Dietary Guidelines and Implementation for Celiac Disease

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Medical nutrition therapy is the only accepted treatment for celiac disease. This paper summarizes a review of scientific studies using the gluten-free diet, nutritional risk factors, controversial elements of the diet, and its implementation in treating celiac disease. Treatment for celiac disease requires elimination of the storage proteins found in wheat, rye, and barley. The inclusion of oats and wheat starch is controversial. Research supports that oats may be acceptable for patients with celiac disease and can improve the nutritional quality of the diet. However, use of oats is not widely recommended in the United States because of concerns of potential contamination of commercial oats. Studies assessing the contamination of commercial oats are limited. Research indicates no differences in patients choosing a strict wheat starch-containing, gluten-free diet vs. a naturally gluten-free diet. Factors other than trace gluten may be the cause of continued villous atrophy in some patients. The impact of nutrient malabsorption caused from untreated celiac disease is well documented. The diet and gluten-free products are often low in B vitamins, calcium, vitamin D, iron, zinc, magnesium, and fiber. Few gluten-free products are enriched or fortified, adding to the risk of nutrient deficiencies. Patients newly diagnosed or inadequately treated have low bone mineral density, imbalanced macronutrients, low fiber intake, and micronutrient deficiencies. Also troubling is the increased incidence of obesity seen in persons with celiac disease following a gluten-free diet. Because of the nutritional risks associated with celiac disease, a registered dietitian must be part of the health care team that monitors the patient's nutritional status and compliance on a regular basis.

Medical nutrition therapy (MNT) is the only accepted treatment for celiac disease (CD). The gluten-free (GF) diet (GFD) is sometimes called the "drug of choice" by patients. Medical nutrition therapy is a strict GFD for life. E. Hartsook, PhD, in the 1970s, developed the comprehensive GFD guidelines used in America. Her work was based on scientific research available at the time and was the basis of the Dietary Guidelines used by the American Dietetic Association for a number of years. Until the time of her death in 1996, she was the leading research dietitian in CD in the United States. Her work focused on areas of concern for patients' health and providing dietary guidelines and support based on scientific evidence. Four national US celiac patient support organizations have been formed since 1975. Some of these organizations extrapolated life experiences and added antidotally unsubstantiated restrictions to the GFD. In 1975 and for several years after, research related to the management of CD, specifically the impact of the GFD was limited. Little was known about the effects of malabsorption on the celiac patient, the impact of following the GFD, and what the guidelines for management should include. In the late 1990s, a handful of dietitians in the United States and Canada took up the cause for celiac patients and began the long ordeal of reevaluating claims and restrictions made to the GFD. Based on updated scientific information, the dietary guidelines were rewritten for the American Dietetic Association in 2000, cooperatively by dietitians in Canada and the United States.[1]

This paper is a comprehensive review of scientific literature on the management of CD through the use of the GFD. It looks at the current GFD, areas of controversy, and nutritional risk factors of persons with CD at diagnosis and following the GFD and the implementation and management of CD utilizing the GFD.

Background

The GFD avoids intact storage proteins found in wheat, rye, barley, and hybrids of these grains, such as kamut and triticale. Several studies indicate that these grains contain epitopes in which the deamidation is important for the binding of DQ2 and T-cell recognition, leading to the damage seen in CD.[2–6] Historically, rice, corn, and potatoes were substitutes for gluten-containing grains. Today a number of nutrient-dense grains, seeds, legumes, and nut flours offer increased

Abbreviations used in this paper: CD, celiac disease; GF, gluten-free; GFD, gluten-free diet; MNT, medical nutrition therapy; WSB, wheat starch based.

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Table 1. Grain, Seeds, and Other Starches Sources in the GFD

Storage proteins allowed	Storage proteins not allowed
Amaranth[a]	Wheat (Spelt, semolina, durum)
Arrowroot	Rye
Buckwheat[a]	Barley
Corn/maize	Triticale
Indian Rice Grass (Montina)	Kamut
Legumes[a]	
Mesquite	
Millet	
Nuts	
Potato	
Quinoa[a]	
Rice	
Sorghum/Milo[a]	
Soy[a]	
Tapioca	
Tef/Teff[a]	
Wild rice	

[a]These sources are more nutritious than other starches in the GFD; higher fiber, protein, calcium, iron.

variety, improved palatability, and higher nutritional quality to the GFD. These grains and seeds include the following: amaranth, buckwheat, flax, Indian rice grass, millet, tef, quinoa, and sorghum.[7] See Table 1 for a listing of GF grains and seeds.

Oats

The inclusion of oats and wheat starch in the GFD is controversial, with no clear-cut guidelines for their use. Short- and long-term studies, involving adults[8–12] and children[13,14] during the last decade suggest that oats can be included safely in the GFD. Størsrud found that the use of oats increased the patient's intake of iron, dietary fiber, thiamin, and zinc.[10] Although a number of studies have been done in conjunction with use of oats in the GFD, they have been relatively small, few have been double blind or randomized, and only one has been greater than 1-year duration. However, use of oats in the GFD is not widely recommended in the United States and Canada because of concerns of unacceptable high levels of cross contamination. A study by Lundin et al, in Norway, confirms that contamination of commercial oats can vary widely.[15] Lundin et al found contamination levels between <1.5 ppm and >400 ppm in commercial oats from a single bag. In the sample with the highest levels, it was difficult to determine the source of contamination, but Lundin et al suspected barley, not wheat, as the source. Testing of the "bottom of the bag" of the same product found contamination of <1.5 ppm. Furthermore, Lundin et al demonstrated that even pure oats caused villous atrophy and dermatitis in at least 1 patient. This may be a rare situation but does cause concern.[15] Research supports that oats may be acceptable for the majority but not all patients with CD. Lundin et al also suggest that there may be a subset of CD patients who have an exaggerated sensitivity to oats, not related to CD. Although some patients experience increased flatus and gastrointestinal (GI) discomfort when consuming oats, this may be related to the increase in fiber while eating oats, rather than contamination. At this time, there are no large-scale studies available to assess the potential contamination of commercial oats. Continued research in this area is warranted.

Wheat Starch

Wheat starch is used in some European countries as part of the GFD. A food product is considered GF by Codex standards if it contains less than 0.05 g nitrogen per 100 g dry product matter. Wheat starch-containing GF products therefore may contain as much as 40–60 mg gluten/100 g dry product (20–30 mg gliadin). According to Codex standards, wheat starch must contain not more than 0.3% protein in the dry matter.[16–18] European wheat starch used in GF food products is industrially purified to meet the Codex standards for GF. It is estimated that the Codex-GFD contains 2.5 mg gliadin in the form of malt and wheat starch.[19]

Inclusion of wheat starch-based (WSB) products has been controversial for years. Despite the accepted use of wheat starch-based diets in Europe, wheat starch is currently not recommended for use in North America. Early studies indicating a negative impact of wheat starch in CD were short-term open or cross-sectional studies.[19] The open challenge study by Chartrand et al showed that wheat starch GF products caused abdominal symptoms.[20] Faulkner-Hogg et al[21] studied adult CD patients who had continuing GI symptoms while following a GFD: 56% of the participants were following a GFD as defined by the WHO/FAO Codex. All participants were required to change to a "no-detectible gluten" GFD. Those who continued to be symptomatic underwent diet studies to detect other nongluten food or food chemical intolerances. Symptoms either resolved (23%) or were reduced (45%) by changing to a "no-detectible gluten" GFD in 23% and 45%, respectively. Thirty-one patients participated in an elimination diet for food intolerances. Faulkner-Hogg et al suggest that the trace amounts of gluten allowed by the Codex may be responsible for continued symptoms seen in a subgroup of patients with increased sensitivity and that a "no-detectable gluten" GFD may be required in these patients.[21] However, this study also reveals that 24 of the 37 patients, who under-

went an elimination diet, had at least 1 food intolerance other than gluten.

Selby et al found that some patients who had been on a GFD for 8 years continued to have mucosal abnormalities and that there were no differences between patients on a Codex-GFD and those on a "no added gluten-gluten free diet."[22] In a cross-sectional study of 89 adult subjects, Selby et al[22] confirm early studies by Ciclitira et al that the small amount of gluten allowed by Codex, generally found as wheat starch or malt, is not responsible for the villous atrophy, increased intraepithelial lymphocytes (IEL) counts, and low lactase levels seen in some patients.[23,24] In a study of children and adults with CD and dermatitis herpetiformis (DH), Kaukinen et al also indicate no differences in villous architecture, density of IEL, serum antibodies, bone mineral density, or quality of life in patients choosing a strict wheat starch-containing GFD vs. a naturally GFD.[25] In this study, Kaukinen et al studied subjects following a GFD long-term (range 4–10 years), as well as those newly diagnosed. Only 76% of the long-term GFD subjects were actually on a strict WSB-GFD. On this diet, the calculated mean consumption of gluten was 34 mg (5–150 mg). Only subjects admitting to dietary indiscretions were found to have subtotal or severe partial villous atrophy. Complaints of adverse GI symptoms were limited but did not alter by the patient's chosen diet. Kaukinen et al[25] conclude that, even with long-term ingestion of wheat starch, as allowed by the Codex, no harmful effects are seen in the small bowel mucosa as a result of the gluten ingestion. The findings of Lohiniemi et al[26] concur with Kaukinen et al[25] and add that, when wheat starch is added to the GFD, the average fiber intake is lower than recommended at 13 g/day.[26] Selby et al,[22] Kaukinen et al,[25] and Lohiniemi et al[26] all suggest that factors other than trace amounts of gluten, such as dietary noncompliance or other food intolerances, may cause continued villous atrophy in some patients.

Recently, Peräaho et al conducted a randomized, year-long study of 57 adults newly diagnosed between 1998 and 2000, who were randomized to either a WSB GFD or a natural GFD.[27] The groups were similar with respect to age, sex, and initial symptoms. At the initiation and end of the study period, participants underwent histology and serology studies, nutritional assessment, dietary intake evaluations, and body mass index and bone density measurements. The dietitian also provided dietary education to patients and assessed the daily consumption of GF flours. The mean consumption of GF flours after 3 months and 9 months in the study averaged 79 and 77 g/day in the naturally GFD and 82 and 81 g/day in the WSB GFD, respectively. Quality of life studies were also conducted. Although mucosal recovery was not complete in all patients, Peräaho et al[27] found that there were no differences between the 2 groups in the mucosal morphology, the density of IEL, serum antibodies, bone mineral density, nutritional status, or quality of life tests after 1 year. In patients from both groups who had dietary lapses (4 and 2, respectively), inadequate mucosal, serology, and clinical recovery was observed.

Recent studies suggest that wheat starch is a safe and well-tolerated addition to the GFD when the GFD is otherwise strict. Wheat starch is not currently accepted in the United States or Canadian GFD; however, if Codex-grade wheat starch is available in the United States, it is prudent to further evaluate its inclusion in the GFD.

GF Standards

Worldwide, there is debate regarding the accepted definition for what constitutes "gluten-free." Products labeled "gluten-free" in Canada must meet standards of less than 20 ppm gluten (=20 mg gluten/1 kg), whereas other countries use 200 ppm, and still others prefer a double standard for products rendered GF and those naturally GF. This debate fuels confusion about labeling products GF. The current Codex standard for "Gluten-Free Foods" was adopted by the Codex Alimentarius Commission in 1976 and amended in 1983. In this document, gluten is defined as those storage proteins commonly found in wheat, triticale, rye, barley, or oats. The definition came under review in the1990s. As of the 25th Session of the Codex Alimentarius Commission, the definition of GF continues to remain at step 7 while the committee awaits research on the scientific basis for the establishment of a tolerance level and a method of detection is clarified.[16,28] The Working Group on Prolamin Analysis and Toxicity is currently evaluating a sandwich R5-ELISA system as proposed by the Codex Alimentarius Commission. This new system has good reproducibility (8.7%) and repeatability (7.7%). In a study by Valdés et al,[29] the R5-ELISA was able to identify gliadins, hordeins, and secalins with sensitivities of 0.78, 0.39, and 0.39 ng/mL, respectively. The assay's detection limit was 1.56 ppm gliadins or 3.2 ppm gluten.[29]

Acceptance of R5-ELISA by the Codex Commission and results of ongoing research on tolerance levels will allow the commission to advance toward a revised definition of "gluten-free." Collin et al[30] have estimated a safe and rational threshold for daily gluten at 100 ppm gluten (=100 mg gluten/1 kg), providing that the total daily GF flour intake does not exceed 300 grams. This

Table 2. Common Nutrient Deficiencies in Celiac Disease

At Diagnosis[a]	GFD[a]	GF products[a]	Long-term GFD[b]
Calorie/protein			
Fiber	Fiber	Fiber	Fiber
Iron	Iron	Iron	
Calcium	Calcium		
Vitamin D	Vitamin D		
Magnesium	Magnesium		
Zinc			
Folate, niacin, B_{12}, riboflavin	Folate, niacin, B_{12}, riboflavin	Folate, thiamin, riboflavin, niacin	Folate, niacin, B_{12} (w/supplements)

[a]Thompson.[38,39]
[b]Hallert et al.[34]

level was determined by taking into consideration the amount of residual gluten found in GF products and the total intake of these products. At this level of intake, studies indicate good mucosal recovery. This study also shows that gluten cannot be totally avoided, and many GF products, whether naturally GF or WSB, contain varying amounts of gluten. Furthermore, in Finland, long-term compliance with the WSB GFD was better and the incidence of intestinal lymphoma lower than reported in other studies with a naturally GFD.

The American Dietetic Association (ADA), in conjunction with the Dietitians of Canada, revised the GFD guidelines in 2000. Currently, the ADA is involved in a National Gluten-Free Diet Project to review current science to provide evidence-based support for the dietary recommendations and restrictions of the GFD.[1]

Nutritional Deficiencies

Numerous studies document the impact of nutrient malabsorption caused from CD in both children and adults. Intestinal motor function caused by nutrient malabsorption may be partially responsible for the delayed gastric emptying seen in children according to Perri et al.[31] A study by Bona et al indicates that low dietary intake or malabsorption of B vitamins, iron, and folic acid appears partially responsible for delayed puberty in children with CD.[32] Jameson reports a correlation between zinc deficiencies and the severity of villous atrophy in adults. He also reports that the more pronounced the lesion, the lower the levels are seen for iron, copper, folate and vitamin B-12.[33] Hallert et al[34] assessed the total plasma homocysteine levels in patients following a GFD. Compared with controls, persons following a GFD showed poorer vitamin status for folate and vitamins B-6 and B-12, even when taking nutrient supplements.[34] Studies report an incidence of an average of 4% anemia in the patients with newly diagnosed CD in the United States. Although vitamin B-12 deficiency is not unusual in CD, pernicious anemia is considered uncommon.[35,36] Recovery from iron-deficiency anemia is possible with a GFD alone.[37] Bone disease in CD of adults and children is well documented in the literature. Calcium, vitamin D, magnesium, and fiber, especially soluble fiber, are also limited in the GFD. In the United States, very few GF products are enriched, as are wheat-containing products, adding to the increased possibility of prolonged nutrient deficiencies. GF products, without enrichment are lower in fiber, iron, folate, thiamin, riboflavin, and niacin.[38,39] Table 2 summarizes common nutrient deficiency concerns in CD and the diet. Additionally, some patients report other food sensitivities and intolerances, most commonly to dairy products, eggs, soy, and rice. Although these sensitivities may be temporary and resolve with healing of the small intestine, additional restrictions to the GFD increase risk of overall nutritional deficiencies.

In an Italian study of body composition and dietary intakes of adults with CD following a strict GFD, weight and body mass index of CD patients were significantly lower than that of controls, as were fat and lean body mass. Bone mineral content of women diagnosed as adults was significantly lower than controls. The diets of these patients were unbalanced and had a higher percentage of calories from fat and less from carbohydrates.[40] Mariani et al showed similar results in the nutritional analysis of children with CD. They found that the children complying with a strict GFD had significantly greater nutrition imbalance in their diet than did children cheating on their GFD. More troubling, the incidence of children overweight or obese was more frequent (72%) in the strict GFD group, compared with the children not following a strict GFD (51%) and healthy age-matched controls (47%).[41]

Vitamin and mineral supplementation can be useful adjunct therapy to the GFD. Studies have not specifically looked at the efficacy of nutrient supplementation in

Table 3. Problem Ingredients in Medication

Drug ingredient	Comments
Starch	Source must be known Gluten-free: made from corn, rice, tapioca, or potato Not safe: Made from wheat
Pregelatinized starch	Gluten-free: Made from corn or tapioca; Safety of drugs with wheat starch questionable
Dextrimaltose	Source must be known Processed by enzymatic action of barley malt or corn flour
Flour, gluten, dusting powder	Source must be known Generally not GF
Malt, malt syrup	Derived from barley and used in production of other ingredients
Dextrin, dextrates, cylcodextrins	Source must be known GF if from corn or potato starch Not GF if from wheat
Maltodextrin	Source must be known Derived from caramel color; in the United States, it is generally corn based. Possibly from wheat or oat.
Sodium starch glycolate (carboxymethyl starch)	Source must be known GF if from potato, corn, rice, or tapioca starch. Can be made from wheat
Caramel color	Derived from barley malt syrup or unidentified starch hydrolysates Could request "dye-free" drugs
Alcohol (distilled ethanol)	Gluten free

treatment of CD. However, improving nutrient malabsorption and comorbid conditions related to nutritional deficiencies could be safely hastened with vitamin and mineral therapy. As with any oral medication, GF status of vitamin and mineral supplements must be assured. FDA regulations for ingredients differ between medications and foods. Problems with medications are generally caused by the source of inactive ingredients and are of concern in oral medications. Table 3 reviews some problematic ingredients in medications and vitamin/mineral supplements. It is difficult to assure the safety of ingredients in nonregulated herbal medications and similar nutritional supplements. The responsibility for safety of medications and supplements starts with the ordering physician. It would be an impractical possibility for physicians to know which medications are GF. However, adding a statement such as "As ordered if gluten-free or provide a gluten-free equivalent" obligates the pharmacist to verify medication safety. It may also be useful to avoid generic substitutions, whose sources could change frequently.

Because of the nutritional inadequacies and potential health concerns caused by CD, a registered dietitian must be an integral part of the health care team. Also, persons with CD are experiencing other health risk factors, such as excess weight gains, possibly because of overfeeding as the intestine heals, elevated lipids because of the lack of total fiber and soluble fiber sources in the GFD, and combined diets for comorbid conditions. When properly instructed by a dietitian with expert knowledge in CD, the GFD can be nutritionally adequate, allow healing and return to good health, and decrease risk of associated health conditions, as well as allow catch-up growth in most children. Historically, training for dietitians in CD and GFD was limited. Because of the limited access of registered dietitians experienced in CD, patient support organizations took on the role of making and revising diet recommendations, restrictions, and guidelines used in the United States, often without scientific, evidence-based qualifications for the recommendations. Over time, these modifications have caused a great deal of confusion for patients and may add to increased noncompliance. Today, within the ADA, there is a specialty group of dietitians, Dietitians in Gluten Intolerance Diseases (DIGID), involved in celiac disease. It is important that patients receive MNT from dietitians knowledgeable about this disease. The diet is complicated and can be overwhelming if not presented using a proactive approach. A patient's current nutritional status, instruction in the GFD, and correction of nutritional deficiencies and complications must be addressed by nutrition experts to help minimize additional complications of malnutrition and malabsorption, as well as noncompliance. Studies indicate that compliance to the GFD is compromised by a number of factors, including a lack of education and continued support by a physician and dietitian. In a study by Ciacci et al, dietary compliance and the extent of intestinal damage on follow-up examination could be predicted by baseline education.[40] This study supports the need for frequent reinforcement and accurate explanation of dietary recommendations. MNT is currently the only treatment for management of CD. Maintaining an optimal nutritional state with a GFD and avoidance of potential complica-

tions caused from inadequate care and treatment can be difficult.

Implementing the GFD

Once the diagnosis is made, patients may or may not be referred to a dietitian for education and support, or outdated and incorrect materials may be handed to the patient; care generally stops there. The GFD diet is complex and can easily overwhelm patients. It is best to complete nutrition education in multiple visits, following the needs and learning ability of the patient. An initial assessment of the patient's current nutritional status and potential risk factors for associated complications must be made and psychosocial, learning ability, and economic concerns addressed. Nutritional supplements may be necessary, as well as referrals to social services for support of the person as he or she adjusts to this life-altering condition. Initial education should include basics and survival skills. Follow-up education sessions should expand to include more detailed information and skills, as well as weight management and adjustments to improved nutritional balance of the diet. Long-term, patients with CD should receive a follow-up session with the dietitian at least annually, possibly more frequently with children, pregnant and lactating women, and elderly patients. For this to be practical and feasible, CD should be considered for addition to the MNT payment structure.

Research is Lacking

Studies related to nutritional aspects of CD, especially in the United States, have been limited in size, duration, and study design. Those studies done have not addressed many areas related to long-term use of the GFD, including risk and consequence of increased lipids, chronic inadequacy of micronutrients to overall health, and weight management. As well, case studies indicate the potential for altered eating patterns in children and young adult women, further compromising health. It is important that regular nutritional therapy be a part of the management of CD, that access to care is readily available to all patients, that initial and routine follow-up nutrition therapy is not limited, and that insurance reimbursement is available. To have access to adequate numbers of patients for nutrition studies, establishment of a national patient registry should be considered.

Mandated fortification and enrichment of GFD products would improve the quality of the diet long-term. This warrants further evaluation. Changes in absorption of oral medications and nutrient supplementation related to short- and long-term intestinal damage is a problem. Studies are needed in this area.

In addition to CD, in the gluten sensitivity spectrum are other conditions in which persons respond favorably to gluten withdrawal. Scientifically based research in the pathology and physiology of these conditions is lacking, making the ability to make sound, scientific recommendations for treatment unavailable.

Finally, it is vital that role delineation be clearly defined between the health care team and support organizations. Scientists and health care professionals are the responsible parties for determining the guidelines used for medical and nutrition management. When expert health care professionals set the guidelines, support organizations are able to better provide consistent, reliable information to the consumer.

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