

American Gastroenterological Association Medical Position Statement: Guidelines for the Evaluation and Management of Chronic Diarrhea

This document presents the official recommendations of the American Gastroenterological Association (AGA) on the Evaluation and Management of Chronic Diarrhea. It was approved by the Clinical Practice and Practice Economics Committee on September 27, 1998, and by the AGA Governing Board on November 8, 1998.

Chronic diarrhea, defined as the production of loose stools with or without increased stool frequency for more than 4 weeks, is a common symptom that has a prevalence in the United States of approximately 3%–5%. Chronic diarrhea may be caused by any one of many conditions; accordingly, evaluation of patients with this problem can be complex. Nevertheless, correlation of data from history, physical examination, laboratory tests, radiographic studies, and endoscopic examinations usually results in an accurate diagnosis.

This document provides gastroenterologists with recommendations for the evaluation and management of chronic diarrhea. It is based on the American Gastroenterological Association Technical Review on Chronic Diarrhea,¹ which should be consulted for additional information. As pointed out in that review, many of these recommendations have not been subjected to systematic, prospective testing and instead represent the consensus of experts in the field.

History

A careful history can provide clues to the cause of chronic diarrhea. The following 14 points should be assessed as part of a comprehensive history in a patient with chronic diarrhea:

1. The characteristics of the onset of diarrhea should be noted as precisely as possible. Note should be made of whether it was congenital, abrupt, or gradual in onset.
2. The pattern of diarrhea should be recorded: Are loose stools continuous or intermittent?
3. The duration of symptoms should be identified clearly.
4. Epidemiological factors, such as travel before the onset of illness, exposure to potentially contaminated food or water, and illness in other family members should be elicited.
5. Stool characteristics should be investigated. Specifically, the patient should be queried as to whether stools are watery, bloody, or fatty.
6. The presence or absence of fecal incontinence should be determined. Some individuals complain of diarrhea when their major difficulty is disordered continence.
7. The presence or absence of abdominal pain and its characteristics should be evaluated. Pain often is present in patients with inflammatory bowel disease, irritable bowel syndrome, and mesenteric ischemia.
8. The presence of weight loss should be determined if possible by reference to objective measurement of body weight. Weight loss can be seen in any diarrheal disease, because patients often reduce intake in an effort to control symptoms; however, substantial weight loss is more likely to be caused by nutrient malabsorption, neoplasm, or ischemia.
9. Aggravating factors, such as diet and stress, should be recorded.
10. Mitigating factors, such as alteration of diet and use of both prescription and over-the-counter drugs, should be listed.
11. Previous evaluations should be reviewed whenever possible. Objective records may be inspected, and radiograms and biopsy specimens should be reexamined before new studies are ordered.
12. Iatrogenic causes of diarrhea should be investigated by obtaining a detailed medication history and a history of radiation therapy or surgery.
13. Factitious diarrhea caused by surreptitious laxative ingestion should be considered in every patient with chronic diarrhea. Markers of factitious diarrhea, such as a history of eating disorders, secondary gain, or a history of malingering, should be sought.
14. A careful review of systems should be conducted to look for systemic diseases, such as hyperthyroidism, diabetes mellitus, collagen-vascular diseases and other inflammatory conditions, tumor syndromes, acquired immunodeficiency syndrome, and other immune problems.

Physical Examination

A complete physical examination can yield important clues about the severity of diarrhea and may suggest

the cause of diarrhea, but only in a few cases. The most important conclusions to draw from the physical examination are the extent of fluid and nutritional depletion. Other features of diagnostic significance include the presence of flushing or rashes on the skin, mouth ulcers, thyroid masses, wheezing, arthritis, heart murmurs, hepatomegaly or abdominal masses, ascites, and edema. Special attention should be paid to the anorectal examination as regards anal sphincter tone and contractility and the presence of perianal fistula or abscess.

Routine Laboratory Tests

A complete blood count provides evidence of anemia and helps to classify an anemia, if present. Leukocytosis suggests the presence of inflammation, and eosinophilia is seen with neoplasms, allergy, collagen-vascular diseases, parasitic infestation, and eosinophilic gastroenteritis or colitis. Serum chemistry screening can provide important information about the patient's fluid and electrolyte status, his or her nutritional status, liver problems, and dysproteinemia.

Therapeutic Trials

At this point in the evaluation, a specific diagnosis may be obvious and may warrant a specific therapeutic trial. For example, if a particular drug seems to be responsible for diarrhea, it may be reasonable to discontinue the drug and see if the diarrhea resolves. Similarly, in areas where infectious diarrhea is particularly common, it may be reasonable to perform empirical trials of metronidazole for protozoal diarrhea or a fluoroquinolone drug for presumed enteric bacterial diarrhea before undertaking further evaluation. Any such therapeutic trial should be conducted with specific end points in mind, so that further evaluation is not delayed unnecessarily.

Stool Analysis

In most instances, a quantitative stool collection and analysis can yield important objective information about the type of diarrhea and its severity. When this is impractical, a spot stool collection can yield almost as much information. In addition to stool weight, six groups of studies should be obtained to classify the diarrhea as watery diarrhea (either secretory or osmotic), inflammatory diarrhea, or fatty diarrhea and to gain insight into specific diagnoses:

1. Sodium and potassium concentrations in stool water may be measured, so that the fecal osmotic gap can be calculated. The fecal osmotic gap is best calculated as $290 - 2([\text{Na}^+] + [\text{K}^+])$. Osmotic diarrheas are

characterized by osmotic gaps >125 mOsm/kg, whereas secretory diarrheas typically have osmotic gaps <50 mOsm/kg.

2. Stool pH may be assessed. Values of <5.6 are consistent with carbohydrate malabsorption.
3. Fecal occult blood testing with any of the available agents should be conducted. A positive test result suggests the presence of inflammatory bowel disease, neoplastic diseases, or celiac sprue or other spruelike syndromes.
4. The presence of white blood cells in the stool suggests an inflammatory diarrhea. This can be assessed by microscopic examination of a stool smear stained with Wright's stain or during a stool ova and parasite examination. A latex agglutination test for the neutrophil granule protein lactoferrin may also be useful.
5. The presence of excess stool fat should be evaluated by means of a Sudan stain or by direct measurement. The presence of excessively large and numerous fat globules by stain or measured stool fat excretion >14 g/24 h suggests malabsorption or maldigestion. Stool fat concentration of $>8\%$ strongly suggests pancreatic exocrine insufficiency.
6. Laxative screening should be done in any patient with chronic diarrhea that has defied diagnosis.

Further Evaluation of Patients With Chronic Secretory Diarrhea

Patients with chronic watery diarrhea who have little or no osmotic gap as calculated from stool electrolytes should be evaluated with three sets of investigations:

1. Although bacterial infection rarely causes chronic diarrhea, it can be excluded by stool culture, including culture on special media for *Aeromonas* and *Pleisiomonas*. In addition, the stool should be examined microscopically for ova and parasites, with special tests for *Cryptosporidium*, *Microsporidium*, and *Giardia*. *Giardia* antigen, measured in stool by enzyme-linked immunosorbent assay, is the most sensitive test for giardiasis. An aspirate of small bowel contents for quantitative culture or breath tests with glucose or isotopically labeled xylose can be used to establish the presence of small bowel bacterial overgrowth but is likely to be meaningful only in patients with disorders predisposing them to bacterial overgrowth.
2. Structural disease should be excluded by radiography of the small bowel, sigmoidoscopy, or colonoscopy with multiple biopsies of the colonic mucosa, computerized tomography of the abdomen, and endoscopic biopsy of the proximal small bowel mucosa. A small

bowel follow-through examination is preferable to an enteroclysis study for the radiographic evaluation of patients with chronic diarrhea.

3. Selective testing for plasma peptides such as gastrin, calcitonin, vasoactive intestinal polypeptide, and somatostatin, as well as urine excretion of 5-hydroxyindole acetic acid, metanephrine, or histamine and other tests of endocrine function, such as measurement of thyroid-stimulating hormone and serum thyroxine levels or an adrenocorticotropin-stimulation test for adrenal insufficiency, can be valuable. Because peptide-secreting tumor syndromes causing chronic diarrhea are very rare, measurement of serum peptide concentrations (e.g., gastrin, vasoactive intestinal polypeptide, calcitonin) should be done only when a tumor syndrome seems likely from the clinical presentation or findings on radiographic studies.

Further Evaluation of Patients With Chronic Osmotic Diarrhea

Most osmotic diarrhea not associated with steatorrhea is caused by ingestion of poorly absorbable carbohydrates or magnesium salts. A low stool pH suggests carbohydrate malabsorption, and a high stool magnesium concentration or output suggests magnesium ingestion. If carbohydrate malabsorption is suspected, a careful dietary history and judicious use of breath hydrogen testing with lactose as the test sugar or measurement of lactase in a mucosal biopsy specimen can be diagnostic. Patients with high stool magnesium outputs should be evaluated for inadvertent ingestion of magnesium in mineral supplements or antacids and for surreptitious laxative abuse.

Further Evaluation of Chronic Inflammatory Diarrhea

Patients with blood and pus in the stool should undergo radiographic evaluation of the small bowel with barium (small bowel follow-through examination) and sigmoidoscopy or colonoscopy with biopsies of the colonic mucosa. Stool culture and analysis of stool for *Clostridium difficile* toxin may identify infectious causes of inflammation.

Evaluation of Chronic Fatty Diarrhea

Patients with evidence of steatorrhea should undergo small bowel follow-through radiographic studies to

exclude structural problems. Small bowel biopsy specimens and an aspirate of small bowel contents for quantitative culture should be obtained, and pancreatic exocrine insufficiency should be assessed by direct tests, such as the secretin test, or by indirect tests, such as measurement of stool chymotrypsin activity or a bentiromide test. Studies such as D-xylose absorption tests and the Schilling test have little application in the evaluation of these patients.

Empirical Therapy for Chronic Diarrhea

Empirical therapy is used in three situations: as a temporizing or initial treatment before diagnostic testing, after diagnostic testing has failed to confirm a diagnosis, and when a diagnosis has been made, but no specific treatment is available or specific treatment fails to effect a cure. Empirical trials of antimicrobial therapy may be justified if the prevalence of bacterial or protozoal infection is high in a specific community or situation. An empirical trial of bile acid-binding resins, such as cholestyramine, may be the least expensive way to diagnose bile acid-induced diarrhea. Opiates are the most effective nonspecific antidiarrheal agents. Octreotide should be reserved as a secondary agent. Adequate hydration is an essential part of the treatment of diarrheal diseases, and oral rehydration solutions may be necessary in some instances. Some patients, particularly those with postresection diarrhea, may need long-term intravenous fluid administration. Parenteral nutrition should be reserved for patients who are unable to maintain an adequate nutritional status because of the diarrheal disease.

References

1. Fine KD, Schiller LR. AGA technical review on the evaluation and management of chronic diarrhea. *Gastroenterology* 1999;116:1464-1486.

This Medical Position Statement has been endorsed in principle by the American Association for the Study of Liver Diseases, the American College of Gastroenterology, and the American Society for Gastrointestinal Endoscopy.

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