WGO-OMGE Practice Guideline
Celiac Disease

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† Professor Zeballos, co-chairman of the Celiac Disease Review Team, passed away suddenly just as work on this guideline started. The WGO-OMGE Celiac Disease Team acknowledge his contribution and are greatly saddened by his death.

Contents

- 1. Definition
- 2. Key Points
- 3. Epidemiology
- 4. Pathology, natural history and associated conditions
- 5. Diagnosis of celiac disease
- 6. Management of celiac disease
- 7. Screening for celiac disease
- 8. Useful Websites
- 9. Guidelines, listserv, and further reading
- 10. Queries and Feedback from you

1. Definition

Celiac disease:
An enteropathy affecting the (small) intestine in genetically predisposed children and adults, precipitated by the ingestion of gluten-containing foods.
It is also referred to as celiac sprue, gluten-sensitive enteropathy, or nontropical sprue.

Gluten:
The storage proteins of wheat, rye and barley that give the dough its desired baking properties.
2. Key Points

Key points to remember:

- The prevalence of celiac disease in a healthy adult population varies between roughly one in 100 and one in 300 in most parts of the world.
- Many patients with celiac disease have minimal symptoms, or present atypically.
- For a diagnosis of celiac disease to be made, the patient should have:
  - Characteristic histopathologic changes in an intestinal biopsy; and
  - Clinical improvement in response to a gluten-free diet
- Serological tests have a role in:
  - Confirming celiac disease
  - Screening individuals who are at risk and not at risk
    - Identifying patients in whom biopsy might be warranted
    - Investigating patients with an increased risk of the disease
- Patients with celiac disease should not eat wheat, rye, or barley.
- Patients usually need to follow a strictly gluten-free diet for the rest of their lives.
- Patients with active (clinically manifest) celiac disease have an increased risk of death compared with the general population. However, this excess death rate returns to normal after three to five years on a strictly gluten-free diet.
- In adults, celiac disease (CD) is diagnosed on average > 10 years after the first symptoms.
- It is not true that only Caucasians are affected.
- Oats may be eaten, but must be pure; a small subgroup (below 5%) of patients with celiac diseases should not eat oats.
- Corn and rice-based diets are also acceptable.
- First-degree and (to a lesser extent) second-degree relatives are at an increased risk for CD.

3. Epidemiology

Introduction of key points

Not so long ago, it was thought that CD was a rare condition and that it occurred only in Caucasians, mostly in children, with a typical presentation of weight loss and diarrhea. We know now that this is not true.

- CD is common worldwide and affects around 1:100 to 1:300.
- The female-to-male ratio is 2:1.
- CD occurs frequently without gastrointestinal symptoms
- There is no substantial difference as regards symptomatic patients and "not-at-risk" patients in all those countries or geographic areas in which epidemiological studies have been carried out.
- CD epidemiology has iceberg characteristics - there are far more undiagnosed cases (below the waterline) than diagnosed cases (above the waterline).
- The risks are much greater in first-degree relatives (up to 10%) and less so in second-degree relatives, as well in people with diabetes and other autoimmune diseases, Down's...
syndrome and a number of other associated diseases (see 5.7).
- Fertility is affected in a subset of celiac disease patients.
- Pregnancy may present with an unfavorable course in undiagnosed CD patients, especially in those who have had symptoms earlier.
- A clinically severe picture can develop during pregnancy or during the puerperium in up to 17% of women patients.

3.1 Prevalence and incidence

The prevalence of CD - that is, the number of cases that are present in a population at a given time - is similar in different regions of the world. It is uncertain whether the number of new cases of CD found in a specific period in a given population (the incidence) is increasing locally or globally.

All experts agree on the iceberg image: prevalence here refers to the total size of the iceberg, while the area below the waterline represents the total number of undiagnosed cases in a given population at a particular point in time. The area above the waterline - the tip of the iceberg - represents the number of clinically diagnosed cases.

The iceberg

In 1991 Richard Logan published his idea of a celiac iceberg. In Europe, for every case of celiac disease diagnosed on clinical suspicion, there would be many that remained undiagnosed, either because they were latent, silent, misdiagnosed, or asymptomatic. The ratio of diagnosed to undiagnosed CD in Europe is around 5 : 1 to 13 : 1.

A key study in 2003 by Fasano et al. found that the prevalence of CD was as follows:

- At risk - first-degree relatives: 1 : 10
- At risk - second-degree relatives: 1 : 39

Figure 1. The celiac iceberg.
It is now accepted that the total size of the iceberg is more or less the same worldwide, although the "waterline" may differ from continent to continent.

In Europe and the USA, for example, the prevalence is similar in a healthy population and in "at-risk" groups, but the iceberg appears to be more submerged in the USA - fewer cases are diagnosed there than in Europe. Celiac disease goes hand in hand with the prevalence of DQ2 and to a minor degree DQ8.

It is also associated with an extended ancestral haplotype including class I and class II HLA (A,B,DR,DQ).

This is a necessary but not a sufficient condition for the development of CD.

Gluten load is a key factor - there is no CD without gluten.

Populations that do not have DQ2 - e.g., Chinese and Japanese - are not expected to develop celiac disease, with the exception of individuals with DQ8.

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### 4. Pathogenesis, natural history and associated conditions

#### 4.1. Pathogenesis and genetic predisposition

CD - also referred to as celiac sprue, gluten-sensitive enteropathy, or nontropical sprue - is thought to result from the activation of both a cell-mediated (T-cell) and humoral (B-cell) immune response upon exposure to the glutens (prolamins and glutenins) of wheat, barley, rye, and (rarely) oats, in a genetically susceptible person. Genetic susceptibility is suggested by a high concordance among monozygotic twins of close to 70%, and an association with certain type II human leukocyte antigens (HLA). HLA-DQ2 is found in up to 95% of CD patients, while most of the remaining patients have HLA-DQ8.

The expression of these HLA-DQ2 or HLA-DQ8 molecules is necessary, but not sufficient, for the disease to develop.

The results of studies in siblings (sib recurrence risk for celiac disease is 10%) and identical twins suggest that HLA genes are essential but are not the only genes required for the disease to become manifest. HLA genes are estimated to contribute to about one-third of the genetic variance of the disease.

**Genetic predisposition risk (unconfirmed)**

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population</td>
<td>1%</td>
</tr>
<tr>
<td>Individual DQ2 or DQ8+</td>
<td>2-3%</td>
</tr>
<tr>
<td>First-degree relatives, unknown HLA</td>
<td>10-15%</td>
</tr>
<tr>
<td>First-degree relatives, DQ2 or DQ8+</td>
<td>20-30%</td>
</tr>
</tbody>
</table>
The presence of autoantibodies to the connective-tissue element surrounding smooth muscle known as endomysium is highly specific for CD. The target of these autoantibodies is now known to be the enzyme tissue transglutaminase (tTG). This enzyme may play a prominent role in the pathogenesis of CD by deamidating gliadin, resulting in a greater proliferative response of gliadin-specific T-cells, which contributes to mucosal inflammation and further B-cell activation in patients with HLA-DQ2 or -DQ8.

4.2. Natural history

The natural history of clinically silent CD remains unclear; further research is needed to improve our understanding of the natural history in asymptomatic CD patients.

Most of our current knowledge is related to the natural history and clinical course of clinically manifest CD in diagnosed patients (most of them at the severe end of the clinical spectrum).

If CD remains unrecognized, it can increase the risk of life-threatening complications that are difficult to manage - for example, intestinal lymphoma.

Table 1 If CD remains undiagnosed

- Cancer (overall 1.3 : 1.0) (excluding colorectal cancer)
- Malignant lymphomas
- Small-bowel neoplasia
- Oropharyngeal tumors
- Large-intestine adenocarcinomas
- Unexplained infertility (12%)
- Osteoporosis (increased risk for classically symptomatic patients)
- Stunted growth
- Autoimmune diseases

4.3. Associated conditions

4.3.1. Malignant disease

Malignant diseases are more frequent in patients with long-term untreated classical CD. Small-bowel adenocarcinoma, esophageal and oropharyngeal squamous-cell carcinoma and non-Hodgkin’s lymphoma occur more often in CD patients than in healthy control individuals. A gluten-free diet is thought to be protective against the development of malignant disease, although this might not be the case for the development of enteropathy-associated T-cell lymphomas in celiac patients diagnosed over the age of 50.

4.3.2. Osteoporosis

Measurement of bone mineral density is recommended when CD has been diagnosed, as reduced bone density is common in both adults and children with CD. The reduction in bone density is more severe in symptomatic CD than in the silent form and is associated with an increased risk of fracture. Bone mineral density improves after a gluten-free diet, but may not return to the normal range.

4.3.3. Fertility

CD may be associated with delayed menarche, premature menopause, amenorrhea, recurrent abortions, and fewer children. Studies have reported infertility in subsets of patients, but also a
normal number of pregnancies and children in other patients. Further research is needed.

Patients with CD are also reported to have babies with low birthweight, increased perinatal mortality, and a shorter duration of breast feeding. Adherence to a gluten-free diet is associated with a return to normal outcomes.

CD may manifest clinically for the first time during pregnancy or in the puerperium. Undiagnosed CD has been detected in infertile women who were screened for the disease, but not in all studies.

Infertility in men is also associated with CD. Furthermore, men with the disease also tend to have children with a shorter gestation and lower birthweight than those without the disease.

4.3.4. Autoimmune disorders

Whether CD is an inflammatory disorder with secondary autoimmune reactions or whether it is a primary autoimmune disease induced by a known exogenous factor remains unclear. Autoimmune disorders occur ten times more frequently in adult patients with celiac disease than in the general population.

Such disorders include:
- Insulin-dependent type 1 diabetes
- Thyroid disease
- Sjögren's syndrome
- Addison's disease
- Autoimmune liver disease
- Cardiomyopathy
- Neurological disorders

When both autoimmune disease and CD occur in a patient, CD is frequently silent, and as a result the autoimmune disorder is usually diagnosed first.

4.3.5. Dermatitis herpetiformis

Dermatitis herpetiformis is considered to be a cutaneous manifestation of gluten sensitivity in patients with CD.

Dermatitis herpetiformis (DH) is a severe itchy, blistering skin disease. The rash usually occurs on the elbows, knees, and buttocks. Although people with DH do not usually have digestive-tract symptoms, they usually have the intestinal damage characteristic of CD.

DH is diagnosed by skin biopsy. It is treated with a gluten-free diet (GFD) and medication to control the rash - for example, with dapsone or sulfapyridine. This treatment may last for several years.

Both the skin and the small-bowel diseases are gluten-dependent and are strongly associated with HLA-DQ, with no genetic differences to explain the two phenotypes.

5. Diagnosis of celiac disease
5.1. Introduction

The clinical classification of CD has undergone a change; today, most experts agree with the following classification:

Classical
 Mostly gastrointestinal symptoms
Atypical
 Mostly nongastrointestinal symptoms - usually monosymptomatic or oligosymptomatic
Silent
 No symptoms despite the presence of a characteristic intestinal lesion

5.2. Differential diagnosis

CD presents a very complex and protean clinical picture, and there are many diseases with mucosal changes similar to those of CD.

Table 2 Conditions with mucosal changes similar to those in CD

- Tropical sprue
- HIV enteropathy
- Combined immunodeficiency states
- Radiation damage
- Recent chemotherapy
- Graft-vs.-host disease
- Chronic ischemia
- Giardiasis
- Crohn's disease
- Eosinophilic gastroenteritis
- Zollinger-Ellison syndrome
- Autoimmune enteropathy
- Enteropathy-associated T-cell lymphoma
- Refractory sprue
- Collagenous sprue

(The last four are probably related to CD)

5.3. Diagnostic tests

Only endoscopy with biopsy of the small intestine plus a positive CD serology provide a definitive diagnosis. This is the gold standard.

Table 3. Diagnosis of celiac disease.
Role of endoscopy for suspicion of celiac disease
Although endoscopy may provide an indication for intestinal biopsy, it may not be sufficiently sensitive to detect all manifestations of CD in a population.

The characteristic findings of an endoscopy include:
- Scalloped folds, fissures and mosaic pattern
- Flattened folds
- Smaller size and or disappearing of folds with maximum insufflation

Intestinal biopsy
Intestinal biopsies together with a positive serology represent the gold standard for diagnosing celiac disease.

Multiple biopsies are taken from the second or third part of the duodenum. Endoscopy has become the most convenient method of obtaining biopsies of the small-intestinal mucosa. Suction biopsy (Crosby capsule) provides the best samples.

Histological characteristics of celiac enteropathy
CD affects the mucosa of the proximal small intestine, with damage gradually decreasing in severity towards the distal small intestine, although in severe cases the lesions can extend to the ileum. The degree of proximal damage varies greatly depending on the severity of the disease. The proximal damage may be very mild in "silent" cases, with little or no abnormality detectable histologically in the mid-jejunum. Abnormalities in the gastric and rectal mucosa may be observed in some cases.
Occasionally, the lesion in the duodenum/upper jejunum can be patchy, which may justify a second biopsy immediately in selected patients with positive endomysial antibody (EMA). However this is only warranted if all three samples of the first biopsy show a normal histology.

**Marsh’s classification of small-intestinal lesions:**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Preinfiltrative mucosa; 5% of patients with DH have small-intestinal biopsy specimens that appear normal.</td>
</tr>
<tr>
<td>I</td>
<td>Increase in the number of intraepithelial lymphocytes (IELs) to more than 30 per 100 enterocytes.</td>
</tr>
<tr>
<td>II</td>
<td>Crypt hyperplasia. In addition to the increased IELs, there is an increase in crypt depth without a reduction in villus height. Gluten challenge can induce these changes, which are seen in 20% of untreated DH and CD patients.</td>
</tr>
<tr>
<td>III</td>
<td>Villous atrophy; A partial, B subtotal, C total. This is the classical celiac lesion. It is found in 40% of DH patients and 10-20% of first-degree relatives of celiac patients. Despite marked mucosal changes, many individuals are asymptomatic and therefore classified as having subclinical or silent cases. This lesion is characteristic of, but not diagnostic for, CD and can also be seen with severe giardiasis, infantile food sensitivities, graft-versus-host disease, chronic ischemia of the small intestine, tropical sprue, immunoglobulin deficiencies, and other immune deficiencies and allograft rejection.</td>
</tr>
<tr>
<td>IV</td>
<td>Total villous atrophy. This can be considered the end-stage lesion in a very small group of patients who are unresponsive to gluten withdrawal and may develop malignant complications. There can be deposition of collagen in the mucosa and submucosa (collagenous sprue, a disorder that may be related to CD). Patients with type IV lesions are usually unresponsive to treatment with steroids, immunosuppressive agents, or chemotherapy.</td>
</tr>
</tbody>
</table>

5.4. **Use of serum antibodies to diagnose celiac disease**

- IgA endomysial antibody (IgA EMA; highest diagnostic accuracy)
- IgA tissue transglutaminase antibody (IgA tTG)
- IgA antigliadin antibody (IgA AGA)
- IgG antigliadin antibody (IgG AGA)

Serologic studies for celiac disease can be divided into two groups, based on the target antigens:

- Anti-tTG antibody tests
- Antigliadin antibody tests

**IgA EMA** - IgA endomysial antibodies bind to endomysium, the connective tissue around smooth muscle, producing a characteristic staining pattern that is visualized by indirect immunofluorescence.

The test result is reported simply as positive or negative, since even low titers of serum IgA endomysial antibodies are specific for CD. The target antigen has been identified as tissue transglutaminase (tTG or transglutaminase 2).

IgA endomysial antibody testing is moderately sensitive and highly specific for untreated (active) CD

**Anti-tissue transglutaminase antibodies (IgA tTG).** The antigen against which antiendomysial antibodies are directed is tTG. Anti-tTG antibodies are highly sensitive and specific for the diagnosis of CD.

Enzyme-linked immunosorbent assay (ELISA) tests for IgA anti-tTG antibodies are now widely available and are easier to perform, less observer-dependent and less costly than the
immunofluorescence assay used to detect IgA endomysial antibodies. The diagnostic accuracy of IgA anti-tTG immunoassays has been improved further by the use of human tTG in place of the nonhuman tTG preparations used in earlier immunoassay kits.

**Antigliadin antibody assays (IgA AGA and IgG AGA).** Gliadins are the major proteins of the wheat storage proteins collectively termed gluten.

Purified gliadin is readily available and is used as the antigen for ELISA tests to detect serum antigliadin antibodies.

Serum antigliadin antibody levels are frequently elevated in untreated CD, and antigliadin assays have been used for some years as a diagnostic aid.

Although these tests demonstrate moderate sensitivity and specificity, with the IgA tests being superior, their positive predictive value in the general population is relatively poor.

AGA tests are no longer routinely recommended, because of their lower sensitivity and specificity.

### 5.5. Key symptoms

**Adults: gastrointestinal symptoms**

- Chronic diarrhea (most common symptom)
- Weight loss
- Anemia
- Abdominal distension
- Lassitude and malaise

**Children: gastrointestinal symptoms**

- Failure to thrive, weight loss, down-shift of weight or height centile, short stature
- Vomiting
- Diarrhea
- Recurrent abdominal pain
- Muscle wasting
- Irritable bowel
- Hypoproteinemia
- Irritability and unhappiness

**Adults and children: nongastrointestinal symptoms**

- Iron deficiency/anemia
- Dermatitis herpetiformis
- Peripheral neuropathy
- Folic acid deficiency
- Reduced bone density
- Unexplained infertility

**Consider CD in cases of:**

- Unexplained folic acid, iron, or B12 deficiency
- Reduced serum albumin
• Unexplained hypertransaminasemia
• Osteoporosis and osteomalacia
• Recurrent abdominal pain or bloating
• Skin rashes

Why is celiac disease difficult to diagnose?

• Alternative diagnoses (often irritable bowel syndrome)
• The condition may be oligosymptomatic or asymptomatic
• The condition may have latent periods
• Clinicians are "unaware" and there are several "myths":
  o CD is rare
  o CD occurs in Caucasians only
  o CD occurs mostly in Europe and the USA
  o CD occurs only in childhood
  o CD can be cured after (a period of) treatment

5.6. Risks

An elevated risk for CD exists in:

• First-degree and second-degree relatives (5-15% basic, 10-30% if DQ2 or DQ8+; see section 3.1)
• Down's syndrome (12%)
• Autoimmune thyroid disease (5%)
• Chronic active hepatitis
• Type 1 diabetes mellitus (5-6%)
• Lymphocytic colitis (15-27%)
• Chronic fatigue syndrome (2%)
• Irritable bowel syndrome

Those with (long-term untreated) CD have an elevated risk for:

• Cancer (overall 1.3 : 1.0)
• Malignant lymphomas
• Small-bowel neoplasia
• Oropharyngeal tumors
• Unexplained infertility (12%)
• Osteoporosis (increased risk for classically symptomatic CD patients).

5.7. The global aspect

Global epidemiology

CD is common throughout the world and affects between approximately one in 100 and one in 300 individuals.

The prevalence of CD is likely to be similar in different regions of the world - so that while the size of the iceberg probably remains the same, the water line is very different. The waterline determines the ratio of diagnosed to undiagnosed cases. It depends on: 1) awareness of CD, 2) the availability of diagnostic resources and 3) variations in clinical manifestation (for example, as a result of local diet).
In developing countries, the area above the waterline - the tip of the iceberg (i.e., the number of clinically diagnosed cases) - is probably much smaller. Here almost the entire iceberg is submerged.

The diagnosis of CD can be made with different diagnostic technologies in different parts of the world, depending on the available resources, but the specificity and validity of the results may vary when tools poorer than those of the "gold standard" are used.

Depending on available resources, diagnostic options can be cascaded from a highly resourced setting in which the above gold standard can be used - endoscopy followed by small-bowel biopsy and specific serology for confirmation or case finding - to a situation in which very few resources are available and only the minimum can be done.

If biopsy is not available, "serology only" remains a feasible method for diagnosing CD, also because serological tests are cheaper than endoscopy and biopsy and their statistical value is very similar.

In the absence of a biopsy, the criteria are:

- The presence of auto-antibodies
- Gluten dependency of the auto-antibody titer
- Clinical symptoms, when present
- Improvements in symptoms and reduction in the anti-tTG antibody titer on a gluten-free diet
- In children, catch-up growth, when applicable

The easiest and cheapest serological test would be the dot ELISA. Once a bedside IgA anti tTG test becomes available and sufficiently sensitive and specific, it would be ideal for low-income regions.

If a geographic area has very limited resources, clinical aspects become the most important diagnostic tool. A rice-based or corn-based GFD is the final and vital step in confirming a diagnosis of CD.

Table 4 Cascade for diagnosing CD

| 1. | Autoantibodies and endoscopy with intestinal biopsy (gold standard) |
| 2. | Endoscopy with intestinal biopsy |
| 3. | Autoantibodies |
Although endoscopy is a very useful tool for detecting CD, it cannot be relied on as a single diagnostic procedure. The presence of markers of mucosal atrophy may be highly suggestive of CD in places where the disease is common, but in other areas of the world there may be several differential diagnoses - for example, tropical sprue, malnutrition, heavy-chain disease, etc. Nevertheless, the procedure is very helpful when markers are elevated in the course of endoscopies ordered for other reasons. Then the endoscopist must be alert and proceed to intestinal biopsy.

6. Management of celiac disease

6.1. Management

The current treatment for CD is a strictly gluten-free diet for life. In the gluten-free diet, wheat, barley, and rye are avoided. Oats are not toxic in > 95% of patients with CD or dermatitis herpetiformis, but there is a small subgroup (< 5%) for whom oats are not safe.

Additionally, there is a reluctance in some countries to advise liberal use of oats because of the difficulty in guaranteeing that commercially available oats will be free of contamination with other grains. Rice and corn can be part of a GFD.

Initial approach:

- Prescribe a "natural" gluten-free diet
- Refer to a dietician and/or support group (see web sites listed below)
- Screen for iron and folate deficiency
- Advise bone-density tests (in some cases)
- Advise vitamin D and calcium supplementation if the patient is osteoporotic
- Advise serological screening for first-degree and second-degree relatives

Most patients have a rapid clinical response to a gluten-free diet (within 2 weeks), although the rate of response varies. Patients who are extremely ill may require hospital admission, repletion of fluids and electrolytes, intravenous alimentation, and, occasionally, steroids. Patients should be encouraged to eat natural high-iron and high-folate foods, especially if a deficiency in these minerals is documented.

Patients should also have a consultation with a dietician who is knowledgeable about gluten-free diets. However, not all dieticians are familiar with the intricacies of a gluten-free diet, and for this reason local or national support groups provide most of the required information.

For adults, quality of life is improved on a gluten-free diet, even in those whose disease was detected by screening. Children on a gluten-free diet reported a quality of life comparable to that of a reference population. Adolescents have difficulty with dietary compliance.

6.2. The gluten-free diet
The most effective treatment is a rigorous gluten-free diet (GFD) for life. This means no wheat, rye, or barley. Oats - provided they are pure and not contaminated with other grains (even minimal amounts of wheat, rye or barley) - are safe to eat in > 95% of cases.

Plain meat, fish, rice, corn, fruits, and vegetables do not contain gluten. Examples of foods that are safe to eat and those that are not can be found online. Useful online CD information sites are listed in sections 8 and 9.

A gluten-free diet is low in fiber. Patients should be advised to eat a high-fiber diet supplemented with whole-grain rice, maize, potatoes and ample vegetables.

Correct any dietary deficiencies such as iron, folic acid, calcium and (very rarely) B12 deficiency.

### 6.3. Persistence of symptoms

A common difficulty with the GFD is the presence of occult gluten in processed foods and/or medicines (although this is rare). The persistence of symptoms is almost always caused by continued ingestion of gluten.

Reasons for persistence of symptoms:

- (Inadvertent) gluten ingestion (this is the most common reason)
- Wrong diagnosis
- Lactose or fructose intolerance
- Other food intolerances
- Pancreatic insufficiency
- Microscopic colitis
- Bacterial overgrowth
- Collagenous colitis or collagenous sprue
- Irritable bowel syndrome
- Ulcerative jejunitis
- Enteropathy-associated T-cell lymphoma
- Refractory CD

The last three can be regarded as complications of long-lasting CD.

### 6.4. Refractory celiac disease

The diagnosis of refractory CD is considered in patients with features of CD who have persistent symptoms, villous atrophy, and failure to respond to a gluten-free diet. This may occur at presentation, or after an initial response to a gluten-free diet.
Refractory CD is considered to be a form of low-grade intraepithelial lymphoma, revealed by severe malabsorption that is not responsive to a gluten-free diet.

This diagnosis must be considered particularly in celiac disease patients who are diagnosed over the age of 50.

### 7. Screening for celiac disease

#### 7.1. Screening for celiac disease

Good health and growth, as well as quality of life, are key reasons for screening.

CD also reduces life expectancy because of a higher risk of malignancies such as:

- Small-bowel lymphoma
- Small-bowel adenocarcinoma
- Esophageal carcinoma
- Ulcerative jejunitis
- Refractory CD
- Enteropathy-associated T-cell lymphoma

Screening is therefore attractive and meets the five WHO criteria for justifying general screening in the population:

- Early detection could be difficult on a clinical basis
- Must be a common disorder causing significant morbidity in the general population
- Tests must be highly sensitive and specific
- Treatment must be available
- If not recognized, the disease could result in severe complications difficult to manage

However, there are resource implications - is this the best use of available limited resources? There are also ethical implications.

The current view is that there is not enough evidence to support a decision to carry out mass screening of the general population, nor is there enough evidence to assess the risks of undetected CD.

#### 7.2. The Future

With the identification of the critically important epitopes within gliadin and gluten and related proteins, and with plans to develop a mouse model of CD, research is focusing on either modifying these proteins or improving tolerance of these proteins in CD patients or in those with a susceptibility to CD. In the meantime, oats (in > 95% of cases), corn and rice and possibly industrially purified wheat/starch protein can be used to expand the relatively limited range of a GFD.

The celiac genetics research community has established sound foundations for the identification of additional disease genes. In addition, alternative, nondietary treatments may soon become available following the identification of the relevant gluten epitopes, with destruction of these epitopes with specific proteases and blockade of HLA-DQ2 and HLA-DQ8.
8. Useful websites

Center for Celiac Research (University of Maryland)  
www.celiaccenter.org
The Celiac Center of BIDMC, Harvard Medical School  
http://bidmc.harvard.edu/display.asp?node_id=5449
The Celiac Disease Foundation  
http://www.celiac.org
The Celiac Sprue Association  
http://www.csaceliacs.org
The Celiac Disease and Gluten-free Diet Support Page  
http://www.celiac.com
The Gluten-Free Pantry  
http://www.glutenfree.com
World Gastroenterology Association  
http://www.omge.org
US National Institutes of Diabetes, Digestive, and Kidney Disorders  
http://digestive.niddk.nih.gov/ddiseases/pubs/celiac/
The Gluten Intolerance Group  
http://www.gluten.net/
Celiac Helpline  
http://www.celiac.co.uk
The Wheat-Free Zone  
http://www.nowheat.com/grfx/nowheat/index.htm
US National Digestive Disease Clearinghouse (NDDIC)  
WGO-OMGE “Ask a Librarian” for Celiac Disease Research support  
http://www.omge.org

9. Guidelines, list server and further reading

9.1. Celiac disease guidelines

7. Celiac disease list server. St. Johns Celiac Listserv Newsgroup. To subscribe, send an e-mail to the following address: listserv@maelstrom.stjohns.edu, in the body of the letter, put the following: SUB CELIAC followed by your first and last name - for example, "SUB CELIAC Bob Jones".

9.2. Further reading

10. Queries and Feedback from you

**Invitation to comment**

The Practice Guidelines Committee welcomes any comments and queries you may have. Do you feel we neglect some aspect? Do you feel some procedures carry extra risk? Tell us your experiences. Click the link below and let us know your views. Together we can make it better.

E-mail