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Nutritional and Dietary Aspects of Celiac Disease

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Celiac disease (CD) is a primarily digestive systemic disease triggered and maintained by the ingestion of gluten in the diet. Its has a wide clinical spectrum of manifestations, particularly varied in adult patients, in whom, because of their frequent negative serology and mild, nonspecific symptoms, there is a considerable delay in diagnosis. The intestinal lesion caused by CD leads to various deficiencies of nutrients, vitamins, and dietary minerals, with ferropenia, vitamin B12, folic acid, and fat-soluble vitamin deficiencies being especially frequent. The deficiencies, together with dairy intolerance, cause low bone density and an increased risk of fractures. Treatment using a gluten-free diet (GFD) does involve certain complications, since gluten is found in up to 70% of manufactured food products and manufacturing regulations are not standard in all countries. In addition, certain nutrient deficiencies require specific management. This article reviews the nutritional aspects of CD and provides practical guidelines to correct these deficiencies and to ensure optimum GFD compliance. (*Nutr Clin Pract*. 2011;26:163-173)

Keywords: celiac disease; diet; gluten-free; glutens; gliadin; nutrition therapy; nutritional deficiencies

Celiac disease (CD) dates far back in history: In I AC, Aretaeus de Cappadocia described an illness with characteristics similar to gluten-sensitive enteropathy, but the first accurate clinical description of the disease was made by Dr Samuel Gee. In 1887, Dr. Gee provided such an accurate description of this entity that a better description has not been obtained since then,[1] recommending dietary treatment of a disease he called "celiac affection." However, it was after the Second World War in 1953 when, a Dutch pediatrician, Willem Dicke, made a connection between the origin of the disease and wheat, observing how wheat supply shortages during the postwar period were linked to improvement shown by affected patients, clearly implying that gluten proteins were precipitants.[2]

At present, CD is considered to be a primarily digestive systemic disorder consisting of a common inflammatory disease of the small intestine triggered and maintained mainly by an immunological response following exposure to gluten in the diet.[3]

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Etiopathogeny

Genetic and environmental factors are involved in the origin of CD. CD can be considered an autoimmune disease of known etiology triggered by the ingestion of gluten-containing foods. It appears in genetically susceptible individuals and leads to different degrees of lesions in the small bowel mucosa, ranging from mild intraepithelial lymphocytosis to severe mononuclear infiltration resulting in total villous atrophy at the most evolved stages.[4,5] The characteristic clinical response is triggered by exposure to gluten, the name given to the proteins present in a group of cereals including mainly gliadin (wheat), secalin (rye), hordein (barley), and triticale (hybrid of wheat and rye).

Between 1% and 3% of the general population in Europe and the United States is affected by CD at some point in their lives.[6-8] CD has a strong MHC class II association, higher than that previously found in many other autoimmune diseases.[9] Approximately 90% of celiac patients carry the HLA-DQ2 heterodimer, which is encoded by the DQA1*05 and DQB1*02 genes carried either in cis position on the DR3-DQ2 haplotype, which is common to many autoimmune diseases, or in trans, where the a chain is encoded on the DR5-DQ7 haplotype on one chromosome and the b chain on the DR7-DQ2 haplotype on the other chromosome.[10] Most patients who are DQ2 negative carry the DQ8 genotype. DQ2 and DQ8 molecules present gluten peptides or related antigens to disease-specific CD4+ T cells.

The pathogenesis of CD includes the activation of cytotoxic T lymphocytes in the duodenal lamina propia[11] and the production of characteristic autoimmune antibodies, which can provoke several lesions in other tissues and organs similar to those observed in the small bowel. The systemic manifestations of CD include a wide clinical spectrum, involving endocrinological, cutaneous, and neurological manifestations, among others. Like most autoimmune diseases, CD predominantly affects women at a ratio of 2:1.

HLA haplotypes conferring risk for CD are not enough to develop the disease alone and are expressed in up to 25% of the general population. Consequently, other factors conditioning the onset of the disease should be taken into consideration. With regard to its forms of presentation during childhood, the age at which gluten is introduced seems to be a risk factor for developing CD, to the extent that a greater risk has been reported if gluten is introduced before the age of 3 months or after 7 months, whereas it is shown to be a protective factor if it is introduced during breast-feeding.[12,13]

Until 20 years ago, CD was considered to be associated with children. However, in recent years, we have attended an increasing number of cases diagnosed in adults. It is common for many patients to go undiagnosed for many years because CD has mild and nonspecific symptoms in adults. It has been estimated that for every new patient diagnosed with CD, between 2 and 7 cases could go undiagnosed, and the average period of evolution of symptoms in adults prior to being diagnosed is calculated to be 11 years.[6]

Clinical Manifestations

CD is no longer a children's disease and can appear at any stage of life, causing anomalies in the structure of the intestine, which can also lead to various disorders relating to the absorption of vitamins and dietary minerals. It is one of the main causes of malabsorption in developed countries.[14]

The classic form of the disease is characterized by the appearance of severe symptoms of malabsorption (diarrhea, steatorrhea, lack of appetite, growth retardation, and deficiencies in fat-soluble vitamins, iron, calcium, and folic acid), positive serum antibodies, and severe villous atrophy, which is the typical presentation in children between the ages of 9 and 24 months. After the age of 3 years, loose stools, short stature, treatment-resistant ferropenic anemia, and mood alterations are frequent. When the disease evolves without any treatment, particularly in the case of children between the ages of 1 and 2 years, severe forms may appear (celiac crisis), involving severe cutaneous or digestive bleeding (due to deficiency in the synthesis of vitamin K and other vitamin K–dependant hemostatic factors), hypocalcemic tetany, and edema caused by hypoalbuminemia.

From adolescence onward and in adulthood, the clinical symptoms are more larvate, and digestive symptoms are either absent or of secondary importance. The most characteristic clinical symptoms at this age are fatigue, which may or may not be associated with anemia (82%), abdominal pain (77%), meteorism (defined as accumulation of gas in the abdomen or the intestine, usually with distension; 73%), ferropenic anemia (63%), as well as delayed menarche and irregular menstruation. Constipation is present in 50% of cases,[15] irritable bowel syndrome is frequently diagnosed (30%), and even the classic image of a thin patient contrasts starkly with reality since up to 30% of patients show evident signs of being overweight. Osteomalacia, osteopenia, and osteoporosis are common (36%), even in the absence of malabsorption, leading to a concomitant increase in bone fractures. In this respect, most adult cases do not stand out as a result of their digestive clinical symptoms, which can also manifest as osteoporosis, infertility, asthenia, or other neurological alterations (such as ataxia) and neuropsychiatric disorders (such as depression).[16] In some cases the disease is asymptomatic, even if duodenal histological lesions are present and there is positive serology. More than half of the diagnosed cases of CD currently occur in individuals older than 50 years,[17] precisely in those in whom CD often has mildly symptomatic manifestations.

Diagnosis

The diagnosis of CD is complex and tends to require a high level of clinical suspicion. The study of all suspected patients should begin with a blood test so that specific antibodies can be determined.

Serological Tests

These are very useful indicators of CD. They identify the patients who need to undergo a biopsy of the small intestine, which is still the gold standard. The negativity of these markers does not definitively rule out diagnosis, since it is very common for adults with CD to have negative serology, and a genetic study is sometimes required if there is very strong suspicion. The absence of risk alleles certainly allows us to exclude the disease, but their presence is not a confirmation because of their high prevalence in the general population. However, the good clinical and laboratory test response to a gluten-free diet (GFD) in a patient exhibiting risk alleles can confirm the disease.[15]

Three antibodies have been useful in diagnosing CD. IgA-class antigliadin antibodies were the first to be introduced. They are more efficient in screening for CD in

children than in adults, but in both cases have low sensitivity and specificity. Antiendomysial antibody tests, which are costly to perform, do not afford clear advantages either. Lastly, the use of IgA anti-tissue transglutaminase antibodies, currently considered to be the most useful markers, is unanimously regarded the best marker for CD screening. In the case of children at least, it should be noted that the anti-transglutaminase antibody titers correlate with the degree of the histological lesion and are very low in children in whom only lymphocytic enteritis is observed, which, on the other hand, is the most common finding in the adult forms. Thus, it is estimated that their sensitivity, which exceeds 90% in the case of childhood CD, is reduced to approximately a mere 15% to 30% in screening for CD in adults,[18] for whom a positivity threshold of 2 U/mL is recommended.[19]

Biopsy of the Small Intestine

A small intestine biopsy should be performed to confirm the serological results if they are positive and also if there is clinical suspicion, even though the serum tests are negative. Multiple biopsies should be taken from the duodenum (from the bulbus to the distal duodenum or even from the proximal jejunum where possible), provided that the patient has followed a diet containing gluten during the previous 6 weeks (3-4 slices of bread per day are usually sufficient). Given that patients with CD are frequently deficient in vitamin K, a coagulation study should be performed before the biopsy. The result of the anatomopathological study confirms the existence of compatible lesions classified into different stages of increasing severity, in accordance with the Marsh classification.[5]

The diagnostic criteria established in 1970 by the European Society for Paediatric Gastroenterology Hepatology and Nutrition included performing at least 3 intestinal biopsies, where it was essential for the patient to consume gluten at the time the first biopsy was being taken. After a gluten-free period had elapsed showing histological normalization, it was recommended to reintroduce (or provoke the introduction of) gluten into the diet, where 3 biopsies in total were required to accurately confirm the diagnosis. These criteria were subsequently reviewed in 1990, when it was indicated that the second and third biopsies would be required in small children only if the histological findings from the first were doubtful or nonspecific or when the clinical response to the exclusion of gluten proved inconclusive.

The presence of serological markets and their normalization after following a GFD support the diagnosis, but it is not a sufficient criterion, per se. Gluten should never be excluded from the diet without being justified by an intestinal biopsy beforehand.

Gluten-sensitive enteropathy with significant clinical repercussions has also been described in individuals with preserved mucosal architecture. Dr Esteve showed that a strategy based on the genetic study of first-degree relatives followed by biopsies in positive cases diagnosed 3 times the number of cases compared with using serology only.[19]

Nutrition Implications of CD

The nutrition status of patients diagnosed with CD in the past was severely compromised as a result of late diagnosis and because only the cases in which the intestine was significantly affected were diagnosed. Today, we know that the nutrition status at diagnosis depends on the length of time the disease is active and has not been treated, the extent of the intestinal damage, and the degree of malabsorption. As already shown, the classical clinical presentation includes steatorrhea and fat-soluble vitamin deficiency.[20] The malabsorption of iron, folic acid, and calcium is also frequent, as they are absorbed in the first section of the intestine, which is the most frequently affected by CD.[21] Monitoring common nutrient deficiencies after beginning a GFD may be useful to achieve an efficient, complete recovery.

The physiology and anatomy of the intestine are modified to a similar extent, which is important in terms of intestinal absorption, since any damage to the intestinal mucosa, for whatever reason, leads to a decrease in the secretion of cholecystokinin,[22] a hormone that stimulates the secretion of pancreatic enzymes required for the absorption of nutrients. This merely exacerbates malabsorption. More than half of celiac patients have low levels of elastase-1 in their stools, a marker of exocrine pancreatic function[23]; these levels return to normal a year after commencing a GFD. Based on these premises, Leeds et al[24] have shown the benefits of supplementation using pancreatic enzymes for patients with persistent gastrointestinal symptoms, despite having correctly followed a GFD.

Iron Deficiency

Iron deficiency occurs very frequently because iron is absorbed at the place that is most severely affected by CD. CD should be considered in the differential diagnosis of unexplained anemia,[25] given that iron deficiency can be the sole manifestation of CD. In fact, certain authors consider it to be the most usual clinical presentation[26-28]; 49% of patients diagnosed with CD previously suffered from anemia,[29] and up to 8% of anemia cases caused by iron deficiency resisting treatment using oral iron supplements can be attributed to CD.[30] The prevalence of CD in patients referred to a digestive endoscopy unit to study ferropenic anemia ranges from 3% to 12%.[31] Once gluten is excluded from the diet, ferropenia can persist until the morphology of the intestine has been

restored and the deposits have been replenished,[32-34] which is why ferritin levels should be determined in all patients for monitoring purposes.[35] Iron levels are restored after following a GFD, although foods rich in iron, such as red meat, can be recommended and even supplements can be prescribed because of the reduced iron content of cereals suitable for patients with CD.[36,37]

If iron supplements are required, it could be advisable to keep using them for up to 6 months after beginning the GFD,[35] the minimum period to normalize the intestinal anatomy. In any case, supplements should be administered with foods rich in vitamin C to optimize their dosage.[38]

B12 Deficiency

In theory, vitamin B12 deficiency was considered to be infrequent as it affects different sections of the intestine to CD. However, at present, we know it is a very important deficiency in patients with CD because different studies have reported a prevalence between 8% and 41%.[39-42]

Vitamin D and Calcium Deficiencies

Both vitamin D and calcium deficiencies are frequent in CD; this may be caused by various mechanisms, first, as a result of their malabsorption and, second, because of frequent lactose intolerance often shown by patients prior to diagnosis, which is why they eliminate milk products from their diet. Of patients with CD, 62% ingest less than the recommended amount of vitamin D, and together with the high prevalence of osteopenia, it might be necessary for patients who do not ingest minimum amounts, or who have a low bone mineral density demonstrated in a bone mineral densitometry test, to resort to supplementation.[43]

Folic Acid Deficiency

Folic acid is absorbed in the jejunum, where the initial sections can be inflamed by the disease. Supplementation is therefore required in cases of severe malabsorption or anemia since the serum levels might not be a fair reflection of the intraerythrocyte levels. It is also essential to ensure that an adequate amount is taken by patients who are planning to give birth, particularly when it is known that the pregnancy is evolving unfavorably, at least in undiagnosed patients. In those requiring supplementation and who are being treated with proton-pump inhibitors, recent studies suggest that it is probably more appropriate to use the methylated form of folic acid.[44]

Other Fat-Soluble Vitamins

There is no universal recommendation for fat-soluble vitamin supplementation; thus, recommendations should be tailored to each individual. However, some authors are in favor of their universal supplementation at diagnosis and then tailoring the doses in each case.[45] This is because 10% of patients with CD are deficient in vitamin K at diagnosis, which is why it is important to correct this even before carrying out the confirmation biopsies in order to ensure adequate blood coagulation.

Other Micronutrients and Mineral Deficiencies

Patients with CD have been reported to be deficient in vitamin B_6, copper, selenium, and zinc.[46] However, universal screening and supplementation is not recommended because these deficiencies reverse rapidly once patients start following a GFD.

Treatment of Celiac Disease: The Gluten-Free Diet

The treatment of CD is based on strictly and permanently eliminating gluten, which is followed by rapid clinical improvement, especially in children. However, it is difficult to follow a GFD on an ongoing basis at any age, and noncompliance with the diet is very frequent, with rates between 50% and 80%,[47,48] Children and adolescents require special care where the diet's limitations can be perceived as a loss. In this respect, various studies have shown that the GFD causes a decrease in quality of life,[49,50] which means that up to 23% of children feel sad most of the time as a result.[51]

Patients should be advised not to consume gluten once they start to gain weight and feel better because even small amounts of gluten can lead to mucosal alterations after several weeks, with modifications in the intestinal biopsy.[52] It should be noted that patients with active CD (clinically manifested) have a greater risk of death than the general population.[17] However, this higher death rate normalizes 3 to 5 years after a GFD has been strictly followed.[17]

The GFD is based on 2 fundamental premises: (1) the elimination of all products containing wheat, barley, spelt, rye, and oats, and (2) the elimination of any products deriving from these cereals (starch, flour, semolina, bread, pasta, pastries, and cakes) and of all the by-products of these grains in food products, beverages, and medication.[53,54] The inclusion of oats is still controversial because commercial oats are often contaminated with wheat or barley. Recent studies have shown that the moderate consumption of oats (50 g/d) is tolerated, provided that they have not been contaminated by gluten from other toxic cereals during the preparation process. Less than 5% of patients should not consume oats as a result of intolerance.[6]

Current consensus recommendations consider that only patients with villous atrophy should follow a GFD[55]; however, patients at stage 1 of the Marsh classification or with lymphocytic enteritis in the duodenal biopsy present the same clinical manifestations as the others[55] and benefit in the same way from the GFD, which is why these recommendations are obsolete and should be reviewed.

Despite its simple appearance, in practice, it is very difficult to follow a GFD in the Western world where wheat is the most widely consumed and used cereal, since 70% of manufactured food products may contain gluten, which is included as a carrier for preservatives, aromas, food coloring, thickeners, additives, moisture barriers, and so forth. Also, until recently, the food industry was not obliged to label the existence of gluten or wheat starch if it amounted to less than 25% of the final weight of the product.[56] Wheat ear, the international wheat-free symbol, does not guarantee the total absence of gluten from food as these products may contain up to 200 parts per million (ppm), an excessively high amount.[57] For this reason, certain countries such as Italy, Australia, Canada, and the United States chose to legally ban the use of wheat starch in the preparation of gluten-free products as they were unable to guarantee levels lower than 200 ppm. Recently, under new legislation, products labeled *gluten-free* should not contain more than 20 ppm, and all products containing any of the 8 most common allergens must be correctly labeled.[58] Be that as it may, the diet should be based on natural foods, and manufactured products should be avoided as far as possible (Table 1).

To prevent patients from receiving incorrect information on the GFD, they should be referred to an experienced dietitian as soon as possible.[60] Alternatively, placing them in contact with a support group or association for celiac patients can provide them with accurate and useful information.[49,61] Table 2 contains the contact details for these support groups (celiac.com).

The GFD should meet an individual's nutrition needs and involve a balanced diet containing optimum macronutrients and micronutrients. It has been observed that limiting the consumption of carbohydrates has led many patients to increase their consumption of fat.[62] This may be a frequent practice in patients with CD, in whom an increased fat intake is usually observed by replacing gluten-containing flour and cereals with others lacking gluten, which must be taken into account to avoid weight gain. The traditional image of patients with CD characterized by thin and diarrheic individuals contrast with the subsequent situation, as up to 30% of all patients are overweight and 50% suffer from constipation.[63]

Prior to commencing the GFD, patients may have certain nutrient deficiencies that may require correction through supplementation for a certain period of time until the optimum absorption capacity of the intestine has been completely restored.[64] In this respect, it is important to monitor the patients' blood tests, not only at the start of the diet but also in the long term, as nutrient deficiencies are also frequent after having followed a GFD for years as shown by Hallert et al,[65] mainly due to the low fortification of specific foods. One month after beginning the GFD, it may be necessary to limit the consumption of lactose because of the relative deficiency of lactase present in about 30% to 60% of newly diagnosed cases of CD, especially in worse cases of affectation and malabsorption.[35,66,67] In these cases, calcium and vitamin D supplementation should be considered using lactose-free foods. Certain authors suggest that exocrine pancreatic insufficiency is responsible for relative lactase deficiency, to the extent that trypsin is required for the enzymatic activation of lactase.[68]

In cases of intense diarrhea, electrolyte supplements may be required during the first days of treatment. If malabsorption is severe, blood concentrations of calcium and magnesium may be low, which, together with the frequent association of CD with osteoporosis, makes it essential for all adults diagnosed with CD to undergo a bone mineral densitometry test, supplemented with calcium and vitamin D in the long term, using bone status criteria if blood levels are normal. For children in the growth phase, calcium with vitamin D supplementation is also very important.

Patients with anemia should be administered iron, folate, and vitamin B12 preparations in accordance with their needs, although different studies show that the GFD alone is capable of reversing anemia in patients by 78%-94%.[35]

A high number of patients with CD (up to one-third has been calculated) have dyspepsia or gastroesophageal reflux,[21,69] which are often treated using proton-pump inhibitor drugs. The increase in intragastic pH reduces the digestion of proteins in the diet and increases the stimulation of the immune system.[70] While it prevents nutrients from being digested correctly, it facilitates the entry of pathogenic microorganisms and the inactivation of digestive enzymes.[71]

Nutrition support via enteral nutrition (EN) is rarely required, but it could be assessed occasionally in extreme cases of malnutrition, using EN formulas that include medium-chain triglycerides, oligopeptides, and/or amino acids. In patients who do not respond to treatment and who have a high nutrition risk, a gluten-free enteral or oral feeding trial used as the sole source of ingestion could be beneficial at diagnosis, thereby allowing a distinction to be drawn between true refractoriness to GFD and poor compliance due to the inadvertent ingestion of gluten.

Between 70% and 95% of patients with CD show rapid clinical improvement with the disappearance of symptoms 2 weeks after commencing the GFD[26,61,72]; the serum antibody titers can take from 6 to 12 weeks to normalize and, lastly, complete histological resolution may

Table 1. Gluten Content of Foods[a]

Gluten-Free	Contains or May Contain Gluten
Meat and meat by-products	
Fresh, frozen, and canned meat and entrails in brine	Canned meats, meat pies
Cured beef and ham	Meatballs and hamburgers
Prime home-cooked ham	Charcuterie: sausages
Homemade cold meats and sausages	Cold cuts such as chopped pork, mortadela, chorizo, etc
	Patés
Fish, seafood, and by-products	
Fresh and frozen fish not coated in breadcrumbs or batter	Frozen fish or fish coated in breadcrumbs or batter
Fresh seafood	Fish and seafood substitutes
Canned fish or seafood in brine or in oil	Canned fish and/or seafood: in sauce, tomato, *a la marinera* style, pickled, in their ink
Eggs and by-products	
Fresh, refrigerated, and desiccated eggs	
Milk and dairy by-products	
Any form of fresh milk	Milk foods
Curds, rennet, cottage cheese, and kefir	Powdered curds
Cream	Petit Suisse yogurts
Fresh, cured, and semicured cheeses	Melted, spreadable, grated, or pizza-topping cheeses
Natural or flavored yogurts	Chocolate, cereal, fiber yogurts, or yogurts containing pieces of fruit
Homemade dairy desserts	Some ice cream
Edible fats	
Olive oil, butter, and margarine not containing fiber	Oil used to fry food containing gluten
	Margarine, minarines containing fiber
Legumes	
Fresh or precooked in brine	Cooked and canned
Vegetables, root vegetables, and tubers	
Fresh vegetables	Frozen vegetables in cream or béchamel sauce
Fresh and sweet potatoes	Frozen salads: may contain small pieces of cold meats
Homemade chips	Frozen foods: precooked chips
Instant mashed potatoes	Fast-food chips
	Potato-based aperitifs
	Potatoes filled with ketchup, mustard
Cereals	
Rice, corn, tapioca, quinoa, amaranth, soya, millet	Wheat, spelt, rye, barley, oats, and their by-products (starch, semolina, wheat germ, hydrolyzed protein)
Breakfast cereals prepared using gluten- and malt-free products	
Flour, pasta, and by-products	
Flour, starch, and semolina from all kinds of permitted legumes, tubers, and cereals	Flour, pasta, bread, or cakes made with wheat, spelt, barley, rye, and oats and their by-products
Special gluten-free flour for patients with celiac disease	
Gluten-free macaroni, spaghetti, noodles, bread, pasta, or cakes sold in specialized shops	
Fruit and by-products	
Fresh fruit and fruit in syrup	Jellies, fruit preserves, sweet and fruit purées, industrially produced quince
Homemade jellies and fruit preserves using gluten-free ingredients	
Dried fruit and nuts	
Fresh fruit and nuts	Toasted and fried dried fruit and nuts (especially if they contain salt, which is usually mixed with flour so that it sticks)
	Dried figs

(*continued*)

Table 1. (continued)

Gluten-Free	Contains or May Contain Gluten
Manufactured foods	
Purées and soups made using gluten-free products	Stock or bouillon cubes
Dark, white, or milk chocolate	Chocolate bars containing gluten
Pure cocoa	Drinking chocolate
	Chocolate candies filled with jelly
	Candies
Sugar	
Sugar and honey	Candies, gumdrops, and other sweets (licorice)
Other	
Coffee beans or ground coffee, infusions without aromas, orange and lemon sodas, and cola	Coffee substitutes and other machine beverages
Tea	Malted beverages
Pickled onions, cucumbers, olives	Beverages distilled or fermented from cereals: beer, whisky, barley water, certain spirits
Sparkling wines and beverages	Sauces, condiments, seasonings, food coloring
Salt, vinegar, and spices	

[a]Modified from Racondio AM, Arroyo M. Dieta controlada en gluten. En: Salas-Salvado J, Bonada A, Trallero R, Salo ME, Burgos R. Nutricion Y Dietetica Clinica. 2nd Ed. Elsevier Espana, S.L. Masson, Barcelona, 2008. 292-299.[73]

not occur until the GFD has been followed for 2 years.[73] From then onward, *celiac condition* can be referred to instead of *celiac disease*. The objectives of nutrition care in all age groups are the remission of symptoms, normalization of the absorptive function, and regeneration of the villi of the intestinal mucosa. In addition, with infants and children, the objectives primarily include optimum growth, development, and activity.

Common Causes of Failure of the Diet

The lack of response to the GFD can be due to ulceration of the intestinal mucosa, the severe secondary decrease in lactase activity, or to another concurrent disease such as refractory pancreatic insufficiency or intestinal lymphoma. However, the most common cause is poor compliance with the GFD due to various reasons:

1. Patients adapt poorly to the disease as they see that certain foods are being eliminated from their daily diet (eg, bread, pasta, cakes).
2. The accidental consumption of gluten contained in unusual products or the accidental ingestion of small amounts can trigger a clinical relapse.
3. Their difficulty is in following the GFD for life.

Nutrition Characteristics and Following the Diet in a Practical Manner

Gluten is found exclusively is wheat, spelt, barley, rye, and oats. All the foods and by-products of these should therefore be excluded from the diet. Although gluten is present in very few foods, it is very difficult to do without them in the diet. The extended use of emulsifiers, thickeners, and other processed additives make it extremely difficult to follow a GFD strictly. It is advisable to systematically read the labels of food products and avoid those that mention the use of "suspicious" foods, which the manufacturer cannot verify as being gluten free. Suspicious terminology on the labels includes reference to flour, thickening agents, malt, semolina, cereal additives, starch, modified food starch, cereals, emulsifiers, stabilizing essence, stabilizers, vegetable protein, hydrolyzed vegetable protein, flavorings, vegetable gum, toasted rice syrup, monoglycerides, and diglycerides.

At the beginning of treatment, a protein- and energy-rich diet should be encouraged, especially if the patient has significant weight loss and deficiencies caused by malabsorption. Normal kilocalorie and protein recommendation can be made as soon as malabsorption abates. At the outset, the administration of vitamin and mineral supplements should be assessed. However, they should be discontinued as soon as absorption improves, which is assumed to happen in clinical practice when anemia improves or when the antibody titers decrease to normal levels, due to the difficulty in obtaining objective tests, such as a new biopsy. For most patients, 6 months after starting the GFD seems to be a prudential period for receiving a response.

Gluten-free foods have an additional economic cost and tend to be considerably more expensive than conventional foods. In some countries, patients receive economic assistance to compensate for this higher cost. However, such assistance varies considerably from country to country and even within different regions of the

Table 2. Celiac Associations by Country[a]

Andorra	celiacsandorra.org
Germany	dzg-online.de
Argentina	acela.org.ar
	celiaco.org.ar
	soyceliaco.com.ar
Australia	coeliac.org.au
Austria	zoeliakie.or.at
Belgium	vcv.coeliakie.be/tiki-index.php
	sbc-asbl.be
	coeliakie.be/prt
Brazil	acelbra.org.br
Canada	celiac.ca
	fqmc.org
Chile	coacel.cl
Croatia	celijakija.hr
Denmark	coeliaki.dk
United States	csaceliacs.org
	celiac.org
	gluten.net
	celiac.com
Slovakia	celiakia.sk
Slovenia	drustvo-celiakija.si
Spain	celiacos.org
	controladoporface.es
Finland	keliakialiitto.fi
France	afdiag.org
Greece	koiliokaki.com
The Netherlands	coeliakievereniging.nl
Hungary	coeliac.hu
Ireland	coeliac.ie
Israel	celiac.org.il
Italy	celiachia.it
Luxembourg	alig.lu
Malta	coeliacmalta.org
Morocco	amig.ifrance.com
Mexico	celiacosdemexico.org.mx
Norway	ncf.no
Portugal	celiacos.org.pt
United Kingdom	coeliac.org.uk
Czech Republic	celiac.cz
	coeliac.cz/en
Romania	celiachie.uniserve.ro
Russia	celiac.ru
	celiac.spb.ru
Sweden	celiaki.se
Switzerland	zoeliakie.ch
	coeliakie.ch
	celiachia.ch
Uruguay	acelu.org
AOECS	aoecs.org
The Coeliac Youth of Europe	cyeweb.eu

[a]Taken from http://www.celiacos.org/otras_asociaciones.php (accessed January 8, 2010).

same country. In some countries, gluten-free foods receive 100% financing; in others, they are tax deductible; and in most European countries, patients receive monthly assistance of between 20 and 200 Euros to finance the products. The regional associations of CD patients can provide specific information in this connection (Table 2).

A Balanced Diet and GFD

The GFD should be balanced and rational as well as varied, pleasant, and sufficient. It must provide enough energy to meet individual daily recommendations. The distribution of nutrients must be established by committees of experts and take into account the following:

1. Daily energy requirements should be based on age, gender, and physical activity.
2. The carbohydrate intake should represent 50% to 60% of the diet's total energy value, and fats should amount to between 30% and 35%. Proteins should contribute approximately 10% to 15%.
3. The number of meals recommended depends on habits, time tables, and pace of life. In general, between 3 and 6 meals per day are recommended.
4. The daily intake of vitamins, minerals, water, and fiber recommended for the general population by the World Health Organization guidelines should be ensured.

Practical Rules and Advice

1. A GFD should not be started without having performed an intestinal biopsy beforehand that may show intolerance thereto, due to alteration of the mucosa. The diet must be strictly followed for life. The consumption of small amounts of gluten can cause lesions of the intestinal villi, although they are not always accompanied by clinical symptoms.
2. To the extent possible, consume natural foods: milk, meat, fish, eggs, vegetables, legumes, and gluten-free cereals (rice and corn). Avoid manufactured products if their composition and form of preparation are not fully guaranteed.
3. Take the relevant precautions with regard to handling food at home, in bars, in restaurants, and in school dining halls.
4. Be careful with corn flour, rice flour, and other gluten-free sources for sale at bakeries or supermarkets that do not certify the absence of gluten. They can be contaminated if they have been milled at the same place other cereals are also milled such as wheat or oats. Do not purchase cornbread from bakeries that are not overseen by celiac associations.
5. At public establishments, it is advisable to speak to the maitre d' or manager for information purposes to guarantee that the appropriate safety standards are in place. If there is any doubt, avoid elaborate dishes and

Table 3 List of Ingredients That Usually Appear on the Labels of Food Products That Contain or May Contain Gluten

Cereals
Flour
Modified starch: E-1404, E-1410, E-1412, E-1413, E-1414, E-1420, E-1422, E1440, E-1442, E-1450
Starch
Fiber
Thickeners
Semolina
Protein
Vegetable protein
Hydrolyzed protein
Malt
Malt extract
Yeast or yeast extract
Spices and aromas

opt for salads and grilled fish or meat. An internal control system should be established in school dining halls to avoid risk of contamination: raw materials should be stored separately with a distance of at least 1 m between them or by using a partition.

6. If there is a person affected by CD in the house, food should always be prepared and handled separately from the rest, and if separate areas are not available, start by preparing the gluten-free meal. Do not use the same cooking utensils to prepare gluten-free and gluten-containing foods. Avoiding cross-contamination between both kinds of food is a fundamental matter in the practical management of CD. The washing of cooking utensils constitutes a central point to take into account. Gluten particles can travel from one food to another merely by using a cooking utensil that has not been properly washed or when it is shared in preparing a different kind of food. Gluten-free food must be prepared at the beginning using only clean instruments. After that, food containing gluten can be prepared. Some cooking instruments, such as colanders, skimmers, food mixers, oven moulds, and so forth, are difficult to clean due to their characteristics. As a solution, a small set of cooking utensils to be used exclusively for GFDs should be available, and prepared food could be isolated by using aluminum foil. Take flour and wheat breadcrumbs off the family menu and use gluten-free flour and breadcrumbs instead or instant potato flakes to coat food or thicken sauces.
7. Take precautions with imported foods because in accordance with regulations in different countries, the same manufacturer can use different ingredients for a product sold under the same brand name. The criteria for gluten content and health controls can vary significantly in terms of the country of origin; for example, there are no common European regulations governing the maximum content of gluten-free foods.
8. Do not consume bulk, farmhouse, or unlabelled products. The list of ingredients that usually appears on the labels of food products that contain or may contain gluten are contained in Table 3.
9. Pharmaceutical products may use gluten, flour, starch, or other by-products in the preparation of its excipients. Pharmaceutical specialties for human consumption containing gluten, flour, starch, or other by-products thereof as excipients deriving from wheat, triticale, oats, barley, or rye should list their primary and secondary packaging materials and the quantity present under "composition." The leaflets of the related specialties must contain a warning for individuals with CD.
10. If there is any doubt as to whether a product may contain gluten, it should not be used.

Conclusion

CD leads to various deficiencies of nutrients, vitamins, and dietary minerals, which should be evaluated and restored. Following a GFD, the specific therapy for CD involves certain difficulties since gluten is widely found in common diets. Several practical measures such as those reviewed in this article should be taken to ensure GFD compliance.

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