Complete Summary

GUIDELINE TITLE

WGO-OMGE practice guideline: celiac disease.

BIBLIOGRAPHIC SOURCE(S)

World Gastroenterology Organisation (WGO-OMGE). WGO-OMGE practice guideline: celiac disease. Paris (France): World Gastroenterology Organisation (WGO-OMGE); 2005 Feb. 18 p.

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
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SCOPE

DISEASE/CONDITION(S)

Celiac diseases

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Risk Assessment
Treatment

CLINICAL SPECIALTY

Allergy and Immunology
Family Practice

Gastroenterology
Internal Medicine
Nutrition
Oncology
Pathology
Pediatrics

INTENDED USERS

Dietitians
Health Care Providers
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide practice guidelines for the diagnosis and management of celiac disease

TARGET POPULATION

Patients with celiac disease or suspected celiac disease

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Clinical history
2. Physical examination and consideration of symptoms
3. Endoscopy
4. Intestinal biopsy
5. Serology
6. Histological tissue assessment
    - Immunoglobulin A (IgA) endomysial antibody
    - IgA tissue transglutaminase antibody
    - IgA antigliadin antibody (not routinely recommended)
    - IgG antigliadin antibody (not routinely recommended)
7. Differential diagnosis

Management

1. Gluten-free diet
2. Referral to a dietician and/or support group
3. Screening for iron and folate deficiency
4. Bone-density testing
5. Vitamin D and calcium supplementation, if osteoporotic
6. Hospitalization, repletion of fluids and electrolytes, intravenous alimentation, and steroids as needed for extremely ill patients
7. Serological screening for first-degree and second-degree relatives

MAJOR OUTCOMES CONSIDERED

- Sensitivity and specificity of diagnostic tests
- Symptom resolution
- Morbidity and mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

World Gastroenterology Organization's (WGO's) Graded Evidence System

WGO's Grading Evidence System is built to help National Societies of Gastroenterology and all those interested in the practice and research of gastroenterology keep track of the literature in topics covered by WGO Guidelines.

Evidence is classified into three categories:

- Systematic reviews, consensus statements, meta-analyses, evidence-based practice guidelines
- Clinical trials
- Other reading

The following journals are scanned for new evidence:

- Gastroenterology
- Annals of Internal Medicine
- Hepatology
- GUT
- Journal of Hepatology
- Alim. pharmacology & therapeutics
- American Journal of Gastroenterology
- Inflammatory Bowel Disease
- Gastrointestinal Endoscopy
- J. of Pediatric Gastroenterology & Nutrition
- Digestion
- Scandinavian Journal of Gastroenterology
- Eur. J. of Gastroenterology and Hep.
- Digestive Diseases and Sciences
- Endoscopy
- J. of Gastroenterology and Hepatology
- Digestive Surgery
- Digestive Diseases

Plus a selection from the general journals:

- New England Journal of Medicine
- JAMA

- Lancet
- BMJ
- Nature
- Science

Coverage

Graded Evidence is an iterative process—and for that reason need not be so concerned with searching both Medline, Embase and Biosis for example. All top gastrointestinal (GI) journals are covered by both Medline and Embase and in single one-off complex searches unique citations in one or the other are often due either to differences in database currency or differences in coverage of less important journals. In addition to cost issues, the generous republishing and copyright policies of the US National Library of Medicine (NLM) make Medline the preferred choice.

Search Strategies

Search strategies for each topic are based on a combination of controlled access and free text terms. The strategies aim for "precision" rather than "sensitivity." Busy gastroenterologists probably prefer very precise search strategies in top GI journals and thus make sure every major article is found. The WGO Graded Evidence works along the lines of PUBMED Medline "Clinical queries" features. Precise searches only find relevant information. Indexing errors may still be responsible for irrelevant or duplicate records. Case studies and animal studies are not usually included.

Finding Evidence

True evidence-based searches require a deeper understanding of databases and search strategies not necessary for our purpose. WGO Global Guidelines are not systematic reviews. The WGO Library adheres to the Cochrane Collaboration's views that a searcher has to work through a hierarchy of evidence as follows.

- Cochrane Collaboration Systematic Reviews
- DARE Systematic Reviews
- Randomized Clinical Trials (e.g., in the Cochrane Controlled Clinical Trials Database)

As you move down the hierarchy you are more likely to find "opinion" instead of evidence.

NUMBER OF SOURCE DOCUMENTS

- 42 meta-analyses, systematic reviews, and practice guidelines
- 11 clinical trials
- 56 other readings

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review
Review of Published Meta-Analyses

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not applicable

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Diagnosis of Celiac Disease (CD)

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

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. Conditions with Mucosal Changes Similar to Those in CD

- Tropical sprue
- Human immunodeficiency virus (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)

Diagnostic Tests

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

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.

See original guideline document for Marsh's classification of small-intestinal lesions.

Use of Serum Antibodies to Diagnose Celiac Disease

- Immunoglobulin A (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.

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":
    - CD is rare
    - CD occurs in Caucasians only
    - CD occurs mostly in Europe and the USA
    - CD occurs only in childhood
    - CD can be cured after (a period of) treatment

Risks

An elevated risk for CD exists in:

- First-degree and second-degree relatives (5 to 15% basic, 10 to 30% if DQ2 or DQ8+; see section 3.1 in the original guideline document)
- Down's syndrome (12%)
- Autoimmune thyroid disease (5%)
- Chronic active hepatitis
- Type 1 diabetes mellitus (5 to 6%)
- Lymphocytic colitis (15 to 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)

The Global Aspect

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 gluten-free diet (GFD) is the final and vital step in confirming a diagnosis of CD.

Table. Cascade for Diagnosing CD

1. Autoantibodies and endoscopy with intestinal biopsy (gold standard)
2. Endoscopy with intestinal biopsy
3. Autoantibodies
    - EMA or anti-tTG or both (depending on availability and experience)
    - Dot ELISA
4. Diagnosis based on "clinical aspects," with clinical improvement after a corn-based or rice-based GFD

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 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.

Management of Celiac Disease

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.

The Gluten-Free-Diet

The most effective treatment is a rigorous 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 of the original guideline document.

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.

See Table 5 in the original guideline document for foods allowed in a gluten-free-diet.

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.

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.

Screening for Celiac Disease

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.

CLINICAL ALGORITHM(S)

A clinical algorithm for diagnosis of celiac disease is provided in the original guideline document.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Improved diagnosis and management of celiac disease to reduce disease-associated morbidity and improve quality of life

POTENTIAL HARMS

False positive and false negative diagnostic tests

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Foreign Language Translations

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

World Gastroenterology Organisation (WGO-OMGE). WGO-OMGE practice guideline: celiac disease. Paris (France): World Gastroenterology Organisation (WGO-OMGE); 2005 Feb. 18 p.

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 Feb

GUIDELINE DEVELOPER(S)

World Gastroenterology Organisation - Medical Specialty Society

SOURCE(S) OF FUNDING

World Gastroenterology Organisation (WGO-OMGE)

GUIDELINE COMMITTEE

Celiac Disease Review Team

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the World Gastroenterology Organisation (WGO-OMGE) Web site.

Print copies: Available from the World Gastroenterology Organisation (WGO-OMGE), c/o Medconnect GMBH, Brünnsteinster. 10, 81541 Munich, Germany

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Graded evidence. Professor Elewaut's essential reading.
- Spanish, Portuguese, Mandarin, and Russian translations of the original guideline document

Electronic copies: Available from the World Gastroenterology Organisation (WGO-OMGE) Web site.

Print copies: Available from the World Gastroenterology Organisation (WGO-OMGE), c/o Medconnect GMBH, Brünnsteinster. 10, 81541 Munich, Germany

PATIENT RESOURCES

None available

NGC STATUS

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