds. *Rubin's Pathology: Clinicopathologic Foundations of Medicine.* 5th ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008:584.

Atypical signs include indigestion, bloating, excessive gas, fatigue, anemia, depression, bone pain, bone disease (osteopenia, osteoporosis), hair loss, muscle cramps, short stature, growth delay in children, dental enamel defects, infertility or delayed fertility, as well as other symptoms caused by nutritional deficiencies common with celiac disease.[1,5-8] (See *Non-intestinal symptoms of celiac disease.*)

Untreated celiac disease is linked to numerous illnesses (malnutrition, anemia, stunted growth, short stature, low bone density, delayed puberty, infertility, and psychiatric disorders), autoimmune disorders (autoimmune thyroid disease, type 1 diabetes mellitus, and Addison disease), and certain types of cancer (enteropathy-associated T cell lymphoma, non-Hodgkin lymphoma, and intestinal and extraintestinal lymphoma).[5] It is also linked to early mortality in untreated individuals.[3] Evidence further suggests that the longer the patient is exposed to gluten, the greater the risk of autoimmune disorders.[5] It is important that celiac disease is diagnosed and treated early to decrease the morbidity and early mortality associated with long-standing untreated disease.

## Screening

Serologic screening is essential. Although a thorough health history is important, there is no single overt condition or symptom found in every case of celiac disease. Because celiac disease is a common, yet underdiagnosed, disease, NPs in the primary care setting should diligently screen for the disease when warranted.[7,8]

The *American Gastroenterological Association Institute Technical Review on the Diagnosis and Management of Celiac Disease* and its accompanying *Medical Position Statement on the Diagnosis and Management of Celiac Disease* as well as many other resources offer a wealth of information on the prevalence of celiac disease in specific high-risk populations.[1,2,5,7-9] High-risk populations for undiagnosed celiac disease include first-degree relatives of individuals with celiac disease (10% prevalence of celiac disease), as well as second-degree relatives (2.6% to 5.5% prevalence).[1] Adults with unexplained iron deficiency anemia (IDA) are also at increased risk for celiac disease (approximately 2% to 9%) regardless of intestinal symptoms. Individuals with IDA and intestinal symptoms have a higher prevalence of celiac disease (approximately 10% to 15%).[1,5]

Increased prevalence of celiac disease has been identified in adults and children with numerous medical conditions. Adults with type 1 diabetes mellitus have an increased prevalence of 2% to 5% (3% to 8% in children).[5] Individuals with osteoporosis, especially those with early-onset osteoporosis and osteomalacia, have an increased prevalence of celiac disease (approximately 1.5% to 3%).[1,5] Celiac disease prevalence in individuals with unexplained elevated transaminase levels

is 1.5% to 9%; for those with autoimmune hepatitis, 2.9% to 6.4%; and up to 6% in those with primary biliary cirrhosis.[1,5] In individuals with autoimmune thyroid disease the prevalence of celiac disease varies in the range of approximately 1.5% to 6.7%.[5] Other diseases and disorders associated with a known increase in the prevalence of celiac disease include Addison disease, immunoglobulin A (IgA) nephropathy, idiopathic epilepsy, occipital calcifications, Sjögren syndrome, aphthous stomatitis, cardiomyopathy, and peripheral neuropathy.[1,5]

Individuals with genetic disorders also have an increased risk of celiac disease. Its prevalence in Down syndrome can range from 3% to 12%; in Turner syndrome the range is 2% to 10%. Although limited information is available, celiac disease may have increased prevalence in individuals with William syndrome, a rare syndrome with facial and cardiovascular abnormalities.[1,5]

Reproductive disorders are associated with increased prevalence of celiac disease in both males and females. These include delayed menarche, early menopause, decrease in sex hormones, infertility, delayed fertility, fewer live births, preterm birth, and higher rates of miscarriage.[5,7,9]

## Diagnosis

The gold standard for diagnosis of celiac disease is an intestinal biopsy showing the characteristic changes of celiac disease along with improvement when the individual is on a gluten-free diet.[5] The intestinal biopsy should include four to six samples taken by a provider skilled in obtaining samples for diagnosis of celiac disease.[5] A pathologist skilled in evaluating biopsy tissue for celiac disease will review the samples using the Modified Marsh criteria, a scale that rates intestinal damage commonly found in celiac disease.[2,5] The Modified Marsh criteria categorizes intestinal mucosal changes of the duodenum and jejunum that are characteristic of celiac disease into stages assessing the following: increased intraepithelial lymphocytes, crypt lengthening or hyperplasia and villous atrophy.[5]

Recommended serologic screening includes total IgA, endomysial antibodies, and tissue transglutaminase (see *Serologic testing for celiac disease*). It is important to understand that these tests are conducted using IgA. There is a 3% prevalence of selective IgA deficiency in individuals with celiac disease; therefore, utilizing a panel that includes total IgA will rule out false negatives due to selective IgA deficiency. IgG serologic tests may be used in IgA-deficient individuals.[5,8,9]

A recent study indicates that positive serologic testing and negative or equivocal intestinal biopsy have the same biomarkers of untreated celiac disease.[10] These findings suggest that intestinal changes and damage may not be necessary for the presence of symptoms of gluten intolerance or illness, and may prompt changes in diagnostic criteria for celiac disease in the future.

Genetic testing can also rule out celiac disease.[1]

### Symptoms of celiac disease[1,4-8]

**In children**

- Failure to thrive
- Chronic diarrhea or constipation
- Recurring abdominal bloating and pain
- Slow development
- Irritability
- Refusal to eat
- Fatigue

**In adults**

- Abdominal pain
- Abdominal distention, bloating, gas, indigestion
- Constipation
- Diarrhea, chronic or occasional
- Decreased appetite (may also be increased or unchanged)
- Lactose intolerance (common upon diagnosis; may resolve following treatment)
- Nausea and vomiting
- Stools that float, are foul smelling, bloody, or "fatty"
- Unexplained weight loss (although people can be overweight or a normal weight upon diagnosis)

### Nonintestinal symptoms of celiac disease[1,4-8]

- Alopecia
- Anemia
- Bone and joint pain
- Bone disease (osteoporosis, kyphoscoliosis, fracture)
- Bruising easily
- Dental enamel defects and discoloration
- Dyspnea (due to anemia)
- Fatigue
- Foot pain (loss of fat pads)
- Growth delay in children
- Hypoglycemia
- Irritability and behavioral changes
- Liver and biliary tract disorders (transaminitis, fatty liver, primary sclerosing cholangitis)
- Malnutrition
- Mouth ulcers
- Muscle cramps
- Nosebleed
- Peripheral neuropathy
- Psychiatric disorders (anxiety/depression)
- Seizures
- Short stature, unexplained
- Skin disorders (dermatitis herpetiformis)
- Swelling, general or abdominal
- Tingling or numbness in legs
- Unexplained infertility or recurrent miscarriage
- Vitamin or mineral deficiency, single or multiple nutrient (for example, iron, folate, vitamin K)

## Treatment

There are numerous areas of treatment the NP should be aware of including assistance and support for initiation of a gluten-free diet, assessment and treatment of nutritional deficiencies (including vitamin D), bone-density evaluation, recovery monitoring, and management of concomitant disorders. The NP should also carefully review the patient's current prescription and over-the-counter medications for gluten content, and replace with equivalent gluten-free prescriptions or pharmacist-compounded formulations.[9]

The NP can refer the newly diagnosed patient to a nutritionist knowledgeable in a diet appropriate for patients with celiac disease. Strict adherence to a gluten-free lifestyle—not just diet—is crucial. NPs must recognize potential threats including vitamins, teas, and supplements, as well as cookware and appliances (such as bread makers, toasters, broilers) in which gluten remnants cannot be thoroughly removed. Lipsticks, lip balms, and even adhesives on envelopes and stamps can contain gluten. For children, arts and crafts supplies may be a source of gluten due to hand-to-mouth behaviors or not washing hands thoroughly before snacks or meals are served in the school or daycare setting. Cross-contamination when preparing foods in kitchens that are not completely gluten-free can also be a problem. In addition, patients may have difficulty reading food, supplement, and medication labels to determine if products are gluten-free (see *Items to check for gluten content*).[9,11]

NPs should also ensure adequate treatment of anemia or IDA, treatment of B12 and folic acid deficiency, and treatment of other vitamin deficiencies, particularly fat soluble, A, D, E, and K. Calcium levels and bone density also need to be monitored as osteoporosis can occur in patients with celiac disease.

Thyroid studies and cancer screenings are also appropriate for these patients. NPs should always carefully assess other symptoms, monitor, and manage any comorbidities.

### Serologic testing for celiac disease[5,8,9]

| Test | Comments |
|---|---|
| IgA tissue transglutaminase (tTG) | Very specific for celiac disease. Overall sensitivity is probably 90% and specificity 95.3%. |
| IgG tTG | Used in individuals with IgA deficiency. |
| IgA endomysial antibodies | Almost 100% specificity and 93% sensitivity for celiac disease |
| Total IgA antibodies | Used to identify IgA-deficient patients who may have false-negative results unless IgG tests are used to screen for celiac disease. |
| IgA and IgG antigliadin antibodies | Used only in those younger than 2 years of age (not considered specific or sensitive enough for screening in those older than 2 years). |

### Items to check for gluten content[9]

- Food items (including teas, coffee, condiments, spices, and gluten additives)
- Prescription and over-the-counter medications (including nasal sprays and oral sprays)
- Vitamins, minerals, supplements
- Lipsticks and lip balms, toothpaste, mouthwash
- Adhesives on envelopes and stamps
- Arts and crafts supplies
- Kitchen items: toasters, broiler pans, bread makers, coffee makers
- Eating out: friends' or family residences, restaurants, travel
- Situational instances of cross-contamination: unwashed hands, countertops, multiuse containers, conveyer belts at stores

## Restoring healthy weight/monitoring growth and development in children

The NP should assess each patient's weight at the time of diagnosis and initiation of the gluten-free diet. Each patient will need a diet plan designed to provide healing nutrition along with proper calorie intake to normalize weight if underweight or overweight. Underweight patients will need additional calories until normal weight for height is achieved. At that time, the NP and the patient can reassess calorie and nutrient needs to help the patient maintain a healthy weight on the gluten-free diet. Overweight patients will need a diet plan adequate in nutrients, but restricted in calories to achieve normal weight for height. Once a healthy weight is achieved, these patients will need a diet plan to maintain a healthy weight. A dietician or nutritionist with expertise in gluten-free diets and normalization of weight in patients with celiac disease can help develop diet plans that include healing nutrients with a proper calorie count to normalize underweight or overweight patients.

## Implications for practice

Celiac disease is a multisystem immune-mediated disease with varying signs, symptoms, complications, and associated disorders, which occurs in genetically susceptible individuals at any age. While it is not a rare disease, it can take up to 10 years for those with symptoms to be diagnosed.[7] In addition to annual recommended medical screenings for their age-group, the individual with celiac disease needs annual serology testing for celiac disease to ensure adherence to a gluten-free lifestyle, monitoring of bone density, and careful monitoring for complications and associated disorders of celiac disease.[9,11] The disease is managed with a lifelong

adherence to a strict gluten-free diet and lifestyle, which can be expensive, difficult to maintain, and interfere with work and social life. These patients need education and support to maintain a psychological and physiological healthy gluten-free life.[2,7,9]

NPs should educate patients about the harm gluten ingestion causes not only to the intestinal tract, but also throughout the body. Individual and families should be taught to focus on what can be eaten rather than what must be excluded. While a consult with a knowledgeable nutritionist is extremely helpful, most insurance carriers will not reimburse this expense and this should be discussed during the visit. A support or advocacy group can also be helpful for those adjusting to the gluten-free lifestyle, and NPs should provide contact information for local groups.

NPs can be excellent primary care providers for individuals with celiac disease as long they are well-versed in patient education and supportive, patient-centered care.

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The author disclosed that she has no financial relationship pertaining to this article.

DOI-10.1097/01.NPR.0000403289.30513.2d