



Complete Summary

GUIDELINE TITLE

American Gastroenterological Association medical position statement: celiac sprue.

BIBLIOGRAPHIC SOURCE(S)

American Gastroenterological Association medical position statement: celiac sprue. Gastroenterology 2001 May; 120(6): 1522-5.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Celiac sprue (gluten-sensitive enteropathy or celiac disease)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Gastroenterology
Internal Medicine
Pediatrics

INTENDED USERS

Dietitians
Physicians

GUIDELINE OBJECTIVE(S)

- To define celiac sprue
- To document the prevalence
- To summarize available therapy

TARGET POPULATION

Individuals with symptoms consistent with celiac sprue, and a genetic predisposition to malabsorption of dietary gluten, particularly individuals of European descent

INTERVENTIONS AND PRACTICES CONSIDERED

Celiac sprue

Diagnostic assessments (initial and ongoing)

1. Small intestinal biopsy (endoscopic)
2. Hemoglobin concentration, platelet count, and prothrombin time
3. Serologic marker antibodies, such as antibodies to gliadin, reticulin, jejunum, endomysium, and tissue transglutaminase (tTG)
4. Dual energy x-ray absorptiometry (DEXA) for osteoporosis
5. Serum alkaline phosphatase, vitamin D, and parathyroid levels
6. Test for blood film features of hyposplenism
7. Barium radiologic examinations of colon
8. Yearly assessment, including weight, full blood count, folate, calcium, and alkaline phosphatase
9. Monitoring for associated conditions, such as diabetes mellitus, hypothyroidism, pernicious anemia, and hypoadrenalism
10. Hydrogen breath test, bile acid breath test, bacteriologic count in a small intestinal aspirate
11. Enzyme assays of small intestinal biopsy or sugar permeability study for lactose or sucrose intolerance
12. Exploratory laparotomy, abdominal ultrasonography, computer-generated tomography or nuclear magnetic resonance screening for carcinoma of the gastrointestinal tract

Treatment

1. Gluten-free diet
2. Systemic steroids
3. Immunotherapy, such as 6-mercaptopurine, azathioprine, or cyclosporin
4. Antibiotics, such as oxytetracycline, cotrimoxazole, or metronidazole for small bowel bacterial overgrowth

Dermatitis herpetiformis

Diagnosis

1. Demonstration of granular immunoglobulin A in skin areas
2. Small intestinal biopsy

Treatment

1. Dapsone
2. Gluten-free diet

MAJOR OUTCOMES CONSIDERED

- Results of diagnostic tests, such as small intestinal biopsy, radiology exams
- Sensitivity and specificity of antibody tests, such as antireticulin antibodies, antigliadin antibodies, antijejunum antibodies, antiendomysial antibodies, and anti-tTG antibodies
- Response to gluten-free diet
- Relief of symptoms

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

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

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This document was approved by the Clinical Practice and Practice Economics Committee on September 23, 2000, and by the American Gastroenterological Association Governing Board on November 12, 2000.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Clinical Features

Adult presentation usually involves weight loss, diarrhea, lassitude, and anemia. Children frequently present with failure to thrive, vomiting, diarrhea, muscle wasting, signs of hypoproteinemia including possible ascites, and general irritability and unhappiness.

Patients may present at any hospital department with associated conditions. One important example is insulin-dependent diabetes mellitus, in which 6%-8% of sufferers have concomitant celiac sprue. Other conditions include cerebral calcification, Sjögren syndrome, and thyroid disease. The diagnosis should be considered with unexplained folic acid, iron or B₁₂ deficiency, reduced serum albumin, osteoporosis, and osteomalacia. Other presentations may include failure to grow in children, infertility, or recurrent miscarriage.

Dermatitis herpetiformis deserves special mention because it can be considered an extraintestinal manifestation of gluten-sensitive enteropathy. This manifests with a pruritic, blistering rash. The diagnosis depends on the demonstration of granular immunoglobulin (Ig) A in uninvolved skin. Treatment involves dapsone and a gluten-free diet, which, if strictly adhered to, frequently allows, after a period of 6 months, for dapsone to be withdrawn.

Serologic Markers

The main role of these tests is to screen patients who have nonspecific symptoms or an associated condition such as insulin-dependent diabetes mellitus. Immunoglobulin A antiendomysial antibodies are currently the best serologic test for celiac sprue with a sensitivity of 97%-100% and specificity of 98%-99%. Because 2%-3% of individuals with celiac sprue have selective immunoglobulin A deficiency, immunoglobulin A levels should be measured. Alternatively quantifying antigliadin antibody may be the best approach. Recently, the enzyme tissue transglutaminase has been found to be the antigen for antiendomysial antibody. This has allowed the development of a tissue transglutaminase enzyme-linked immunosorbent assay, which is reported to have a sensitivity of 95% and specificity of 94%. The sensitivity of these assays in certain commercial laboratories may not be as high as published from research centers.

Disorders of Bone Metabolism

Osteomalacia is well recognized and responds to calcium and vitamin D supplementation. Bone pain, pseudofractures, or deformity may occur, and the finding of a raised serum alkaline phosphate with normal calcium and phosphate levels may be present.

Osteopenia and osteoporosis are common features. Bone mineral density is almost always reduced. Osteoporosis carries a significant fracture risk, and thus dual energy x-ray absorptiometry (DEXA) screening of celiac sprue patients is important and now recommended. Dual energy x-ray absorptiometry scans suggest osteoporosis if the T values obtained are less than 2.0 standard deviations below the mean values for comparable age-matched controls. If osteoporosis is found, strict adherence to a gluten-free diet should be confirmed. This may provide an indication for consideration of a repeat small intestinal biopsy in those already treated because it suggests possible poor dietary compliance. Treatment may comprise hormone replacement therapy in postmenopausal women, biphosphonates, or calcitonin. Dietary calcium supplementation up to 1500 mg/day has been recommended. Smoking should be discouraged and exercise advised. Monitoring by repeat dual energy x-ray absorptiometry scanning after a year allows an estimate of the rate of change of bone mineral density.

Splenic Atrophy

This occurs in celiac sprue. It has been suggested that pneumococcal immunization be administered, although whether this should be advocated for all celiac sprue patients is unknown.

Diagnosis

The mainstay of diagnosis of celiac sprue is a small intestinal biopsy specimen, which is usually taken at endoscopy. At least 3 biopsy specimens preferably should be taken with "jumbo" forceps from the distal duodenum. Some individuals, especially pediatricians, use a dedicated Watson or Crosby capsule. The characteristic changes involve damage to the normal villous morphology with decreased villous height to crypt depth, decreased epithelial surface cell height, and increased lymphocytic infiltration of the mucosa.

The generally accepted diagnostic criteria are that there should be an abnormal small intestinal mucosa while individuals continue to take a gluten-containing diet. There should then be unequivocal improvement in villous architecture on a repeat small intestinal biopsy procedure after some months on a gluten-free diet with symptomatic improvement. A repeat biopsy should usually be taken 4-6 months after induction of treatment and if there has been no improvement in the small intestinal mucosal morphology, the original diagnosis should be questioned. However, many gastroenterologists do not take a follow-up biopsy specimen and the cost-effectiveness of this approach has not been demonstrated. Most clinicians do not undertake formal gluten challenge to show the resultant deterioration of the small intestinal villous architecture. However, gluten challenge should be performed if there is any doubt concerning the correct diagnosis.

Routine full blood count, urea and electrolytes, liver function tests, serum iron or ferritin, folate or red blood cell folate, and B₁₂ should be measured at initial diagnosis. Liver function tests may be mildly abnormal in patients with celiac disease, even when associated hepatic disorders are absent. Specific deficiencies of iron and folic acid should be therapeutically corrected, although they will not normally be required long-term after introduction of a gluten-free diet. B₁₂ levels usually normalize without specific therapy. A dual energy x-ray absorptiometry scan should be undertaken to seek evidence of osteoporosis because this usually improves on a gluten-free diet, although specific therapy may be required.

Treatment

The cornerstone of treatment is a gluten-free diet. This should involve the advice of a dietician who is experienced in this field. Patients should omit wheat, rye, and barley from their diet. Oats may be permitted, although it should not be forgotten that the majority of commercially available oat flour is contaminated with wheat gluten.

It is important to explain the disease and the toxicity of gluten-containing foods to the patient. This should include information on the avoidance of future ill health or reversal of current problems including anemia, depression, and infertility. Explaining the increased risk of malignancy, particularly small intestinal lymphoma, is debatable and should be decided with discretion on a patient-by-patient basis. Physicians should not frighten patients into dietary compliance but provide them with the necessary facts for them to decide themselves.

It is advisable for patients to join a celiac sprue group that usually publishes lists of locally available gluten-free products. There are now a wide range of gluten-free breads, biscuits, "pasta", etc. that are commercially available in the United States and many European countries, where they can be obtained on a prescription. Specific foods that require some mention include beer and malted breakfast cereals, which should be avoided because they contain celiac toxic barley hordein. Patients with celiac sprue usually experience a rapid symptomatic improvement within a matter of weeks of the exclusion of dietary gluten, and this provides additional diagnostic confirmation.

Nutrient Deficiency

At the time of diagnosis, routine blood tests including full blood count and biochemical profile (which includes albumin concentration, ferritin, serum folate or red cell, and B₁₂) should be measured. Supplements to replace iron and folate and B₁₂ may be required if reduced serum levels of ferritin and folate are found, although levels frequently correct on treatment with a gluten-free diet. Monitoring of antiendomysial or tissue transglutaminase antibody titers, which usually normalize with the institution of a gluten-free diet, may prove useful to check dietary compliance. Occasionally, calcium and vitamin D supplementation may be required. Similarly, life-threatening hypokalemia or hypomagnesemia may occur and should be appropriately corrected.

Nonresponsive Celiac Sprue

The most common cause of nonresponsiveness is continued gluten intake. Should the biopsy remain abnormal, a wheat-free, gluten-free diet should be initiated in which there is avoidance of wheat starch-based gluten-free foods in addition to the standard gluten-free diet. It is important to stress that clinicians should rule out other treatable diseases with similar histology that do not respond to a gluten-free diet.

Steroids can be used, and an acute crisis is managed with parenteral hydrocortisone. Oral corticosteroids may be used in nonresponsive disease but only when other causes of small intestinal villous atrophy have been excluded. 6-Mercaptopurine or azathioprine may be used as steroid-sparing agents if a dose of more than 10 mg/day of prednisolone is required.

Ulcerative Jejunitis

In this condition, there are ulcers affecting the jejunum or ileum. Scarring can lead to stricture formation with intervening areas of dilated bowel. There is a variable degree of villous atrophy in adjacent and distant mucosa. There is a high mortality rate with death often following hemorrhage, perforation, or obstruction possibly on a background of malnutrition. Diagnosis can be difficult, with small intestinal radiology often being unhelpful. If ulceration or lymphoma beyond the second part of the duodenum is thought likely, enteroscopy may be useful to obtain biopsy specimens for histologic assessment.

Surgical resection of the ulcer, especially if localized to one part of the intestine, can be curative. Strictureplasty may be undertaken. A strict gluten-free diet should be initiated, and steroids are often used, sometimes with benefit. If a diagnosis of enteropathy-associated T-cell lymphoma is made, the patient should be referred to an oncologist for appropriate chemotherapy.

Malignancy

There is an increase in overall mortality in celiac sprue. The excess deaths are mainly caused by malignancy, the majority of which involve intestinal lymphoma. Holmes and colleagues found a 5-fold increased risk of developing malignancy in a celiac population with a relative risk of developing non-Hodgkin lymphoma of 40. This risk fell to the level of the normal population after patients had taken a gluten-free diet for 5 years.

Small bowel radiology, enteroscopy, and a computer-aided tomographic radiographic scanning should be undertaken if lymphoma is suspected. Laparotomy may be required. Treatment for enteropathy-associated T-cell lymphoma is unsatisfactory with a low survival rate. After lymphoma, the most common malignancy is adenocarcinoma of the intestine. Presentation may involve anaemia, gastrointestinal blood loss, weight loss, obstruction, vomiting, and abdominal pain.

Follow-up

Some physicians contend that after introduction of a gluten-free diet, most patients remain well. It is generally advocated that yearly weight, full blood count, ferritin, folate, calcium, and alkaline phosphatase should be recorded. Follow-up should be life-long, and this permits reinforcement of the continuing need for strict adherence to the gluten-free diet.

Screening first-degree relatives may be undertaken and other associated conditions may be sought in affected individuals. It is wise, therefore, that follow-up should be undertaken by a physician.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate diagnosis and management of patients with celiac sprue.

POTENTIAL HARMS

Risk of hemorrhage with intestinal biopsy

Hemoglobin concentration, platelet count, and prothrombin time should be checked before biopsy because of the significant number of untreated celiac patients who have an increased prothrombin time. Anemia is not a contraindication to small intestinal biopsy unless very marked because of the risk of hemorrhage with a normal prothrombin time is small.

Subgroups Most Likely to be Harmed:

Celiac patients with increased prothrombin time

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

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)

American Gastroenterological Association medical position statement: celiac sprue. *Gastroenterology* 2001 May; 120(6): 1522-5.

ADAPTATION

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

DATE RELEASED

2000 Nov 12 (reviewed 2001)

GUIDELINE DEVELOPER(S)

American Gastroenterological Association - Medical Specialty Society

SOURCE(S) OF FUNDING

American Gastroenterological Association

GUIDELINE COMMITTEE

American Gastroenterological Association Clinical Practice and Practice Economics Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Not stated

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

According to the guideline developer, the Clinical Practice Committee meets 3 times a year to review all American Gastroenterological Association guidelines. This review includes new literature searches of electronic databases followed by expert committee review of new evidence that has emerged since the original publication date.

This guideline has been reviewed by the developer and is still considered to be current as of Dec 2001.

GUIDELINE AVAILABILITY

Electronic copies: Available from the [American Gastroenterological Association \(AGA\) Gastroenterology journal Web site](#).

Print copies: Available from American Gastroenterological Association, 4930 Del Ray Avenue, Bethesda, MD 20814.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Paul J. Ciclitira. AGA technical review on celiac sprue. *Gastroenterology*. 2001 May; 120(6):1526-40 [46 references].

Electronic copies: Available from the [American Gastroenterological Association \(AGA\) Gastroenterology journal Web site](#).

The following is also available:

- The American Gastroenterological Association standards for office-based gastrointestinal endoscopy services. *Gastroenterology*. 2001 Aug; 121(2):440-443 [8 references].

Electronic copies: Available from the [American Gastroenterological Association \(AGA\) Gastroenterology journal Web site](#).

Print copies: Available from American Gastroenterological Association, 4930 Del Ray Avenue, Bethesda, MD 20814.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on June 5, 2002. The information was verified by the guideline developer on July 12, 2002.

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