

Functional Dyspepsia — Managing the Conundrum

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Every day, in countless examination rooms around the world, patients are consulting their doctors about chronic stomach pain. In industrialized countries, medical evaluation usually uncovers no structural cause for chronic upper abdominal pain or discomfort; the majority of patients have functional, or non-ulcer, dyspepsia. Although some general principles are useful in managing functional dyspepsia, the therapies that have been assessed to date provide little hope of a cure for this perplexing disorder.

Most patients with dyspepsia are first evaluated by primary care practitioners, who should elicit a detailed history to identify patients whose symptoms may be attributable to medication use, gastroesophageal reflux disease, gallstones or, if symptoms are associated with constipation or diarrhea, irritable bowel syndrome. Stopping the use of medications (such as nonsteroidal antiinflammatory agents) that have been implicated as potential sources of such symptoms may help to mitigate dyspepsia. Symptoms of gastroesophageal reflux disease usually improve after treatment with acid inhibitors, whereas symptoms of irritable bowel syndrome do not.

Patients with dyspepsia should be asked about other physical problems, coexisting psychological symptoms, and stressful life events, because these factors influence the severity of the illness and affect its management. Patients undergo a physical ex-

amination for tenderness, which is usually nonspecific. However, it is common to find localized tenderness of the abdominal wall that increases with the contraction of abdominal muscles at painful sites in the upper or lower abdomen. This test (Car-



nett's sign), first described 80 years ago, is an accurate tool for assessing pain from the abdominal wall, and in many patients without weight loss or other worrisome features, no additional investigation is required. However, this test is frequently overlooked, leading to referral to a specialist after fruitless and expensive imaging procedures have been performed and drug therapy has proved unsuccessful.

Much less often, the examiner palpates a tumor or detects a dermatomal cutaneous sensory abnormality or localized paresis of the abdominal wall, both of which are typical of thoracic polyradiculopathy, which occurs

mainly in patients with diabetes. Certain worrisome features — such as the onset of dyspepsia after 55 years of age, unintended weight loss, anemia, and progressive dysphagia — increase the likelihood that the cause is an organic disorder. Unfortunately, a medical history and a physical examination cannot distinguish peptic ulcer disease from functional dyspepsia.

Ultrasonography of the gallbladder should generally be undertaken only in patients with characteristic biliary pain, since they are the most likely to benefit from cholecystectomy. The measurement of gallbladder emptying with the use of cholecystokinin cholescintigraphy in patients without gallstones is unproven as a predictor of the outcome of cholecystectomy, and “diagnostic cholecystectomy,” which may be increasing in frequency as laparoscopic surgery becomes more common, should be discouraged.

If careful history taking, physical examination, and screening laboratory tests in patients with dyspepsia do not lead to a diagnosis, physicians can follow the management guidelines of the American College of Gastroenterology¹ or the American Gastroenterological Association,² which make similar recommendations on the basis of data from both cost analyses and randomized, controlled trials of a variety of treatments. Patients who are older than 55 years, who are members of racial or ethnic groups that are predisposed to early gastric

Treatments for Functional Dyspepsia.
Treatments with limited supporting evidence
<i>H. pylori</i> eradication
Itopride
Proton-pump inhibitors
Psychological therapy (cognitive behavioral therapy, hypnotherapy, psychotherapy)
Treatments with uncertain or no supporting evidence
Antacids
Antispasmodic agents
Bismuth salts
Dietary therapy
Herbal therapy
Histamine H ₂ -receptor antagonists
Misoprostol
Prokinetic agents
Selective serotonin-reuptake inhibitors
Sucralfate
Tricyclic antidepressants (at low doses)

cancer, or who have worrisome features should undergo esophagogastroduodenoscopy with biopsy for *Helicobacter pylori*. Other patients should undergo testing for *H. pylori* with the use of a urea breath test or a test for antigen in the stool. Patients who test positive should be treated for *H. pylori* infection. Patients who test negative for *H. pylori* or who test positive but whose condition does not respond to treatment should receive proton-pump inhibitor therapy for four to eight weeks. In populations with a prevalence of *H. pylori* infection of less than 10 percent, the cost-effectiveness of the test-and-treat policy declines, as compared with that of empirical therapy with a proton-pump inhibitor.

In patients 55 years of age or younger whose condition does not have worrisome features, esophagogastroduodenoscopy is recommended only if the condition does not respond to proton-pump inhibitor therapy. However, such

treatment algorithms have pitfalls for patients with complex disorders, and physicians' actions may be affected by such factors as the uncertain prevalence of *H. pylori* in particular populations, the potential for preventing noncardiac gastric cancer and peptic ulcer disease by eradicating *H. pylori*, the risk of antibiotic-associated *Clostridium difficile* colitis, the risk of induction of bacterial resistance to clarithromycin and other antimicrobial agents, the costs of proton-pump inhibitors and esophagogastroduodenoscopy, and the patient's preferences.

In most patients, esophagogastroduodenoscopy reveals no cause of dyspepsia; this may be reassuring temporarily, but physicians are then challenged to select a treatment from several unimpressive options (see table). Variation among methods complicates the assessment of economic models, trials, and systematic reviews, and publication bias can occur. Trials involving *H. pylori* eradication in

patients whose esophagogastroduodenoscopy results were normal raise the issue of statistically significant versus clinically significant efficacy. The most optimistic meta-analyses of studies involving more than 3000 patients suggest that at least 15 patients with *H. pylori* infection must be treated to cure 1 patient whose condition would not have resolved with placebo — and that condition may in fact be undiagnosed ulcer disease. The critical features of dyspepsia include abnormal gastric emptying, impaired fundic accommodation, increased gastroduodenal sensitivity to mechanical distention, and impaired acid clearance and increased acid sensitivity in the duodenum. However, only a small proportion of patients are tested for these derangements, which correlate poorly with symptoms and with responses to targeted drug therapy. Therefore, the positive trial of itopride — a dopamine D2 antagonist — reported by Holtmann et al. in this issue of the *Journal* (pages 832–840) is important.

Findings from even the best trials of treatments for functional dyspepsia may not translate well into clinical practice. Factors that contribute to this problem include the enrollment of patients from referral centers, who may not be typical of patients treated in primary care, and the inadvertent inclusion of patients with gastroesophageal reflux disease — the symptoms of which can resemble those of dyspepsia — which can bias the results. Moreover, although functional dyspepsia is a chronic disorder, few trials of drugs for this disease exceed eight weeks. In addition, critical aspects of care include demystifying symp-

toms with an explanation of gastrointestinal sensitivity and its relation to stress and allaying anxiety, especially regarding the possibility of cancer — yet many reports do not address such details of physician–patient interactions.

Functional dyspepsia represents more than just abnormal gastrointestinal function — it also involves the interaction of the stomach and intestine with the central nervous system. This interaction underscores the desirability of characterizing the psychological status of participants in drug trials and considering it when choosing outcomes to measure. Trials involving psy-

chological therapy are more difficult to design well than drug trials, and although hypnotherapy shows promise, it is not widely available. Antidepressant therapy could improve patients' global health status by alleviating the symptoms of disorders other than dyspepsia, including anxiety, insomnia, and headache. Multicomponent therapy (e.g., psychotherapy and pharmacotherapy) has not been well studied.

Functional gastrointestinal disorders are complex, and multinational committees have met every few years to revise the diagnostic criteria for research and treatment and to update recommendations for therapy.³ Until ther-

apy for functional dyspepsia is more dependable, our most effective approach is to maximize the physician–patient relationship to help patients cope with their symptoms.

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3. Drossman DA, Corazziari E, Delvaux MM, et al. Rome III: the functional gastrointestinal disorders. *Gastroenterology* (in press).