Celiac Disease

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- Complete the questions at the end of the course.
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Faculty

Diane Thompson, RN, MSN, CDE, CLNC, has an extensive history in nursing and nursing education. She possesses a strong background in diabetes and cardiac care, starting her professional career at the cardiac care area of the Cleveland Clinic in Cleveland, Ohio. Ms. Thompson took the knowledge and experience she learned from the Cleveland Clinic and transferred it into the home health arena in rural Ohio, after which she moved to Florida and obtained further knowledge while working as a PRN nurse in all areas, including medical/surgical, intensive care, emergency, critical care, and cardiology. With a desire to have a specific area to concentrate her profession, Ms. Thompson accepted a position as a pneumonia case manager, which led into a diabetes case manager career. (A complete biography appears at the end of this course.)

Sylvia A. Bower, RN, has an extensive history in the nursing profession. She is a graduate of Grant Hospital School of Nursing and attended Franklin University in Columbus, Ohio and St. Joseph's College in Maine, and attended Liberty University. She has been registered to practice nursing in Ohio, Texas, Missouri, Arizona, Tennessee, and Florida, and she has practiced in public health, emergency, orthopedics, long-term care, occupational health, ambulatory care, nurse recruitment, discharge planning, hospice care, and continuing education. (A complete biography appears at the end of this course.)

Faculty Disclosure

Contributing faculty, Diane Thompson, RN, MSN, CDE, CLNC, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Contributing faculty, Sylvia A. Bower, RN, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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The division planner and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for nurses, dieticians, and allied health professionals who may have a patient with celiac disease primary or secondary to their presenting diagnosis.

Accreditations & Approvals

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A complete Works Cited list begins on page 20.

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About the Sponsor

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Disclosure Statement

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Course Objective

The purpose of this course is to provide healthcare professionals with the information necessary to identify and provide adequate care for those with celiac disease.

Learning Objectives

Upon completion of this course, you should be able to:

1. Discuss the history and epidemiology of celiac disease in the United States.
2. Explain the pathophysiology of celiac disease and risk factors for development.
3. Discuss the clinical signs and symptoms of celiac disease.
4. Describe the methods used for the diagnosis of celiac disease.
5. Identify comorbidities and complications commonly associated with celiac disease.
6. Describe recommended treatment of celiac disease and discuss therapeutic alternatives.
7. Explain the importance of ongoing education and support for the individual and family with celiac disease.

EVIDENCE-BASED PRACTICE RECOMMENDATION

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Celiac disease (CD) is a global health concern, impacting 1% to 3% of the global population and requiring a multidisciplinary approach to care and treatment [1; 2]. Research estimates that as many as 1 in 133 Americans, or approximately 1% of the U.S. population, have CD [3]. CD is a burden to the U.S. healthcare system, with average all-cause costs totaling more than $12,000 in patients with CD, compared with $5,000 in individuals without CD [127]. In addition, undiagnosed CD costs approximately $3,964 per patient over a four-year period [3].

Until the 1970s, the estimated global prevalence of CD was only 0.03%. A Finnish population-based study demonstrated an almost doubled prevalence of CD observed between 1980 (1.03%) and 2001 (1.99%). This overall increase is due to improved awareness, screening, and diagnostics and may also be attributed to environmental changes worldwide [4]. With increased awareness of this disease among adult and pediatric primary care providers, there will undoubtedly be an increase in the number of individuals being evaluated for CD in outpatient diagnostic centers and gastroenterology practices [5].

HISTORY

The term celiac is derived from the Greek word *koiliakos*, meaning "suffering of the bowel." It was first introduced in 250 C.E. by Aretaeus of Cappadocia. Allergies, food intolerances, and sensitivities began when humans learned to cultivate crops, generating a new battery of food antigens, including cereal grains, birds' eggs, and the milk of cows, goats, and donkeys [6]. The first century C.E. provides the earliest documented evidence of CD. The case was a young woman of short stature (140 cm) with a history of anemia and a decreased bone mass with evidence of osteoporosis and bone fragility. The archeologic artifacts from the tomb, and the quality of the burial architecture, suggest that the tomb was built for a wealthy person in an area with an extensive culture of wheat consumption. Clinical presentation and the possible continuous exposure to wheat suggest CD [7].

There have been numerous documented cases of CD since this first observation. In 1888, a British physician, Dr. Samuel Gee, presented clinical studies of CD that included both children and adults. Dr. Gee felt that the regulation of food was the principal component of treatment, and he documented a case of a patient improving after introduction to a gluten-free diet [8]. In 1953, a Dutch pediatrician, Dr. Willem Karel Dicke, wrote his doctoral dissertation based on observations that the ingestion of wheat proteins, not carbohydrates, was the cause of CD. In the mid-1960s, an enteropathy similar to CD was identified in patients with dermatitis herpetiformis. This skin condition was shown to be a manifestation of gluten-sensitive enteropathy. Around that time, adult CD was also noted to be associated with numerous neurologic disorders, including epilepsy, cerebral calcifications, and peripheral neuropathy [9].

In the 1970s, gastrointestinal (GI) endoscopic techniques were introduced. This provided the opportunity to obtain routine biopsy samples, which in turn provided improved opportunities in CD case finding and diagnosis. In the 1980s and 1990s, two human leukocyte antigen molecules (HLA-DQ2 and HLA-DQ8) typically associated with CD were identified, which led to more specific diagnosis [4]. In 1990, the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) published guidelines to achieve higher diagnostic accuracy of CD. A panel of experts established that CD is an autoimmune disease associated with specific genes (DQ2 and DQ8) and identified the autoantigen in CD as the enzyme tissue transglutaminase [2; 135]. In 2012, a working group within ESPGHAN established new guidelines as well as a new definition of CD based on scientific and technical developments; these evidence-based guidelines were further updated and expanded in 2020 [2; 135].

EPIDEMIOLOGY

The ESPGHAN guidelines define CD as "an immune-mediated systemic disorder elicited by gluten and related prolamins in genetically susceptible individuals and characterized by the presence of a variable combination of gluten-dependent clinical manifestations and CD-specific antibodies" [2; 135]. CD, also known as gluten intolerance, gluten-sensitive enteropathy, nontropical sprue, and celiac sprue, is an immune-mediated response to gluten (e.g., wheat, rye, barley) in genetically predisposed individuals [5]. When an individual with CD consumes gluten, it damages the small intestines and results in difficulty absorbing nutrients from foods. As previously noted, approximately 1 in 133 individuals in the United States (or about 1%) have CD. The risk is greater (i.e., 1 in 22) in individuals with a first-degree relative with CD [10].

Until the 1990s, CD was considered rare among non-European and developing nation populations. Prevalence rates are now thought to be similar, due in part to increased awareness of the disease and the introduction of serologic screening tests in the Middle East, India, and North Africa. However, CD is still rarely reported in sub-Saharan African, African American, and East Asian populations [11; 12]. This immune-mediated disorder is more common in individuals with other such disorders (e.g., type 1 diabetes). The individual with type 1 diabetes has a prevalence of approximately 6% of comorbid CD [13]. Although CD is most often recognized as an illness affecting the pediatric population, for adult individuals, the diagnosis is often made between the fourth and sixth decade of life [14].

Individuals with CD often have an inherited predisposition influenced by environmental factors [15]. An estimated 5% to 22% of individuals with CD have an immediate family member (i.e., first-degree relative) who also has the disease [3]. CD affects two to three times as many women as men and is most commonly seen among relatives, especially siblings [16; 17].

There is often a delay in diagnosis due in part to the varied clinical manifestations of CD. The average time to diagnosis from initial presentation of symptoms ranges from 6 to 10 years [3]. In 2004, public awareness of CD was brought to the forefront by the National Institute of Health Consensus Development Conference and its statement on CD. This statement was instrumental in addressing issues of protein manifestations, epidemiology, diagnostic testing, and therapy for CD and resulted in an increase in reported incidence [14].

PATHOPHYSIOLOGY

Gluten is the general term used for storage proteins considered antigenic in CD. Gluten is a complex macromolecule that is largely indigestible and, under normal circumstances, left partly unabsorbed by the GI tract [18]. The gluten in wheat, rye, and barley is toxic to the intestinal epithelial cells of genetically susceptible individuals [19]. Specifically, the alcohol-soluble protein fraction (prolamins) of gliadin in wheat (secalin in rye, hordein in barley) is responsible for initiating the intestinal damage typical of CD [20]. Exactly how gliadin is able to cross the intestinal epithelial barrier is not clear.

CD originates as a result of a combined action that involves both adaptive and innate immunity [18; 21]. Four presentations are recognized (***Table 1***) [18; 21]:

- Typical: GI signs and symptoms
- Atypical (extraintestinal): Minimal or absent GI signs/symptoms, but a number of other manifestations
- Silent: Damaged small intestinal mucosa and no symptoms, but disease can be detected by serology
- Latent: Individual possesses genetic compatibility and may show positive autoimmune serology but normal mucosa, with or without symptoms

CLASSIFICATION OF CELIAC DISEASE[a]				
Type	**Serology (tTG and/or EMA)**	**Age Most Often Affected**	**Symptoms**	**Pathology**
Typical	Positive	Toddler, young child	Abdominal pain, distention, diarrhea, vomiting, anorexia, constipation	Marsh 2–3
Atypical	Positive	Older child, adult	Mostly extraintestinal	Marsh 1–3
Silent	Positive	Adult	None	Marsh 1–3
Latent	Positive or negative	Adult	None, gastrointestinal, extraintestinal	Marsh 0–1 (previous or future gluten enteropathy)
Potential	Positive	Any age	None, gastrointestinal, extraintestinal	Marsh 0–1
[a]In all cases, genetic asset is HLA-DQ2 and/or HLA-DQ8. EMA = endomysial antibody, tTG = tissue transglutaminase.				
Source: [18]				*Table 1*

CD primarily affects the mucosal layer of the small intestine, where a cascade of immune events leads to changes that can be documented by histology [18]. Three distinctive histologic stages, termed the Marsh classification, have been described [18; 22]:

- Type 0 or preinfiltrative stage (normal)
- Type 1 or infiltrative lesion (increased intraepithelial lymphocytes)
- Type 2 or hyperplastic lesion (type 1 plus hyperplastic crypts)
- Type 3 or destructive lesion (type 2 plus villous atrophy of progressively more severe degrees)

Destruction of mucosal cells instigates inflammation. Water and electrolytes are secreted, causing diarrhea. Potassium loss leads to muscle weakness. Magnesium and calcium malabsorption can cause seizures or tetany [19]. Unabsorbed fatty acids combine with calcium, and secondary hyperparathyroidism increases phosphorus excretion, resulting in bone reabsorption. Calcium is no longer available to bind oxalate in the intestine and is absorbed, producing hyperoxaluria [23]. The function of the gallbladder may be abnormal, and bile salt conjugation may be decreased [19]. Vitamin K malabsorption leads to hypoprothrombinemia. In one-third of cases, iron and folic acid malabsorption is manifested as cheilosis, anemia, and a smooth, red tongue. Vitamin B12 absorption is impaired in those with extensive ileal disease, and folate and iron deficiencies are common [19]. Failure to thrive is noted, and hypotonia is common [24]. Extraintestinal manifestations of CD include dermatitis herpetiformis, dental enamel hypoplasia, aphthous ulcers, delayed tooth eruption, and arthritis/arthralgia [18].

RISK FACTORS

As noted, the single most important risk factor for CD is having a first- or second-degree relative (particularly a sibling) in whom the disease is already diagnosed. An incidence of up to 20% has been noted in this population. The risk is greater in families in whom two siblings are affected, especially if one is a man who carries HLA-DQ2 [25]. The presence of another autoimmune disorder (e.g., thyroid disease, type 1 diabetes) may also increase the risk of developing CD [3]. Women appear to be at greater risk than men [26]. Other environmental factors include a high number of gastrointestinal infections before 6 months of age and frequent rotavirus infections in children younger than 4 years of age [27].

Evidence is emerging that early (<3 months of age) or late (>7 months of age) first exposure to gluten may favor the onset of CD in infants predisposed to the disease [28]. Some studies show a protective effect of breastfeeding, while other studies show no effect [29]. Although no studies have shown a long-term preventive effect, researchers agree that it is reasonable to recommend introducing gluten in small amounts between 4 and 6 months of age, while breastfeeding, and that breastfeeding be continued for a minimum of an additional two to three months [29]. Future studies, such as the European multicenter study Prevent CD, may help clarify the association between infant nutrition and the risk of developing CD [30].

DIAGNOSIS

The American Gastroenterological Association recommends diagnostic testing for CD only for symptomatic patients at high risk, with high risk defined as a premature onset of osteoporosis or unexplained elevations in liver transaminase levels or iron-deficient anemia [31; 128]. In addition, the Association notes that testing should be selectively considered for individuals with another autoimmune disease known to be associated with CD or who have a family history of the disease [32].

The differential diagnosis of CD involves the exclusion of several conditions with similar characteristics, including anorexia nervosa, bacterial overgrowth, Crohn disease, multiple sclerosis, and intestinal lymphoma [33; 129]. Irritable bowel syndrome has been diagnosed before the detection of CD in as many as 36% of individuals [33].

There is no one universally accepted diagnostic standard, and the diagnosis of CD should be made on the basis of several factors, including the findings of the history and physical examination, serologic testing, and biopsy of the small intestine [34; 35]. Diagnostic testing should be done while the patient's diet includes foods that contain gluten [128].

CLINICAL SIGNS AND SYMPTOMS

Adults with CD commonly present with weight loss, diarrhea, lassitude, and anemia. Very young children (9 to 24 months of age) often present with failure to thrive, vomiting, chronic diarrhea, muscle wasting, anorexia, abdominal distension, and irritability. Symptoms may begin at various times after the introduction of gluten-containing foods. Older children present with nausea, recurrent abdominal pain, bloating, constipation, and intermittent diarrhea [18]. Other symptoms in both children and adults may include itchy skin rash, headache, depression, and bone and/or joint pain [3; 36]. Symptoms may vary widely from patient to patient; some patients are asymptomatic or minimally symptomatic, especially older children and adults [18]. Many symptoms of CD mimic those of other diseases, leading to a high rate of misdiagnosis [37]. Dermatitis herpetiformis may be an extraintestinal manifestation of gluten-sensitive enteropathy, manifesting as a pruritic, blistering rash [36]. The reversible nature of CD makes prompt diagnosis important [38].

SEROLOGIC MARKERS

Three antibodies commonly appear in patients with CD: antibodies to tissue transglutaminase (tTG), antiendomysial antibodies, and antigliadin antibodies. The American Gastroenterological Association and the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition recommend using serologic markers to screen patients with either nonspecific symptoms of CD or medical conditions that increase the risk of CD; small intestinal biopsy should be performed to confirm the diagnosis [38]. The ESPGHAN recommends foregoing the confirmatory duodenal biopsy in selected cases of children and adolescents to reduce the burden on patients and their families [2; 135].

Four serum antibody assays can help to identify candidates for biopsy [38]:

- Immunoglobulin A anti-tissue transglutaminase (IgA anti-tTG)

- IgA endomysial antibody (IgA EMA)
- IgA antigliadin antibody (IgA AGA)
- IgG antigliadin antibody (IgG AGA)

The IgA EMA assay is highly specific for CD, with 99% accuracy [39]. The test has a variable sensitivity of 70% to 100%, due in part to the high technical difficulty in performing it [39]. Because 2% to 3% of individuals with CD have selective IgA deficiency, IgA levels should be measured [96]. The IgA tTG assay is the preferred screening method, with a sensitivity of 93% and a specificity or more than 98% [39; 96]. No statistically significant difference has been found between IgA EMA and IgA tTG. The IgA AGA assay has a reported sensitivity of 80% to 90% and a specificity of 85% to 95%. The IgG AGA has a reported sensitivity and specificity of 80% [38].

EVIDENCE-BASED PRACTICE RECOMMENDATION

The American College of Gastroenterology asserts that serology is a crucial component of the detection and diagnosis of celiac disease, particularly tissue transglutaminase-immunoglobulin A (TG2-IgA), IgA testing, and less frequently, endomysial IgA testing.

(https://www.gastrojournal.org/article/S0016-5085(18)35408-8/fulltext. Last accessed November 22, 2022.)

Level of Evidence: Expert Opinion/Consensus Statement

Routine full blood count, urea and electrolytes, liver function tests, serum iron or ferritin, folate or red blood cell folate, and vitamin B12 should also be measured at initial diagnosis [36].

INTESTINAL BIOPSY

Esophagogastroduodenoscopy (EGD) with duodenal biopsy is considered the criterion standard to confirm the diagnosis of CD. During EGD, a small flexible endoscope is introduced through the mouth or nose and advanced through the pharynx, esophagus, stomach, and duodenum. Most endoscopes use a video chip, which provides the best imaging. Moderate sedation and topical anesthesia are used in the United States to ensure patient comfort and cooperation. Benzodiazepines (e.g., midazolam, diazepam) and opioids (e.g., meperidine, fentanyl) are the most commonly used sedative agents. EGD is contraindicated in patients who are medically unstable or unwilling. Possible complications (occurring in 1 in 1,000 procedures) include bleeding, infection, perforation, and cardiopulmonary problems caused by the sedation agent [41; 42]. Diagnostic criteria include abnormal small intestinal mucosa, usually accompanied by increased intraepithelial lymphocytosis, followed by objective clinical response and unequivocal improvement in villous architecture on a gluten-free diet [36; 43]. Experts recommend that six biopsy samples be obtained from the distal and proximal areas of the small intestine to protect against missed diagnoses [96]. In the past, repeat biopsy was the standard of care, but this is now often avoided [36].

The histologic lesions characteristic of CD may be missed in some cases, even with multiple duodenal biopsies [44; 45]. Also, some patients with clinical presentation highly suggestive of CD may have a normal EGD and nondiagnostic biopsy [41]. These patients may benefit from video capsule endoscopy (VCE). VCE, also referred to as physiologic endoscopy, is a noninvasive procedure that provides high-resolution magnified views of the small intestinal mucosa, with a reported sensitivity of 76% to 99% and specificity of 56% to 100% [46]. It is mainly used to evaluate patients with CD in whom the disease course after diagnosis has been unfavorable and a diagnosis of adenocarcinoma, lymphoma, or refractory CD is suspected [36; 43; 96]. Other indications for the use of VCE include iron-deficiency anemia, chronic diarrhea, and abdominal pain due to suspected Crohn disease [43]. No well-designed trial has tested for noninferiority or equivalence between VCE and EGD with biopsy [43].

OTHER TESTING

Some argue that small intestine biopsy can, under certain circumstances, be replaced by serology testing. Positive CD serology has been linked to an increase in mortality rates; however, the predictive value and long-term consequences of CD serology in individuals with normal mucosa are unknown [47]. Additional tests to confirm the diagnosis of CD may include [16]:

- Malabsorption studies
- Glucose tolerance test: Demonstrates poor absorption of glucose
- D-xylose tolerance test: Demonstrates low urine and blood levels of xylose (<3 grams over a five-hour period); the presence of renal failure may contribute to a false-positive result
- Serum carotene levels: Measure absorption; low levels indicate malabsorption
- Stool analysis: Analyzed for fat and pancreatic function; done to rule out cystic fibrosis
- Barium studies of the small bowel: Show protracted barium passage; barium shows up in a segmented, coarse, scattered, clumped pattern; jejunum shows generalized dilatation
- Hemoglobin, hematocrit, leukocyte, and platelet counts: Low levels indicative of possible CD
- Albumin, sodium, potassium, cholesterol, and phospholipid levels: May be reduced with CD
- Prothrombin (PT) times: Diminished in patients with CD

SCREENING

Screening for CD is not routinely performed in the United States; however, it is recommended for first-degree relatives of individuals with the disease [96]. Four to twelve percent of an affected individual's first-degree relatives will also have the disease [48]. Screening for CD is also recommended for patients with type 1 diabetes and any digestive symptoms or signs or laboratory evidence suggestive of CD [96].

COMORBIDITIES AND COMPLICATIONS OF CELIAC DISEASE

Two theories have been proposed to explain the association between CD and other autoimmune disorders [49]. The first suggests that untreated CD leads to the onset of another disorder in genetically susceptible individuals. This theory is supported by the prevalence of autoimmune disorders in patients with CD in relation to the duration of gluten exposure and by an increased prevalence of comorbid autoimmune disorders in first-degree relatives of individuals with CD [50; 51; 52]. The second theory suggests that the association is secondary to a more frequent than expected, simultaneous occurrence of genes that predispose individuals for both the autoimmune disorder and CD [49]. Authors of one study screened for the presence of autoimmune disorders in 605 healthy controls and 422 patients with CD. Both groups included individuals 16 to 84 years of age who had been on a gluten-free diet for at least one year. A three-fold higher prevalence of autoimmunity was found in patients with CD as compared to the controls [53]. The autoimmune disorders associated with CD were both organ-specific (e.g., type 1 diabetes, thyroid disease) and nonorgan-specific (e.g., rheumatoid arthritis) [49].

TYPE 1 DIABETES

CD is one of the most frequent autoimmune disorders co-occurring in patients with type 1 diabetes. The prevalence of CD is eight times higher in patients with type 1 diabetes than in the general population. The prevalence varies from 3% to 16%, with a mean prevalence of 8% worldwide, as confirmed by duodenal biopsy [18; 54; 129].

The close association between CD and type 1 diabetes may be due to the same HLA pattern, specifically HLA-DQ2 and/or HLA-DQ8, which predisposes individuals to both disorders. Consumption of gluten may also be a causative factor, and undiagnosed CD may favor the onset of type 1 diabetes [54]. Because symptoms (e.g., bloating, diarrhea) of the two disorders are similar, diagnosis of CD may be missed unless screening is performed [18].

MULTIPLE SCLEROSIS

Multiple sclerosis is an immune-mediated autoimmune disease characterized by inflammation in the central nervous system that damages the myelin surrounding nerve fiber, thereby causing neurologic symptoms. Approximately 10% of individuals with multiple sclerosis have co-occurring CD. In addition, multiple sclerosis and CD share several of the same symptoms, including constipation, depression, and changes in vision. Like CD, multiple sclerosis occurs more frequently in women than men [129; 130].

THYROID DISEASE

Hashimoto thyroiditis is the most common type of thyroid disease and involves inflammation and eventual destruction and fibrosis of the thyroid gland, resulting in hypothyroidism [3; 55]. The prevalence of CD in individuals with Hashimoto thyroiditis is estimated to be 3% to 7% [3; 53].

Graves disease, though rare, is the most common cause of hyperthyroidism in the United States. One large study confirmed the presence of CD in 4.5% of adults with Graves disease [3].

The prevalence of CD has invariably been higher in patients with autoimmune thyroid diseases than in controls [56; 57; 58; 59]. Adherence to a gluten-free diet has occasionally been reported to result in improvement in thyroid disease management after the detection and treatment of comorbid CD [60]. Therefore, individuals with autoimmune thyroid disorders should be screened and tested for CD [3].

DOWN SYNDROME

Approximately 8% to 12% of individuals with Down syndrome also suffer from CD [18]. This is largely because individuals with Down syndrome are at higher risk of developing autoimmune diseases than the general population [3; 61]. Two-thirds of individuals with Down syndrome who have CD have some GI symptoms (e.g., abdominal bloating, anorexia) [18]. Children with Down syndrome should be screened for CD, as prompt treatment can improve quality of life [62].

DERMATITIS HERPETIFORMIS

Dermatitis herpetiformis is a severe, itchy, blistering skin manifestation of CD. It occurs in approximately 10% of people with CD, affecting men more frequently than women and generally presenting in adults 20 to 55 years of age [63]. It may occur in children, although this is uncommon. Approximately 80% of individuals with dermatitis herpetiformis have some degree of villous atrophy, and approximately 20% have intestinal symptoms of CD. A small percentage of patients with CD will develop dermatitis herpetiformis despite adherence to a gluten-free diet [3; 131].

DEPRESSION

Depression is present in a higher percentage of patients with CD than in the general population. A combination of factors (e.g., genetic, psychologic, environmental) can cause depression in patients with CD. Some studies have suggested that depression in individuals with CD is the result of a connection between brain functions and the malabsorption of vitamins, minerals, and other essential nutrients [3]. Other studies attribute the association between depression and CD to the real and perceived social, emotional, and physical demands of adhering to a gluten-free diet and living with a chronic illness [64; 65; 66]. One year of adherence to a gluten-free diet fails to significantly affect depressive symptoms, suggesting that these patients need psychologic support [66; 67; 68].

AUTISM

Autism is a developmental neurologic disorder that impacts the functioning and development of the brain [3]. The causes of autism remain unclear but are thought to include psychologic, physiologic, and sociologic factors [16]. Studies have found that the opiates in gluten and casein are released even when the gluten and casein are only partially digested [3]. When the GI tract is not functioning properly, as with CD, the opiates are released into the bloodstream, where they impair brain function (worsening autism symptoms) and produce cravings for gluten- and casein-containing foods, perpetuating the problem. Although trial periods on diets that are gluten- and casein-free have demonstrated improvements in behavior and functioning in children with autism, no direct link between CD and autism has been established [3].In the largest study of its kind, researchers found no link between autism and CD. However, they confirmed a strong association between autism and the presence of antibodies to gluten [69].

INFERTILITY

Several studies have examined the link between CD and infertility and found that women suffering from unexplained infertility may have silent CD with minimal or no symptoms [70; 71]. The prevalence of CD in women reporting infertility is estimated to be 2.5% to 3.5% higher than in the general population [70]. CD also represents a risk for recurrent spontaneous abortion, low-birth-weight infants, stillbirth, and short breastfeeding duration [72; 73]. The malabsorption of folic acid and other nutrients resulting from CD may explain the unfavorable outcomes of pregnancy; however, additional research is required [70; 71]. Men with CD have demonstrated gonadal dysfunction, which may contribute to fertility complications. Patients presenting with unexplained infertility or recurrent spontaneous abortion should be screened for CD [3].

INTESTINAL CANCER

CD is associated with intestinal lymphoma and other forms of cancer, especially adenocarcinoma of the small intestine, pharynx, and esophagus. Enteropathy-associated T-cell lymphoma is a rare form of high-grade non-Hodgkin lymphoma of the upper small intestine that is specifically associated with CD [74]. A significant increase in the incidence of enteropathy-associated T-cell lymphoma has been noted in the United States that correlates to the increase in CD diagnoses [75]. Long duration or undiagnosed or silent CD appears to increase the risk of cancer of the small intestine. Adherence to a gluten-free diet for several years can lower the risk of lymphoma for patients with CD, especially when started early [74; 76].

MIGRAINE

An association between migraine and CD has been reported. A 2003 study found that migraine sufferers have a higher risk of CD than the general population [77]. Of the 90 patients with migraine included in the study, 4.4% were found to have CD compared with 0.4% of the controls. During a six-month gluten-free diet, those with CD experienced an improvement in frequency, duration, and intensity of migraine.

A study published in 2011 included 100 children with migraine headache (classified according to criteria of the International Headache Society) [78]. Serum total IgA and anti-tTGA antibodies were measured. Duodenal biopsy was performed to confirm CD in children with positive serologic results. Researchers found the same prevalence (2%) of positive serologic results for CD in both groups.

A study published in 2013 included 502 subjects: 188 with CD, 111 with inflammatory bowel disease, 25 with gluten sensitivity, and 178 controls [78]. Thirty percent of the subjects with CD reported chronic headaches; 72% of these patients graded their migraines as severe in impact. The study authors recommend screening patients with migraine for CD.

OSTEOPOROSIS/OSTEOPENIA

Osteoporosis can be a complication of untreated CD [79]. More than 75% of adults with untreated CD with overt malabsorption syndrome at diagnosis suffer from loss of bone mass [80]. A variety of factors contribute to the risk of osteoporosis in the individual with CD, including individual body composition (e.g., thinness, small frame), vitamin D deficiency, malabsorption of calcium and magnesium (leading to low bone density and fracture risk), and inflammation [80].

Calcium metabolism defects are common in children with untreated CD and return to normal after initiation of a gluten-free diet [81]. Normalization of bone mineral density (BMD) levels in childhood CD may be complete as early as after two years of adherence to a gluten-free diet [80]. Studies have described a 35% to 85% prevalence of osteoporosis among children with untreated CD.

A study published in 2012 measured BMD in 35 adult patients with CD (19 receiving a gluten-free diet, 16 not) and 36 controls [82]. The patients with CD also received calcium and a vitamin D analog daily for one year. Reduced BMD was diagnosed in 57% to 77% of the patients with CD. Patients on the gluten-free diet had higher BMD than those not on the diet but lower BMD than the controls. In this study, a gluten-free diet increased BMD in patients with CD.

TURNER SYNDROME

Turner syndrome is a chromosomal condition that affects only girls and commonly results in short stature and lack of sexual development at puberty [3]. The prevalence of CD in girls with Turner syndrome is estimated to be 2% to 8%, much higher than in the general population [3; 83; 84]. The National Foundation for Celiac Awareness recommends that girls with Turner syndrome be tested for CD [3].

JUVENILE IDIOPATHIC ARTHRITIS

Juvenile idiopathic arthritis is the most common form of arthritis in children. The cause is poorly understood but is believed to be related to both genetic and environmental factors. Symptoms include joint inflammation, contracture, and alteration or change in growth. The estimated prevalence of CD in children with juvenile idiopathic arthritis is 1.5% to 6.6%. As with CD and other autoimmune diseases, the onset of juvenile idiopathic arthritis usually occurs before CD is diagnosed [3].

PERIPHERAL NEUROPATHY

Peripheral neuropathy is one of the most frequently reported neurologic manifestations of CD. An estimated 5% of patients with peripheral neuropathy have CD. Common symptoms include severe burning, stinging, and electric shock-type pain. Adherence to a gluten-free diet is the recommended treatment, but there are data that indicate that neurologic manifestations may persist independent of gluten exposure [85; 86]. One review of more than 28,000 patients with biopsy-verified CD found that CD was associated with a 2.5-fold increased risk of developing neuropathy in the future. Based on the findings, researchers recommend that patients with neuropathy be screened for CD [132].

LIVER DISEASE

The disease-causing mechanism of liver damage in patients with CD is poorly understood, and the spectrum of liver abnormalities associated with CD is wide [87]. The most frequent occurrence, present in approximately 50% of patients with untreated CD, expresses as mild liver impairment (i.e., celiac hepatitis), which reverts to normal after a few months of gluten withdrawal [87; 88]. More severe liver injury (chronic hepatitis or liver cirrhosis) presents in only a few cases of patients with CD and may improve after gluten withdrawal. Autoimmune liver dysfunction is rare and usually does not improve after gluten withdrawal [87].

SJÖGREN SYNDROME

Sjögren syndrome is a slowly progressing autoimmune disease characterized by dry eyes and dry mouth [89]. Although the pathogenesis of the disease is poorly understood, environmental, genetic, and hormonal factors appear to be involved. Sjögren syndrome has been reported in up to 15% of patients with biopsy-proven CD [90].

WILLIAMS-BEUREN SYNDROME

Williams-Beuren syndrome is a rare congenital disorder occurring in 1 in 20,000 live births [3]. The prevalence of Williams-Beuren syndrome in patients with CD is comparable to that reported in Down syndrome and Turner syndrome [91]. One study of limited participants found the frequency of CD to be higher in individuals with Williams-Beuren syndrome than in the general population [92]. However, the association between Williams-Beuren syndrome and CD is poorly understood.

MANAGEMENT

THE GLUTEN-FREE DIET

A strict, lifelong gluten-free diet and supportive nutritional care (for iron, calcium, and vitamin deficiencies) is the only recommended treatment for CD [93; 94; 95; 96]. Adherence to a gluten-free diet improves health and quality of life in the majority of patients. However, an estimated 2% to 5% of patients with CD develop refractory disease, a serious complication associated with a 50% risk of developing lymphoma. The gluten-free diet does help prevent malignant complications such as lymphoma and small bowel adenocarcinoma in these patients [93; 95; 97]. People with newly diagnosed CD should undergo testing and treatment for micronutrient deficiencies (e.g., iron, folic acid, vitamin D, vitamin B12) [96].

Medical nutrition therapy provided by a registered dietitian as part of a team-based approach is strongly recommended for the individual with CD [96]. The dietitian can assess the individual's food- and nutrition-related history (e.g., intake, medication/supplement use, patient knowledge/willingness to change behaviors) to effectively determine nutritional needs and appropriate dietary interventions [98]. The dietitian can also help monitor the patient's compliance with the diet and can identify dietary nutrient deficiencies, inadequate fiber intake, and excess weight gain, each of which may be associated with adherence to the gluten-free diet [96]. Research on individuals with CD reports that long-term compliance with a gluten-free diet improves outcomes related to bone density, iron-deficiency anemia, villous atrophy, GI and neurologic symptoms, pregnancy outcomes, and quality of life [98].

Adherence to a gluten-free dietary pattern involves all foods containing or derived from wheat, barley, and rye (***Table 2***). This may result in a diet that is low in carbohydrates, iron, folate, niacin, zinc, and fiber. Individuals with CD often suffer from malabsorption and can develop vitamin and mineral deficiencies despite adequate intake. Age-specific gluten-free vitamin and mineral supplements are an important addition to the diets of persons with CD [98]. Iron supplements are recommended for iron-deficiency anemia, and folic acid and vitamin B12 should be taken to avoid anemia due to folate or B12 deficiencies. Vitamin K is necessary for individuals with abnormal PT times. Calcium and vitamin D supplements should be encouraged for individuals with low blood calcium levels or osteoporosis.

EVIDENCE-BASED PRACTICE RECOMMENDATION

The American College of Gastroenterology recommends that people with newly diagnosed celiac disease should undergo testing and treatment for micronutrient deficiencies. Deficiencies to be considered for testing should include, but not be limited to, iron, folic acid, vitamin D, and vitamin B12.

(https://journals.lww.com/ajg/Fulltext/2013/05000/ACG_Clinical_Guidelines__Diagnosis_and_Management.7.aspx. Last accessed November 22, 2022.)

Level of Evidence: Low (Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate)

GLUTEN IN FOODS		
Acceptable	**Use Caution (May Contain Gluten)**	**Avoid**
Brown rice, corn, flax, Montina, millet, sorghum, teff, wild rice, amaranth, buckwheat, quinoa, arrowroot, bean flours, black-eyed peas, legumes, lentils, lima beans, mesquite, Northern beans, nuts, pinto beans, potato flour/starch, soy, tapioca, gluten-free oats[a]	Imitation seafood, marinades, processed meats, sauces and gravies, broth, candy, coating mixes, meat substitutes, soy sauce, thickeners, imitation bacon, croutons	Barley, einkorn, malt vinegar, bulgar, farina, malt/malt flavoring, couscous, faro, cracked wheat, graham, matzo, durum, Khorasan wheat (Kamut), seitan, semolina, spelt, triticale, wheat, wheat germ, wheat starch
[a]Individuals who can tolerate may gradually include in the diet (approximately 50 g dry oats/daily).		
Source: Compiled by Author		*Table 2*

POTENTIAL ALTERNATIVE THERAPIES FOR PATIENTS WITH CELIAC DISEASE	
Therapeutic Aim	**Therapies**
Decrease Gluten Exposure	
Manipulation or selection of dietary components	Engineer gluten-free grains Polymeric gliadin binders and neutralizers
Enzymatic degradation of gluten	*Aspergillus niger*-derived prolyl endopeptidase ALV003 enzyme cocktail Probiotics
Inhibit Intestinal Permeability	
Zonulin inhibition	Larazotide acetate
Modulate the Immune Response	
Decrease adaptive immune activity	Block transglutaminase 2 (TG2) antibodies Block antigen presentation by HLA-DQ2 and HLA-DQ8
Induce oral tolerance to gluten	Gluten peptide vaccine
Source: [93; 94; 95; 101; 102; 133; 134]	*Table 3*

The treatment of CD also includes the management of complications. Dapsone can be used to treat dermatitis herpetiformis until the gluten-free diet has had effect; the drug typically relieves symptoms within one to three days [37; 99]. Because of the potential for dapsone to cause hemolysis in some individuals, a baseline blood count and periodic follow-up testing are recommended [99]. The use of bisphosphonates for osteoporosis may be appropriate, although their use for osteoporosis related to CD has not been studied extensively [34].

THERAPEUTIC ALTERNATIVES

Adherence to a gluten-free diet can be difficult to sustain due to gluten cross-contamination in food products, higher costs and limited availability of gluten-free products, lower palatability (resulting in low compliance), and cultural practices [93; 95; 100]. Therapeutic alternatives have been developed to reduce the need for a gluten-free diet based on available insights into the pathogenesis of the disease (***Table 3***). Clinical trials for some of these alternative therapies are ongoing, and none are widely recommended as of 2022 [93; 101; 134].

REFRACTORY CELIAC DISEASE

Refractory CD is a malabsorption syndrome defined by villous atrophy and usually an increase of intraepithelial lymphocytes in the small bowel despite strict adherence to a gluten-free diet [103]. The real prevalence of refractory CD is unknown but likely rare; however, it may be the cause of underlying persistent or recurrent symptoms in 10% to 18% of patients treated for CD. It affects two to three times more women than men [104]. Common symptoms include persistent diarrhea, abdominal pain, and involuntary weight loss. Vitamin deficiencies, anemia, fatigue, and malaise are also frequent. Refractory CD is most often diagnosed following development of new symptoms or recurrence of diarrhea after initial clinical response to a gluten-free diet for years.

Refractory CD can be subdivided into types I and II, with phenotypically normal and aberrant intraepithelial T lymphocytes in the small intestinal mucosa, respectively [105; 106]. Type II can be complicated by ulcerative jejunitis or enteropathy-associated lymphoma. The five-year survival rates are 80% to 96% for type I and 44% to 58% for type II, which carries a higher risk of developing lymphoma [106].

Aggressive nutritional support is an important component of the treatment of refractory CD. Total parenteral nutrition is frequently necessary [103; 107; 108]. Correction of trace element deficiencies (e.g., zinc, copper) should also be included. Strict adherence to a gluten-free diet is widely recommended [107; 108; 109]. Depending on the severity of refractory CD, alternative therapies may include prednisone, budesonide, or a combination of prednisone and azathioprine to induce clinical remission and recovery of mucosa [106; 107; 109; 110; 111; 112; 113]. Type II refractory CD is usually resistant to any known therapy. Alternative therapies being investigated include cladribine, autologous stem cell transplantation, and interleukin-15-blocking antibodies [106; 114].

FOLLOW-UP

The American Academy of Nutrition and Dietetics recommends that nutrition therapy be coordinated with a team of clinical professionals (e.g., gastroenterologists, endocrinologists, allergists), depending on the coexisting condition(s) of the individual with CD. Follow-up measures should include: monitoring and evaluation of patient compliance with the gluten-free dietary pattern, evaluation of any persistent GI symptoms, and evaluation of factors affecting the individual's quality of life (e.g., social/medical support, daily stress level) [98]. A survey to assess dietary compliance has been proposed for use in adults [115]. Follow-up measures for the child with CD should also include an assessment of the adequacy of growth and well-being [18].

Healthcare professionals should ensure that patients and their families have the resources, education, motivation, and support to comply with a gluten-free diet. Serologic testing should be done to monitor compliance with a gluten-free diet; strict adherence usually leads to antibody levels becoming normal within 3 to 12 months after starting the diet [34]. A lack of response according to serologic testing may indicate continued exposure to gluten; if the patient has been adhering to the gluten-free diet, the clinician should explore other diagnoses. Among other diseases that appear similar to CD are microscopic colitis, pancreatic insufficiency, inflammatory bowel disease, ulcerative jejunoileitis, collagenous sprue, and T-cell lymphoma [34].

CD is associated with a risk of non-Hodgkin lymphoma that is three to six times higher than for the general population, and the risk for lymphoma is higher for individuals in whom CD is diagnosed later in adulthood [116; 117]. Data have suggested that the risk of lymphoma decreases over time on a strict gluten-free diet [118]. New GI symptoms or other signs of lymphoma should prompt further evaluation. Studies have indicated that the risk of colorectal cancer is not increased among individuals with CD [119; 120].

EDUCATION AND SUPPORT

Healthcare practitioners who treat the individual with CD should be knowledgeable about the importance of a gluten-free diet and should understand the factors (e.g., cost concerns, social stress, feelings of isolation) that contribute to patient noncompliance [121]. Individuals with CD require ongoing education and support that address the physical and psychologic concerns associated with the disease [122]. Sources of gluten may be difficult to detect. Dining at a restaurant or friend's home, attending social gatherings at which food is served, and routine grocery shopping can be stressful events if the individual is not equipped with appropriate management strategies. Patient education should include information about how to create and maintain a gluten-free lifestyle for both adults and children with CD (***Table 4***).

Individuals with CD and their families should be encouraged to participate in CD support and advocacy groups. They also should be encouraged to seek healthcare practitioners who provide supportive patient-centered care and who understand the daily stresses associated with maintaining a gluten-free lifestyle [124]. Healthcare practitioners should be knowledgeable about the coping strategies used by the patient with CD and should assess the impact of these strategies on the individual's quality of life [40; 122; 123].

CASE STUDY

T is a girl, 7 years of age, who presents to her pediatrician, Dr. G, with complaints of fatigue, abdominal cramping, and diarrhea. T weighed eight pounds, three ounces at birth, and her growth and development have been consistent and appropriate. She has no pre-existing conditions and is current on all of her immunizations.

T is afebrile and her vital signs are within normal limits. A diagnosis of viral gastritis is made. Dr. G advises T's mother (Mrs. H) to limit her daughter's diet to bland foods and give the symptoms time to run their course. Mrs. H is advised to call if symptoms do not improve.

At home, T rests and consumes chicken broth and gelatin. After three days, she is feeling better and ready to return to school. At school the next day, T lunches at 11:30 a.m. on tomato soup, a grilled cheese sandwich, and mixed fruit. T is feeling tired but otherwise well. She consumes all of her soup and fruit, but only a few bites of the sandwich. Around 1:00 p.m., T complains to her teacher of stomach cramping and asks to go to the restroom.

Mrs. H picks T up from school at 3:00 p.m.; T continues to experience stomach cramping and tells her mother that she has had three episodes of diarrhea that day. When she arrives home, T consumes nothing but gelatin and ginger ale and spends the rest of the day in bed. Although T feels better the next morning, Mrs. H keeps her at home and in bed and continues to give T only gelatin, chicken broth, and ginger ale. For the next two weeks, Mrs. H keeps T on a diet of soups and liquids to allow her stomach time to recover. When T appears to be improving, Mrs. H decides to slowly introduce other foods back into her diet.

Within two days, T relapses and experiences diarrhea, bloating, and stomach cramping. Mrs. H schedules a follow-up appointment with Dr. G, who re-evaluates T and discovers that she has lost one pound in body weight and that her stomach is tender to palpation. Dr. G orders additional workup, including blood work, with the following results:

- Hemoglobin: 10.8 g/dL (Normal range: 11.5–14.5 g/dL)
- Hematocrit: 34% (Normal range: 35% to 42%)
- Platelets: 225 (Normal range: 250–500)
- Sodium: 127 mEq/L (Normal range: 136–145 mEq/L)
- Potassium: 3.3 mEq/L (Normal range: 3.5–5.0 mEq/L)

TIPS FOR MAINTAINING A GLUTEN-FREE LIFESTYLE			
Location	**Possible Gluten Source**	**Action**	**Comments**
Kitchen, market/grocery store	Foods (e.g., butter, margarine, mayonnaise, mustards, jams, jellies, peanut butter) Utensils Appliances	Dedicate storage for bulk items. Dedicate freezer space. Label foods or ensure kitchen is gluten free. Purchase dedicated cooking appliances, utensils. Learn to read labels. Look for products labeled as "gluten free."	Avoid foods made with wheat, rye, and barley. Avoid oats, unless they are specifically gluten-free. Avoid processed foods, beer, milk/dairy products with lactose. Use caution when purchasing products labeled "gluten free."[a]
Bathroom	Cabinets Medications Shampoos, soaps, cosmetics Toothpaste, mouthwash	Call or check website of product manufacturer. Check with pharmacist and/or pharmaceutical company to ensure medications are gluten free.	Tablets, capsules and vitamins may contain gluten; wheat starch is commonly employed as binding agent. Gluten is used in some cosmetics, but this is generally an issue only if the product is ingested (e.g., lipstick).
Office	Postage stamps Envelopes Stickers	Use wet sponges or self-stick stamps and envelopes.	—
Playroom	Play dough, glue, paint, stickers, paper mâché	Call or check website of product manufacturer.	—
School, daycare, play dates	Cafeteria Sharing lunches Birthday parties Art supplies	Meet with teacher and school nurse. Provide child with bag lunch. Work with cafeteria staff to develop gluten-free options. Provide child with gluten-free treats.	Many schools accommodate children under 504 plans (part of the Rehabilitation Act and the Americans with Disabilities Act).
Restaurants	Difficulty finding gluten-free items on the menu Possible cross-contamination during meal preparation (e.g., the deep fryer)	Call or visit restaurant ahead of time. Avoid busy times. Plan ahead when traveling.	Many restaurants offer gluten-free menu options.
Church	Communion wafers Church socials	Discuss with minister, priest, or church leader.	—
[a]Effective August 2013, the U.S. Food and Drug Administration requires that any food labeled "gluten free" contain less than 20 ppm of gluten.			
Source: [98; 123; 124; 125; 126]			*Table 4*

- Calcium: 6.9 mg/dL (Normal range: 9.0–11.0 mg/dL)
- Albumin: 2.6 g/dL (Normal range: 3.5–5.5 g/dL)

Mrs. H and T return to Dr. G's office to review the results of the blood work. T has continued to have spells of diarrhea and stomach pains, and she has lost an additional six ounces. Dr. G suspects that T has CD. He schedules further evaluation and an EGD.

Two weeks later, Mrs. H and T return to Dr. G's office for a consultation. Dr. G explains the study results, which revealed atrophy of intestinal villi. He explains that T is experiencing malabsorption of important nutrients, likely due to an intolerance to wheat, rye, or barley products in the foods she is eating. T is referred to a dietitian, Ms. D, who specializes in pediatric nutrition and CD.

T and her parents meet with Ms. D, who explains that CD is an immunologic response to wheat, rye, or barley products that causes destruction of the lining of the small intestine, which in turn causes malabsorption of important nutrients. Ms. D further explains that destruction of the lining leads to diarrhea, fatty stools, weight loss, foul-smelling gas, and iron-deficiency anemia. She reassures the family that, although it sounds frightening, CD is easily controlled with dietary changes and provides the family with a list of foods to avoid as well as sources of "hidden" gluten (e.g., school supplies).

Ms. D works with the family to develop one week's worth of gluten-free meals that T will be willing to eat. They openly and at length discuss challenges that the family may encounter. Ms. D recommends that the family explore a nearby CD support group, which can help them with the adjustments they need to make.

T and her mother return to Dr. G's office for a one-year check-up. T's laboratory tests are normal, and she is slowly gaining weight. Mrs. H reports that T has had some minor episodes of bloating and diarrhea after eating something on the forbidden list when at a friend's house. Dr. G states that T is progressing well and indicates that a few slips in the diet are to be expected, but reminds them that these should not be frequent.

One month later, Mrs. H finds T lying on her bed, crying. Mrs. H asks what is wrong, but T responds that she does not want to talk about it. When Mrs. H persists, T tells her that she was not invited to V's sleepover because V's mother is afraid that T will eat something she should not and get sick. She also reports taunting and feeling left out at school.

Mrs. H calls one of the mothers from the support group to discuss what is happening to T, and the mother provides Mrs. H with some helpful tips. Mrs. H then schedules a meeting with T's teacher to educate him about T's CD and to discuss ways to help lessen the alienation T is feeling. Mrs. H asks him to telephone her if another student's parent plans a celebration so that she can send in a special treat for T. He agrees and promises to be more aware of the way that T is being treated by her classmates.

Later in the week, Mrs. H calls V's mother and invites her to meet for coffee. When they meet the next day, Mrs. H explains what CD is and how it is controlled. She tells V's mother that she is not trying to force her to invite T to her home; she simply wants her to know that CD is nothing to fear. V's mother explains that she was not sure she wanted to take the risk of T becoming ill at her home if she ate something she was not supposed to have. Mrs. H responds that T is very knowledgeable about what she can and cannot eat and explains that small amounts of forbidden foods do not cause a severe reaction in T. That evening, V calls and invites T to the sleepover and apologizes for not having invited her sooner.

After the telephone call, Mr. and Mrs. H discussed some of the misconceptions that the school and their community had about CD. They decide to develop an educational program to present to area schools to increase awareness about CD. Six months later, they have presented the program to local schools and received positive responses and many questions. The next year, prior to the start of the school year, the couple is asked to return and present the information again.

T states that her school days improved greatly after the educational programs were presented.

CONCLUSION

CD is an immune-mediated systemic disorder elicited by gluten in genetically susceptible individuals. It is a costly burden to the U.S. healthcare system and a global health concern, impacting 1% to 3% of the global population and requiring a multidisciplinary approach to care and treatment. The symptoms of CD can mimic those of other autoimmune diseases and may vary widely from one individual to another, making diagnosis difficult. However, because CD is reversible, early diagnosis is important in the management of the disease. Strict adherence to a lifelong gluten-free diet is the only recommended treatment for CD. Ongoing education and support are vital to helping the patient (and family) comply with the dietary pattern.

RESOURCES

Academy of Nutrition and Dietetics
https://www.eatright.org

Beyond Celiac
https://www.beyondceliac.org

Canadian Celiac Association
https://www.celiac.ca

Celiac.com
https://www.celiac.com

Celiac Disease Foundation
https://celiac.org

Celiac-Disease (Celiac News and Gluten-Free Diet Resources)
http://celiac-disease.com

National Celiac Association
https://nationalceliac.org

Center for Celiac Research and Treatment: Children
https://www.massgeneral.org/children/celiac-disease

Gluten-Free Drugs
http://www.glutenfreedrugs.com

Gluten Intolerance Group
https://.gluten.org

National Institute of Diabetes and Digestive and Kidney Diseases
https://www. niddk.nih.gov

PreventCD
https://www.preventceliacdisease.com

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

FACULTY BIOGRAPHIES

Diane Thompson, RN, MSN, CDE, CLNC, has an extensive history in nursing and nursing education. She possesses a strong background in diabetes and cardiac care, starting her professional career at the cardiac care area of the Cleveland Clinic in Cleveland, Ohio. Ms. Thompson took the knowledge and experience she learned from the Cleveland Clinic and transferred it into the home health arena in rural Ohio, after which she moved to Florida and obtained further knowledge while working as a PRN nurse in all areas, including medical/surgical, intensive care, emergency, critical care, and cardiology. With a desire to have a specific area to concentrate her profession, Ms. Thompson accepted a position as a pneumonia case manager, which led into a diabetes case manager career.

Ms. Thompson has been employed in diabetes care since 2001, when she was hired as a diabetes case manager. After the completion of 1,000 hours of education to diabetes patients, Ms. Thompson earned her certification as a diabetes educator in 2003. From 2006 to 2018, Ms. Thompson was the Director of Diabetes Healthways at Munroe Regional Medical Center in Ocala, Florida. As the director of the diabetes center, Ms. Thompson was responsible for the hospital diabetes clinicians, hospital wound care clinicians, and out-patient education program. Today, she is the nurse manager of a heart, vascular, and pulmonary ambulatory clinic at Metro Health System in Cleveland, Ohio. Ms. Thompson has also lectured at the local, state, and national level regarding diabetes and the hospital management of hyperglycemia. Ms. Thompson is a member of the ADA, AADE, Florida Nurses Association, and the National Alliance of Certified Legal Nurse Consultants.

Ms. Thompson acknowledges her family as her greatest accomplishment. She is a wife of more than 30 years and a mother of a daughter and son, of which she is very proud. Ms. Thompson credits her husband for the support needed to set a goal and achieve it. He has been by her side through nursing school and completion of her Bachelor's degree and Master's degree, which she was awarded in 2015 from Jacksonville University in Florida.

Sylvia Bower, RN, has an extensive history in the nursing profession. She is a graduate of Grant Hospital School of Nursing and attended Franklin University in Columbus, Ohio and St. Joseph's College in Maine, and attended Liberty University. She has been registered to practice nursing in Ohio, Texas, Missouri, Arizona, Tennessee, and Florida, and she has practiced in public health, emergency, orthopedics, long-term care, occupational health, ambulatory care, nurse recruitment, discharge planning, hospice care, and continuing education.

Ms. Bower has had a lifelong interest in long-term care, working and volunteering in a variety of settings. She has written program development for case management and was certified in nursing administration and case management. Since her retirement, she has worked in hospice as a volunteer at an inpatient unit.

In 1996, Ms. Bower was diagnosed with celiac disease and began gathering research on the history and pathophysiology of the disease. She subsequently authored two books on the topic. She has also lectured extensively on celiac disease to local and national groups. She serves as a board member of the nonprofit Gluten-Free Gang of Central Ohio, which develops, provides, and promotes education, community awareness, and research for those diagnosed with celiac disease and/or gluten intolerance. Her passion is patient education for individuals and families affected by celiac disease.

Her greatest accomplishments are family of three adult children, six grandchildren, and six great-grandchildren.

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