Dyspepsia is a common symptom. Dyspeptic symptoms may be caused by a variety of conditions such as peptic ulcer disease, gastro-oesophageal reflux, and malignancy. Most often, however, no cause is identified and dyspepsia is deemed to be functional. While symptom severity does influence frequency of consultation, dyspeptic consultants also differ from non-consultors with respect to symptom perception and anxiety. This highlights the importance of understanding the patient's agenda early in the course of evaluation. Patients over the age of 55 years or with alarm symptoms should be referred for prompt endoscopy. In the absence of other clinically apparent aetiologies, uninvestigated dyspeptics can be either tested and treated for Helicobacter pylori or empirically treated with proton pump inhibitors. Uninvestigated dyspeptics failing empiric therapy should be referred for evaluation that includes endoscopy. Further therapy with prokinetics, tricyclic antidepressants, fundal relaxants, antidepressants, or psychotherapy is guided by predominant symptoms and assessment of possible psychiatric factors.

DEFINING THE PROBLEM

Defining dyspepsia allows for more accurate study of the problem and the problem is considerable. Studies from the United States, Great Britain, and other parts of the world have shown the prevalence of dyspepsia to be between 26% and 41%. While only 20%–25% of these individuals seek medical care, dyspepsia accounts for 2%–5% of all consultations in primary care. For gastroenterologists, dyspepsia accounts for between 20% and 40% of consultations. It appears that as primary care physicians have grown more comfortable with proton pump inhibitors and Helicobacter pylori eradication, the percentage of attendees in gastroenterology clinics with functional dyspepsia is steadily increasing.

The burden of illness with respect to quality of life and economic consequences of dyspepsia is considerable. Recent data from a large cross sectional survey in the UK suggest dyspepsia may be costing society approximately £1 billion ($1.46 billion) annually. Similar estimates exist for the costs of diagnosis and management of dyspepsia in the United States. A Swedish study estimated direct costs of dyspepsia to be approximately £26 million annually for 8 million people. When indirect costs were included, total costs increased almost 10-fold. This was largely attributable to the average of 26 (1) more days of lost productivity by dyspeptics. Indirect health costs are paralleled by decreased quality of life, which can be profound. Figure 1 shows Psychological General Well Being index scores for healthy controls, patients with functional dyspepsia, and gastroenterics seen in our clinic. Clearly, the burden of dyspepsia is considerable from economic, societal, and personal vantage points.

EARLY INVESTIGATION AND MANAGEMENT OF THE "UNINVESTIGATED DYSPESPICT"

Dyspepsia is a symptom and not a diagnosis. The differential diagnosis of dyspepsia is shown in

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underlying gastro-oesophageal reflux disease or peptic ulcer preferred as they are better tolerated and effectively treat antisecretory or prokinetic agents. Antisecretory agents are these patients may be empirically treated most often using for early endoscopy are termed "uninvestigated dyspeptics". It should be done for valid clinical reasons, endoscopy should be performed. If that cannot be predicted clinically. The most prudent course in these patients is to discontinue non-steroidal. If that cannot be predicted clinically. The most prudent course in these patients is to discontinue non-steroidal anti-inflammatory medication use and these drugs are clearly ulcerogenic. Although most patients with dyspepsia taking non-steroidal anti-inflammatory drugs will not have ulcer, chronic pain syndromes. Patients with dyspeptic symptoms who are not candidates for early endoscopy are termed "uninvestigated dyspeptics". These patients may be empirically treated most often using antisecretory or prokinetic agents. Antisecretory agents are preferred as they are better tolerated and effectively treat underlying gastro-oesophageal reflux disease or peptic ulcer disease. While \( H_2 \) receptor antagonists have been widely used in this setting for many years, proton pump inhibitors should presently be regarded as first line agents. Proton pump inhibitors offer some superiority over \( H_2 \) receptor antagonists in the treatment of peptic ulcer disease and are substantially superior in providing symptom relief in reflux disease. Given the inherent diagnostic uncertainty present when empirically treating dyspepsia, it seems reasonable to not further complicate matters by adding the confounding variable of a suboptimal therapy. Additionally, there are now several studies with omeprazole and lansoprazole demonstrating superiority of these agents over \( H_2 \) receptor antagonists in this setting.5–7 The optimal dose of proton pump inhibitor for a therapeutic trial is not known but given the desired goal of controlling gastric acid secretion and normalising the intraoesophageal pH profile, a twice daily dose of a newer proton pump inhibitor should probably be used.8–10

Some authors have advocated a symptom-tailored approach with proton pump inhibitors given to those patients with principal complaints of upper abdominal pain and prokinetics used initially in patients with fullness, bloating, or early satiety.11 There are no good clinical data to support this approach at present.

Because some dyspepsia will have underlying peptic ulcer disease that can be cured by eradication of \( H\) pylori, the strategy of testing uninvestigated dyspepsia for \( H\) pylori and treating those who are infected has become quite popular. Proponents have argued this strategy eliminates ulcer disease and is cost saving.12–14 The utility of this approach is obviously highly dependent upon the prevalence of \( H\) pylori, the prevalence of peptic ulcer disease, the degree to which eradication of \( H\) pylori improves symptoms of functional dyspepsia, and the cost and availability of alternative management strategies. As shown in fig 2, the prevalence of \( H\) pylori and peptic ulcer disease are highly correlated and vary considerably across the United States. \( H\) pylori and ulcer disease are quite common in urban Detroit but uncommon in suburban and rural practices in Ohio and Pennsylvania.22–26 Obviously, the utility of a test and treat strategy is dependent upon the prevalence of \( H\) pylori in the specific population being treated. Additionally, despite some data to the contrary, the majority of well done clinical trials have failed to demonstrate symptom improvement in functional dyspepsia after \( H\) pylori eradication.27–29

In summary, patients with new onset dyspepsia who are over the age of 55 years or with alarm symptoms should undergo early endoscopy. In the remaining patients, the likelihood of organic pathology is low. "Uninvestigated dyspepsia" can be managed empirically. If the background prevalence of \( H\) pylori and ulcer disease is high, a "test and treat" approach is reasonable. \( H\) pylori negative patients or those not responding to eradication therapy can be given a trial of proton pump inhibitors. If there is a clinical response to either acid suppressive therapy or \( H\) pylori eradication, patients can be managed intermittently for recurrent symptoms. For patients who require additional reassurance, fail empiric therapy, or require chronic treatment, referral for further investigation including upper gastrointestinal endoscopy is indicated.
from H2 receptor antagonists. More recent studies using ulcer and reflux disease have tended to show little benefit of acid suppression in true functional dyspepsia. Studies of patients with dyspepsia attributable to peptic ulcer-like or reflux-like dyspepsia. There additionally appears to be some benefit those patients with dyspepsia due to impaired postprandial relaxation of the proximal stomach. Some investigators have suggested that certain symptoms are associated with altered gastric physiology. Predictors of delayed gastric emptying include female sex, excessive postprandial fullness, and severe vomiting.45 Impaired postprandial relaxation of the proximal stomach has been associated with early satiety.46–48 The acute administration of the interstitial serotonin receptor (5-HT1) agonists, buspirone and sumatriptan, has been shown to improve accommodation and tolerance to balloon distension of the proximal stomach.49–50 While these observations are encouraging, most studies have failed to demonstrate a relationship between disturbed gastrointestinal motor function and symptoms. In particular, there is little evidence that abnormalities of the interstitial serotonin receptor (5-HT1) agonists, buspirone and sumatriptan, have contributed to symptom relief. Studies of the interstitial serotonin receptor (5-HT1) agonists, buspirone and sumatriptan, have been associated with increased frequency in this population.44,45 Understanding these issues is critical to managing patients with functional disorders. The importance of addressing patient concerns and exploring the psychosocial context of symptoms cannot be overstated, particularly in

**Box 2: Potential causes of non-ulcer dyspepsia**

- Duodenogastric reflux.
- Duodenitis.
- Carbohydrate malabsorption (lactose, fructose, sorbitol).
- Cholelithiasis or cholecodocholithiasis.
- Chronic pancreatitis.
- Systemic disorders (diabetes, thyroid, parathyroid, hypoparathyroidism, connective tissue disease).
- Intestinal parasites.
- Psychiatric disorders.
- Visceral hypersensitivity.
- Gastric/small intestinal dysmotility.
- Gallbladder/biliary dysmotility.

**INVESTIGATION OF DYSPESIA AND NON-ULCER DYSPESIA**

Eradication of *H. pylori* and use of acid suppressive therapy will benefit those patients with dyspepsia attributable to peptic ulcer and reflux disease. There additionally appears to be some benefit of acid suppression in true functional dyspepsia. Studies of functional dyspepsia that have aggressively excluded ulcer and reflux disease have tended to show little benefit from H2 receptor antagonists. More recent studies using proton pump inhibitors have demonstrated modest gains in more carefully selected patients. Omeprazole in both 10 mg and 20 mg doses was superior to placebo when using the endpoints of complete symptom relief or sufficient symptom control in two combined trials involving 1262 patients (fig 3). The net therapeutic gain was 10% for omeprazole 20 mg daily and 8% for omeprazole 10 mg daily. There was no significant difference between groups with respect to quality of life and the therapeutic benefits were restricted to those patients with ulcer-like or reflux-like dyspepsia.51 A third double blind, placebo control trial of omeprazole 20 mg daily in 197 patients with functional dyspepsia showed omeprazole to be superior to placebo in providing complete symptom relief after two weeks.52

For patients unresponsive to acid suppressive therapy or *H. pylori* eradication, mechanisms of symptom generation are largely speculative. This means therapeutic interventions are also speculative. A variety of potential causes have been proposed with varying degrees of support (box 2). While patients often complain of excess acid, there is no evidence for abnormal gastric acid secretion. The role of *H. pylori* has already been discussed. It should be kept in mind that “gastritis” is neither an endoscopic diagnosis nor a cause of recognised dyspepsia.

Three aetiologies deserve particular attention: dysmotility, visceral hypersensitivity, and psychiatric disorders. Abnormalities of gastric neuromuscular function can be detected by scintigraphic gastric emptying studies, electrogastrography, or antroduodenal manometry in between 30% and 60% of patients.53,54 In addition to impaired motor function, a subset of dyspeptics has impaired postprandial relaxation of the
patients refractory to standard therapies. Frank discussions in an empathic manner or use of self administered questionnaires such as the Beck Depression Index, Beck Anxiety Index, and Symptom Check List-90 can provide objective documentation that may help further explore these areas.

TREATMENT OF NON-ULCER DYSPEPSIA

Therapy in functional dyspepsia is symptom driven. There are few data to suggest that studies of gastric neuromuscular function allow implementation of therapies that reliably improve symptoms. Patients with functional dyspepsia who have predominant symptoms of upper abdominal pain (ulcer-like) can be initially treated with proton pump inhibitors. Patients with unexplained upper abdominal pain who have failed proton pump inhibitors may be treated with tricyclic antidepressants, although good supporting data are lacking.

Those with dysmotility-like symptoms can be treated initially with either acid suppressive therapy, prokinetic agents, or 5-HT, agonists. Both metoclopramide and domperidone have been shown to be superior to placebo in the treatment of functional dyspepsia. 2–5 Available literature suggests 5-HT, agonists may be efficacious in patients with impaired accommodation. Since formal assessment of accommodation is not widely available, it is reasonable to use these agents in patients with excessive early satiety. The lack of supporting data and the adverse reactions associated with sumatriptan argue against the use of this agent. Buspirone has comparable effects, fewer adverse events, and may provide additional anxiolytic benefits in a non-confrontational way.

For all patients, the psychosocial context of symptoms should be assessed. Patients with a history of psychiatric distress, multiple unexplained physical symptoms, or symptoms refractory to standard therapies should be evaluated for concomitant psychopathology. If identified, appropriate therapy is offered. At present there are no data to support the use of selective serotonin reuptake inhibitors in functional dyspepsia in the absence of disorders for which these medications are otherwise indicated.

SUMMARY

Dyspepsia is a common symptom and is most often functional. Importantly, dyspeptic consulters differ from nonconsulters more in terms of symptom perception and anxiety than objective symptom measures. This highlights the importance of understanding the patient’s agenda early in the course of evaluation. Patients over the age of 55 years or with alarm symptoms should be referred for prompt endoscopy. In the absence of other clinically apparent aetiologies, uninvestigated dyspepsias can be either tested and treated for H pylori or empirically treated with proton pump inhibitors.

Uninvestigated dyspepsias failing empiric therapy should be referred for evaluation that includes endoscopy. Further therapy with prokinetics, tricyclic antidepressants, fundal relaxants, antidepressants, or psychotherapy is guided by predominant symptoms and assessment of possible psychiatric factors.

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Perichondritis: a complication of piercing auricular cartilage

A 20 year old woman presented to the ear, nose, and throat clinic with auricular perichondritis two days after piercing the helix of her left ear with the aid of a piercing gun. Two thirds of the upper part of her auricle was swollen, red, and tender. The lobule (which does not contain cartilage) remained intact, which indicated that the infection was perichondritis and not simply cellulitis. The lobule, which does not contain cartilage, is intact (long arrow) indicating that the infection is perichondritis and not simply cellulitis.

 IMAGES IN MEDICINE

Perichondritis: a complication of piercing auricular cartilage

Figure 1 Perichondritis complicating “high” ear piercing. Two thirds of the upper part of the auricle is swollen and red (wide arrow). The lobule, which does not contain cartilage, is intact (long arrow) indicating that the infection is perichondritis and not simply cellulitis.