DYSPEPSIA MANAGEMENT

Dyspepsia: management guidelines for the millennium

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The annual prevalence of dyspepsia in Western countries is approximately 25%, and the condition accounts for 2–5% of all primary care consultations, yet optimal management remains a subject of considerable debate. Some of the outstanding issues and considerations in the management of dyspepsia are discussed, providing an overview of current thinking and recommendations on patient management by primary care physicians and specialists.

SUMMARY

The optimal management of dyspepsia remains a subject of considerable debate. Careful initial clinical evaluation and history taking are essential in patients with uninvestigated dyspepsia to identify those with gastro-oesophageal reflux disease (GORD) and exclude other diseases. Patients with alarm symptoms, those over a locally identified age threshold, and patients taking standard non-steroidal anti-inflammatory drugs (NSAIDs) regularly should be referred for early upper endoscopy. This may also be indicated to address patient concerns over serious underlying disease. Most patients will be managed initially in primary care without endoscopy. Testing for *Helicobacter pylori* infection and subsequent eradication in infected patients is recommended as this strategy will cure most underlying peptic ulcer disease and prevent future gastroduodenal disease although many infected patients with functional dyspepsia will not gain symptomatic benefit. *H pylori* negative patients, those with residual symptoms following eradication therapy, and patients with an endoscopic diagnosis of functional dyspepsia should be treated empirically, possibly based on their predominant or most bothersome symptom. If symptoms are controlled, a trial of withdrawal of therapy should be considered, with therapy repeated in the case of symptom recurrence. An alternative is on demand therapy with the successful agent. If patients do not respond to the first type of therapy, a switch of treatment should be considered. If symptoms persist, a trial of high dose proton pump inhibitor (PPI) therapy may be considered. Otherwise, the patient should be referred for endoscopy if it has not already been undertaken. In patients with resistant functional dyspepsia, the diagnosis should be re-evaluated, further reassurance given, and behavioural therapy, psychotherapy, or antidepressants considered.

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INTRODUCTION

The annual prevalence of dyspepsia in Western countries is approximately 25%, and the condition accounts for 2–5% of all primary care consultations. Less than half of dyspepsia sufferers in Europe and the USA seek medical help for their complaint,[1] yet it is a major cause of morbidity and economic loss in the community[2] and can have a significant impact on patient quality of life. In patients that do seek help, concern over the cause of symptoms is a significant factor influencing consultation,[3–5] and is a key consideration in managing the condition. However, relief of symptoms and restoration of a normal quality of life, coupled with treatment and, ideally, cure of the underlying cause of symptoms, must also be the aim of interventions in the management of dyspepsia. Yet how are these goals best achieved?

Guidelines for the management of dyspepsia have been proposed by the American Gastroenterology Association,[1] the Digestive Health Foundation in the USA,[6] the Maastricht *H pylori* consensus meeting in Europe,[7] the Canadian *H pylori* consensus conference,[8] two Asian-Pacific consensus meetings,[9 10] and the British Society of Gastroenterology.[11] The role of *H pylori* testing and treatment in patient management is a major component of all of these guidelines. Furthermore, comprehensive guidelines have been proposed for the management of uninvestigated and functional dyspepsia in a Working Party Report for the World Congresses of Gastroenterology in Vienna 1998.[12]

The following article addresses some of the outstanding issues and considerations in the management of dyspepsia, and provides an overview of current thinking and recommendations on patient management for primary care physicians and specialists. There is a considerable body of relevant data that is described in the rest of this supplement, and its impact on the management of dyspepsia is taken into account here.

THE DILEMMAS OF MANAGEMENT

Two outstanding dilemmas in the management of dyspepsia continue to cause considerable debate. These are the overlap between dyspepsia and GORD, and the choice of initial patient management between early endoscopy, empirical therapy, and a *H pylori* test and treat strategy.

Distinguishing GORD from dyspepsia

The definition of dyspepsia as chronic or recurrent pain or discomfort centred in the upper abdomen (that is, the epigastrium), according to the Rome I criteria, stands today as the most

Abbreviations: GORD, gastro-oesophageal reflux disease; NSAIDs, non-steroidal anti-inflammatory drugs; PPI, proton pump inhibitor.

widely accepted and useful definition of dyspepsia.[13] Patients treated in primary care generally have uninvestigated dyspepsia, and their symptoms may have an underlying structural cause, such as peptic ulcer disease, reflux oesophagitis, or endoscopy negative GORD. However, a substantial number of these patients will have functional dyspepsia in which there is no definite structural or biochemical explanation for their symptoms following appropriate investigation.

Functional dyspepsia and GORD are the most frequent causes of dyspepsia in the community, despite the fact that according to the Rome criteria patients with GORD should be excluded in the diagnosis of functional dyspepsia. According to the Rome working team report, for patients to have functional dyspepsia they must have pain or discomfort in the central upper abdomen as their predominant symptom. This should therefore differentiate dyspepsia from GORD, in which the predominant symptom is typically heartburn.[2 14] However, in practice there is considerable overlap between symptoms, and many physicians overlook the issue of identifying the predominant symptom.[15]

A key element of effective management of patients presenting with dyspeptic symptoms is the identification and exclusion of those who have GORD. There are now well documented recommendations to ensure that once diagnosed, these patients receive effective management[14] (see Dent in this supplement **[see page iv67]**). Given that the majority of patients with GORD do not have underlying oesophagitis, accurate symptom diagnosis is particularly important. The availability and validation of questionnaires that accurately describe heartburn may help to improve the identification of dyspeptic patients with underlying GORD.[14] However, confounding factors in this are the likelihood that true dyspepsia is produced by gastro-oesophageal reflux episodes in a minority of patients with dyspepsia and that GORD and functional dyspepsia probably occur together in at least some patients (see Dent in this supplement **[see page ix17]**).

Early endoscopy, empirical treatment, or test and treat?

There are distinct patient groups, such as older patients and those with alarm symptoms, in whom early endoscopy is strongly advisable. This is discussed in more detail below.

However, a major dilemma is the choice of initial management in younger patients who do not have alarm symptoms. There are broadly four options available:

- early endoscopy for all;
- empirical drug therapy for all;
- *H pylori* testing, followed by eradication therapy or endoscopy in infected patients and empirical therapy in uninfected patients; and
- empirical *H pylori* eradication therapy for all, without a screening test for infection.

While there are arguments in favour of early endoscopy for all (see below), this is generally not practical because of cost and availability, and many patients will be treated in primary care without endoscopy. The question in primary care therefore is whether to prescribe empirical therapy or to pursue a course of management based on *H pylori* eradication.

In 1985, guidelines from the American College of Physicians suggested that, in the absence of alarm symptoms, a trial of empirical therapy was appropriate,[16] and this has become the traditional approach to therapy. However, this was prior to the broad recognition that eradication of *H pylori* can cure peptic ulcer disease. Consequently, as discussed below, it is becoming increasingly accepted that a *H pylori* "test and treat" strategy is to be recommended in young patients with dyspepsia and without alarm symptoms presenting in primary care.[1 6 7 9 12] This strategy must be kept under review however in the light of endoscopy costs and availability, and the prevalences of *H pylori* infection and peptic ulcer disease.

An alternative to test and treat is the empirical use of *H pylori* eradication therapy without prior testing for infection. This is generally not recommended as it will result in considerable over treatment, although it may be appropriate in specific areas with a very high prevalence of *H pylori* infection and where referral for endoscopy or testing for infection is not an option.[9]

Early endoscopy, empirical therapy, and *H pylori* test and treat are discussed in greater detail below. The empirical use of *H pylori* eradication therapy without prior testing is not discussed further in this review.

DISCRIMINANT VALUE OF SYMPTOMS AND SYMPTOM SUBGROUPS

Attempts have been made to categorise dyspepsia as ulcer-like, reflux-like, or dysmotility-like according to symptom clusters,[17] with reflux-like dyspepsia generally being synonymous with symptomatic GORD.[13] However, this has proved to be of little value in patients with uninvestigated dyspepsia because of the significant overlap between the symptom subgroupings, the considerable number of patients who do not fit into one of the subgroups[18] and, above all, the lack of adequate value in predicting underlying disease. Patients with dysmotility-like dyspepsia are almost as likely to have underlying peptic ulcer disease as those classified as having ulcer-like dyspepsia,[19] and symptom clusters do not help in defining whether uninvestigated dyspepsia is caused by structural or functional disease.[20–22]

It should be noted however that more recently the subgrouping of patients with functional dyspepsia according to their predominant or most bothersome symptom has been shown to be useful in predicting the response to PPI therapy,[23] and the implications of this for management are addressed in more detail below. One conclusion that can be drawn is that documentation of the patient's most bothersome symptom may prove to be of benefit in guiding treatment.

While the subgrouping of patients with uninvestigated dyspepsia according to symptom clusters is of little value in predicting underlying structural disease or in guiding initial management, this does not detract from the importance of careful clinical evaluation. As discussed above, history taking is extremely important in excluding patients with typical GORD. In addition, clinical evaluation is important in excluding irritable bowel syndrome, abdominal wall and biliary pain, and for exploring the psychosocial factors that often have a major impact on the success of management.

EARLY ENDOSCOPY

Endoscopy remains the gold standard initial approach in the management of uninvestigated dyspepsia, and is the investigation of choice compared with the barium meal. Immediate referral for endoscopy is recommended for patients with sinister or "alarm" symptoms (for example, weight loss, recurrent vomiting, bleeding, anaemia, dysphagia, jaundice, palpable mass)[12] and in older patients with a recent onset of symptoms. More controversially, it is often also recommended in patients receiving traditional NSAIDs. In addition, endoscopy may be indicated to address patient concerns about serious underlying disease. However, while early endoscopy may be theoretically desirable for all patients with dyspepsia, this is currently not practical. When endoscopy is performed, it should be conducted when symptoms are present and after a minimum of one month on no antisecretory therapy.

The age cut off for immediate endoscopy

The recommendation for endoscopy in older patients is made because of concerns over the risk of underlying malignancy with increasing age, and traditionally the age cut off for referral has been 45 years. This is because in Western countries the incidence of gastric cancer is very rare below this age but rises

rapidly in older patients.[24 25] However, this threshold should be defined locally based on the known relationship between age and the incidence of gastric cancer. It has therefore been suggested that an age cut off of 50 years may be more appropriate in Western countries while a lower threshold is advisable in areas where the age specific incidence of gastric cancer takes off at a younger age in the population, as for example in some countries in the Asia-Pacific region.[12]

NSAID users

Endoscopy is recommended in patients presenting with dyspeptic symptoms and who are taking NSAIDs regularly because of the risk of potentially life threatening ulcer complications, such as bleeding. This does not apply with the COX-2 specific NSAIDs. If endoscopy reveals an ulcer, then appropriate healing therapy should be given. Ideally, NSAID therapy should be stopped, in which case, in the absence of an ulcer, dyspeptic symptoms can be treated empirically. However, stopping NSAID therapy is often not practical, and if NSAID therapy is to be continued, then prophylactic therapy against gastroduodenal damage may have to be considered, even if endoscopy only reveals erosions or is normal. The need for prophylactic therapy should be based on the presence of risk factors for complications. The two major risk factors are a previous history of peptic ulcer disease and old age, with the risk increasing as the patient's age increases over 60 years.[26 27] Other risk factors include glucocorticosteroid intake and concomitant use of anticoagulants. If therapy is to be given, a large programme of trials in patients taking concomitant NSAID therapy has shown that proton pump inhibition is superior for both healing and prophylaxis of NSAID associated gastroduodenal damage compared with placebo, misoprostol, and ranitidine.[28–31]

Addressing patient anxiety

Endoscopy may also be indicated to address patient concerns over serious underlying disease as the procedure has been reported to provide reassurance to patients with dyspepsia.[4 32] The psychological general well being score, for example, has been shown to improve in the week following endoscopy in patients with untreated functional dyspepsia, presumably reflecting patient reassurance from the procedure.[32] The importance of assessing the extent of such patient concerns should not be underestimated. However, as discussed below, in the absence of alarm symptoms, a test and treat strategy resulting in a response may be adequate reassurance for the patient.

Early endoscopy for all

Early endoscopy reassures both the physician and the patient, enables targeted therapy of peptic ulcer disease, oesophagitis, and gastric cancer when present, and provides a positive diagnosis of functional dyspepsia. Randomised controlled trial data suggest that prompt endoscopy is associated with greater patient satisfaction than empirical therapy with a H_2 receptor antagonist.[33] Although there was no difference between the two strategies with respect to symptom improvement, the majority of patients treated empirically required subsequent endoscopy and, as discussed above, other studies have reported that dyspeptic patients are reassured following endoscopy.[4 32]

Unfortunately, endoscopy is invasive and carries a risk of complications, albeit small. It can be expensive and is often limited in availability. For these reasons, while endoscopy is recommended in elderly patients, those with alarm symptoms, and those on regular NSAIDs, it is not usually practical to recommend prompt endoscopy for all patients except in areas where endoscopy is widely available and the cost is very low.

EMPIRICAL THERAPY

Empirical therapy with antacids, antisecretory, and prokinetic agents has long been the traditional approach for most primary care physicians in the initial management of patients with uninvestigated dyspepsia. To date, antisecretory therapy has largely been with H_2 receptor antagonists. However, several large studies with omeprazole have now shown that proton pump inhibition is more effective than H_2 receptor antagonists, as well as placebo and antacid-alginate, in relieving symptoms in uninvestigated dyspepsia,[34–36] and lansoprazole has also been shown to be superior to ranitidine.[37]

Empirical therapy can be tailored to predominant symptom presentation and is cheap in those with few or no recurrences. It may be appropriate in young *H pylori* negative patients with dyspepsia, but empirical therapy of uninvestigated dyspepsia with an antisecretory agent will result in inadequate treatment of *H pylori* positive peptic ulcer disease if it is present. More often than not, empirical therapy will only serve to delay eventual investigation and it is therefore unlikely to prove cost effective in most cases. Empirical therapy has thus largely been superseded by *H pylori* test and treat strategies as initial management in uninvestigated dyspepsia. Importantly, however, as discussed later, the empirical therapies described above form the mainstay of treatment for the many patients who prove to be *H pylori* negative or who require further symptomatic treatment despite eradication of *H pylori*.

H PYLORI TEST AND TREAT

Significant numbers of patients presenting in primary care with uninvestigated dyspepsia have underlying peptic ulcer disease and this can largely be cured by eradication of *H pylori*. A number of studies have reported a significantly higher prevalence of peptic ulcer in dyspeptic patients who test positive for *H pylori* compared with those who do not,[38–41] and it is thus logical to use this approach to identify those with dyspepsia who are at a high risk of peptic ulcer disease. Consequently, there is growing support for the use of a test and treat strategy as an initial step in the management of patients with uninvestigated dyspepsia.[1 6 7 9 12]

An alternative is to test for the infection and then endoscope patients who are *H pylori* positive to identify ulcer patients and hence target therapy.[42] This has been rejected by other consensus groups because of cost, inconvenience, and impracticality although it may be of value in areas with a high incidence of gastric cancer and where endoscopy is affordable and available.[9]

A test and treat strategy will result in many infected patients who do not have peptic ulcer disease, largely those with functional dyspepsia, receiving eradication therapy. However, it has previously been pointed out that even in *H pylori* positive dyspeptic patients who do not have peptic ulcer disease, eradication of the bacterium can be viewed as preventative medicine because it is likely to reduce the risk of future gastroduodenal disease.[7]

This is an important consideration given the data from the ORCHID and OCAY studies[43 44] described elsewhere in this supplement. These studies indicate that the eradication of *H pylori* does not relieve symptoms of functional dyspepsia, at least within one year of follow up, although there are contrary data,[45 46] possibly reflecting country specific differences, or alternatively there may be small subgroups of patients who do benefit. For example, we do not know whether periods of longer than one year are required for the complete healing of gastritis and whether this has any influence on symptoms. Based on the available data however physicians should be aware that many patients with functional dyspepsia will not gain symptomatic benefit, at least in the short term, from eradication of *H pylori* infection.

Comparison with early endoscopy

Data are now available from direct comparative studies of early endoscopy and a *H pylori* test and treat strategy[47–50] (see

Moayyedi in this supplement **[see page iv47]**). The studies show that the two strategies have similar efficacy, they are largely comparable with respect to relieving patient anxiety and improvements in patient quality of life, and medical and drug costs are similar. In addition, subsequent endoscopy load is reduced by approximately two thirds by a test and treat strategy. A negative outcome of note with a test and treat strategy in the largest of these trials was a modestly lower level of patient satisfaction, largely due to *H pylori* negative patients not being offered endoscopy.[49] This may be a relevant consideration in patient management. However, the non-invasive nature of the test and treat strategy will probably make it generally preferable to endoscopy from the patient's perspective, given that it is likely to provide adequate reassurance in most cases.

Decision analyses, although somewhat artificial, generally indicate that test and treat is the most cost effective approach in uninvestigated dyspepsia.[51 52] However, relative cost effectiveness compared with early endoscopy is likely to be dependent on the local cost of the two interventions. It is also dependent on the prevalence both of *H pylori* infection in the community and of peptic ulcer in *H pylori* negative patients with dyspepsia. As the prevalence of *H pylori* and associated ulcers falls, the benefit of a test and treat strategy may also decline, and the recommendation of this approach to treatment may thus require future modification.

Data from the new studies addressed elsewhere in this supplement demonstrate that the eradication of *H pylori* does not induce or worsen GORD. However, there are still concerns that a test and treat strategy risks missing cases of Barrett's oesophagus and gastric cancer. The eradication of *H pylori* removes a risk factor for gastric cancer but gastric cancer is uncommon, at least in Western countries. By using an appropriate age threshold for endoscopy, and promptly endoscoping those with alarm symptoms, very few cases of unrecognised gastric cancer will be inappropriately treated by *H pylori* eradication,[25] particularly if follow up is performed. As discussed above, in areas with a high incidence of gastric cancer and where endoscopy is affordable and available, *H pylori* testing followed by endoscopy in positive patients may be appropriate.[9]

Testing for *H pylori* infection following eradication therapy

The question of whether to retest for *H pylori* infection following eradication therapy remains controversial. While it will confirm cure of the infection and provide reassurance, it may be viewed as unnecessary, given the high eradication rates achievable with current regimens. However, if symptoms recur after eradication, then retesting is recommended, with use of a second different eradication regimen in patients who prove to have remained *H pylori* positive.

The choice of *H pylori* test

A test and treat strategy is recommended on the basis that a suitable diagnostic test is used, which for primary care needs to be non-invasive. Use of tests of inadequate sensitivity and specificity may result in inappropriate treatment. A positive result is more likely to be a false positive in populations with a low prevalence of infection, and a negative test is more likely to be a false negative in areas with a high prevalence of infection. A high negative predictive value is also important because patients with a negative *H pylori* test need to be reassured, given that they will usually not be retested. For these reasons, the test for *H pylori* infection in primary care should be a ^{13}C urea breath test or stool test or, if not available or affordable, a locally validated serological test with a sensitivity and specificity of at least 90%.[12] Most currently available whole blood tests are unlikely to be adequate.[53–55]

Treatment of *H pylori* negative patients and patients who remain symptomatic following *H pylori* eradication therapy

Inherent in a test and treat strategy is the need for effective therapy in patients who test *H pylori* negative, and these patients can be assumed to have functional dyspepsia, given that GORD patients have been clinically excluded. Additionally, data from the ORCHID and OCAY studies indicate that a significant proportion of patients with functional dyspepsia will continue to have symptoms following successful eradication of *H pylori* and will also require effective therapy (assuming that, as discussed above, eradication of *H pylori* has been confirmed by retesting for the infection in these patients).[43 44]

The therapeutic options in patients with functional dyspepsia include antacids, H_2 receptor antagonists, PPIs, and prokinetics. Benefits have been shown over placebo for all of these agents with the exception of antacids, but analysis of the available data (see Bytzer in this supplement **[see page iv58]**) reveals that many of the studies with H_2 receptor antagonists and prokinetics are methodologically flawed, the results are often equivocal, and therefore the published results should be evaluated with caution. Despite these limitations, the available data indicate that H_2 receptor antagonists and prokinetics are probably more effective than placebo. In addition, prokinetics are currently the only agents available for dysmotility-like symptoms, underlining the need for improved therapy for this subgroup of patients.

New data from large randomised trials with omeprazole in functional dyspepsia, reviewed elsewhere in this supplement, indicate that omeprazole is effective in relieving symptoms, particularly in the subgroups of patients with predominant symptoms of ulcer-like dyspepsia.[23] Full dose omeprazole, 20 mg once daily, was necessary for the best symptom control although double dose omeprazole may not increase the benefit.[56] Moreover, follow up of patients with successful relief of symptoms over three months indicates that there is a subsequent improvement in quality of life and reduction in costs in patients who are free of symptoms at the end of the acute treatment trial.[57]

Data from studies with omeprazole indicate that a response to therapy may be of value in supporting a symptomatic diagnosis of GORD, and this may also be of value in dyspepsia and in the identification of patients with atypical GORD (see Fennerty in this supplement **[see page iv63]**). This could be of most diagnostic value in *H pylori* negative patients who are not taking NSAIDs and are therefore unlikely to have peptic ulcer disease, but this requires evaluation.

A caveat to the use of a test and treat strategy is the increasing incidence of *H pylori* negative peptic ulcer disease in patients who are not taking NSAIDs.[12] However, these ulcers are healed with PPI therapy which may need to be taken into account when deciding treatment in patients who test *H pylori* negative. This is an area that warrants further study.

MANAGEMENT RECOMMENDATIONS

Based on the above review and discussion, a decision pathway is presented here for the management of dyspepsia, divided into diagnosis, initial therapy, and long term management (fig 1). This is directed at patient management in developed Western countries. In Third World countries, and other regions with a high prevalence of *H pylori* infection and very limited access to healthcare, management needs to be modified and appropriate decision pathways have been suggested elsewhere.[9 12]

Management of dyspepsia in general practice

Careful clinical evaluation and history taking are essential in making a correct diagnosis of dyspepsia and in distinguishing it from GORD and irritable bowel syndrome. Patients above a local age cut off, those with alarm symptoms, and probably

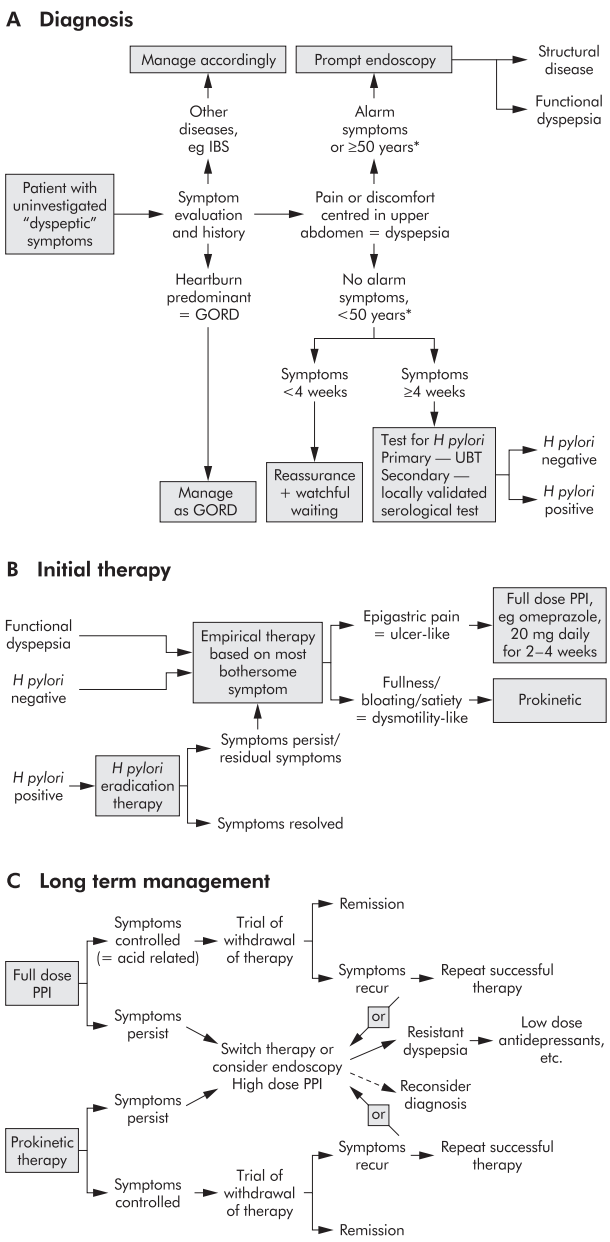

Figure 1 Recommended decision pathway for the management of dyspepsia: (A) diagnosis; (B) initial therapy; (C) long term management. *Age cut off is dependent on local incidence of gastric cancer. IBS, irritable bowel syndrome; PPI, proton pump inhibitor; UBT, urea breath test.

those on regular NSAIDs should be referred for endoscopy, which is addressed in the section below on specialist management. Patients taking NSAIDs chronically may require prophylactic therapy, which has been discussed above.

Patients without alarm symptoms who have had symptoms for less than four weeks may be managed initially with reassurance, over the counter medications, and "watchful waiting". In low risk patients who have had symptoms for four weeks or longer, a strategy of testing for *H pylori* infection and treating the infection in those who are positive is probably cost effective and safe, provided follow up of patients is organised and that an appropriate test is used. This is recommended despite the new data demonstrating that there is no clinically significant benefit in functional dyspeptics one year after *H pylori* eradication. Indeed, primary care physicians must be aware that a test and treat strategy will not reduce dyspeptic symptoms in many infected patients, including some of those who had peptic ulcer disease. Rather than be disheartened by this, physicians should take the view that they have eliminated the issue of peptic ulcer mortality, and treat the residual symptoms accordingly.

The approach to subsequent therapy in patients with residual symptoms following successful *H pylori* eradication therapy is the same as for those who originally test *H pylori* negative, and can be individualised depending on the predominant or most bothersome symptom. The new data for omeprazole in functional dyspepsia indicate that in patients in whom epigastric pain (ulcer-like dyspepsia) is the most bothersome symptom, this is likely to be acid related.[23] Indeed, such symptom classification may be of value in identifying patients who will respond to PPI therapy. The decision pathway only shows patients with epigastric pain, as patients with heartburn should, theoretically, have been identified on initial diagnosis and treated as GORD patients. However, this may often have not been the case. In addition, heartburn may only be apparent as the predominant symptom after eradication of *H pylori*.

Full dose PPI therapy, for example with omeprazole 20 mg once daily, should therefore be the first choice of therapy in patients with ulcer-like dyspepsia, and a response to therapy will confirm the acid related nature of the symptoms. This is consistent with the Genval guidelines for the treatment of symptomatic GORD, which also recommend initial firstline therapy with full dose PPI therapy.[14] In addition, full dose PPI therapy is to be recommended in *H pylori* negative patients to ensure healing of *H pylori* negative peptic ulcer. A further option is an empirical trial of high dose PPI therapy, which may confirm the acid related nature of dyspeptic symptoms, including misclassified GORD patients and patients with atypical GORD.

In patients in whom the predominant symptom is fullness, bloating, or satiety (dysmotility-like dyspepsia), a prokinetic agent is an option, although cisapride can no longer be recommended because of cardiac toxicity (see Bytzer in this supplement **[see page iv58]**).

If symptoms are controlled by an initial course of empirical therapy, a trial of withdrawal of therapy should be considered, with therapy repeated in the case of symptom recurrence. A further option is on demand therapy with the successful agent. Although data are lacking on this treatment approach in functional dyspepsia, it has been shown to be an option in the treatment of GORD.[58] In addition, the ENCORE study, described in this supplement, has shown that improvement in dyspeptic symptoms after acute treatment is followed by reduced subsequent costs and has a positive impact on quality of life over a three month period after cessation of therapy.

Given that patients who do not respond to the first choice of symptomatic therapy may have been misclassified, a switch of treatment, for example from prokinetic to PPI, should be considered. If symptoms still persist following such a switch of therapy, a course of high dose PPI therapy may need to be considered, as discussed above. Otherwise, the patient should be referred for endoscopy, or other treatment options considered, depending on the clinical setting.

Management of dyspepsia by the specialist

A minority of patients with dyspepsia may come direct to the specialist on first presentation, in which case management may be as above, with the obvious difference that early endoscopy is likely to be much more practical than in primary care. In most cases however patients will be referred from primary care. The patient's history and clinical evaluation should be reviewed to ensure that the diagnosis of functional dyspepsia is correct, and further tests should be considered. Suspected atypical GORD can be tested for with 24 hour oesophageal pH monitoring or a high dose diagnostic course of PPI therapy.

In patients referred for evaluation of dyspepsia, endoscopy is indicated, and gastric biopsies should be taken to document *H pylori* status. Structural disease identified on endoscopy can be treated appropriately. Endoscopy provides a positive diagnosis of functional dyspepsia, and patients can be treated according to their most bothersome symptom, as described above.

In patients with resistant functional dyspepsia in whom attempts at symptomatic therapy fail, the diagnosis should be re-evaluated, further reassurance given, and behavioural therapy, psychotherapy, or antidepressants considered.[59–61] In addition, the specialist may be in a position to try more recent visceral analgesic therapies.[62–65] However, the treatment of patients with resistant functional dyspepsia is not based on data from clinical trials and more work is needed in this area.

FUTURE MANAGEMENT ISSUES

The new data with omeprazole indicate that proton pump inhibition provides effective therapy for ulcer-like dyspepsia, which may also be of diagnostic value, although this needs further evaluation. However, there is a clear need for better therapies to treat dysmotility-like dyspepsia, and improved therapies may also be applied as a diagnostic tool for this subgroup of patients. This may be advanced by further work on the relationship between specific symptoms and pathophysiological disturbances, such as early satiety and impaired fundic relaxation.

The potential role of tricyclic antidepressants and selective serotonin reuptake inhibitors, as well as new visceral analgesics, in the management of dyspepsia also warrants further study. Indeed, more research is needed into functional dyspepsia that is resistant to currently available therapies.

Greater access to endoscopy at lower cost would increase the practicalities of early endoscopy in more patients. This may happen with the advent of unsedated transnasal or peroral outpatient endoscopy with small calibre endoscopes[66] although it remains to be seen whether minimal sedation is practical in the primary care setting. High resolution high magnification video endoscopes with chromoscopy will be available in the future, and autofluorescence technology will advance the early detection of dysplasias and malignancies although the cost of such new technologies may be a limitation. In parallel with the potential for cheaper and easier endoscopy, the benefits of test and treat strategies also need to be kept under review in light of the falling prevalence of *H pylori* and associated ulcers in Western countries.

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