DYSPEPSIA MANAGEMENT GUIDELINES

PREFACE

Dyspepsia is a common complaint. Treatments are very effective and investigations sophisticated. More is spent on drugs for dyspepsia than any other treatment for a symptom group. Rational management poses a challenge to those responsible for purchasing, promoting and providing health care.

These guidelines have been compiled on behalf of the British Society of Gastroenterology following consultation with the Primary Care Society of Gastroenterology. The principal objective is to describe good clinical practice for clinicians in primary and secondary care drawing on evidence where it exists and recognising the need to use limited resources effectively. An additional aim is to identify areas where evidence is sparse and where further research is necessary. Purchasers of health care should be interested in both aspects when drafting contracts for service.

INTRODUCTION:

What is Dyspepsia?

Dyspepsia is a group of symptoms which alerts doctors to consider disease of the upper GI tract. It is not a diagnosis and includes symptoms of upper abdominal discomfort, retrosternal pain, anorexia, nausea, vomiting, bloating, fullness, early satiety and heartburn amongst others. A firm clinical diagnosis can be difficult on the basis of these symptoms as few symptoms are discriminatory. Many diseases cause dyspepsia and these include peptic ulcers, oesophagitis, cancer of the stomach or pancreas, and gallstones. In a large proportion of cases no clear pathological cause for a patient’s symptoms can be determined.

Frequency

Dyspepsia is common. Surveys in Western societies have recorded prevalences of between 23 and 41%. For many people dyspeptic symptoms are an acceptable part of living. Why some sufferers (about 25%) seek help from doctors is not clear but concern about symptoms seems to be as important as the symptoms themselves. The minority of sufferers (5% of the population) who do consult are major consumers of resource. In the UK in 1994 more than 400 million pounds was spent on “ ulcer healing” drug prescriptions issued by general practitioners. About 4% of general practice consultations are for dyspepsia and 2% of the entire population receive either an endoscopy or barium meal each year. Time lost from work and interference with quality of life are more difficult to measure but are likely to be considerable.

Only 10% of patients attending their general practitioner with dyspepsia will be referred for hospital consultation or investigation. Universal investigation for dyspepsia is neither desirable nor affordable; thus guidelines for management would be unrealistic if they advised no selection for referral.

COMMON CAUSES OF DYSPEPSIA:

The common diagnoses made at endoscopy in all age groups are:

<table>
<thead>
<tr>
<th>Condition</th>
<th>%</th>
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<tbody>
<tr>
<td>Duodenal ulcer*</td>
<td>10–15</td>
</tr>
<tr>
<td>Gastric ulcer*</td>
<td>5–10</td>
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<tr>
<td>Gastric cancer*</td>
<td>2</td>
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<tr>
<td>Oesophagitis</td>
<td>10–17</td>
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<tr>
<td>Gastritis*, duodenitis*</td>
<td></td>
</tr>
<tr>
<td>and hiatus hernia</td>
<td>30</td>
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<tr>
<td>Normal</td>
<td>30</td>
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*These conditions are strongly associated with Helicobacter pylori infection.
HELIcobacter pylori

This organism lives on the lining of the stomach and is associated with a number of diseases. It is unclear whether it actually causes all the diseases but some are best treated by eradicating this infection.

Testing for Helicobacter pylori

Helicobacter pylori infection can be diagnosed by demonstrating antibodies to the organism in serum, by showing urease activity in the stomach using breath tests, or by analysis of biopsies. Serological methods are simple, non-invasive, and widely available but are not useful in demonstrating successful eradication. Carbon tagged breath tests, which depend upon the principle of urease degradation of urea to produce tagged carbon dioxide which then appears in exhaled breath, are of intermediate cost but are non-invasive. Two methods are commonly used with either $^{14}$C (a tiny radioactive dose, but cheap) or $^{13}$C (a stable, non-radioactive dose but more expensive) labelled urea. The major use for these tests is to confirm successful eradication but they must be performed when patients are not taking proton pump inhibitors, bismuth, or within 4 weeks of antibiotic use. All other methods of identifying Helicobacter involve endoscopy and biopsy and are therefore expensive. Simple biopsy urease tests are a small additional cost to that of endoscopy. Histology, or culture of the organism add significantly to costs.

INVESTIGATION AND DIAGNOSIS

The number of patients with dyspepsia attending general practitioners is believed to exceed the availability of diagnostic procedures. There are approximately 30 attendances per 1000 in general practice amounting to about 210 consultations per GP per annum. Endoscopy is safe but is not totally risk-free. Death from diagnostic endoscopy is reported in the range of 1 in 2,000 - 10,000. In out-patient practice the rate is likely to be even lower. Mechanisms to identify only those patients who may benefit from the procedure and exclude those who would not are worthwhile.

Rationalising the use of endoscopy.

It has been suggested that an age threshold of 45 years is a practical means of limiting endoscopy. This is based on the fact that gastric malignancy is rare below this age. Future guideline revisions may raise or lower this age cut-off if epidemiological data demonstrate temporal changes. Data from the Yorkshire Cancer Registry indicate that less than 3% of the gastric cancer registered occurs in patients under 45, in 1988 representing only 19 cases. Many symptoms of gastric cancer are characteristic and alert clinicians to this possible diagnosis. Indeed the vast majority of patients with gastric cancer present with such symptoms. Thus if endoscopy in people <45y were limited to those with alarm symptoms very few cancers would be “missed”. However, concern about gastric cancer is not the main reason for investigation of dyspepsia in young people. There is evidence that subsequent therapeutic decisions and consulting behaviour change in those investigated even when major diagnoses are absent.

A method of identifying most young patients at risk of gastric neoplasia and peptic ulcer is by testing for evidence of Helicobacter infection. Using modern serological assays and restricting endoscopy in patients under 45 with uncomplicated troublesome dyspepsia to those with evidence of infection has been shown to identify most peptic ulcer disease. The majority of young patients with gastric cancer are seropositive for Helicobacter, so these cases too would be diagnosed, even in the rare absence of alarm symptoms. The major diagnoses that would be missed by such a process are oesophagitis and Barretts oesophagus (columnar lined oesophagus). However, these conditions are best treated with therapy directed at symptom control because treatment directed at healing does not prevent complications or decrease the
recognised additional risk of oesophageal adenocarcinoma. In many cases gastro-oesophageal reflux does not cause erosive oesophagitis and a clinical diagnosis is often the best indication for treatment. In many cases gastro-oesophageal reflux is a long-term problem and some argue that endoscopy should be performed before instigating long-term acid suppressive therapy. Further data are required in this area but endoscopy decreases prescribing costs, consultation rates and leads to management changes even in patients in whom no significant disease is found. The assumption is that the procedure provides reassurance to patients and doctors allowing more rational prescribing. Similar benefits have been reported following negative Helicobacter pylori serology without endoscopy in those in whom endoscopy would otherwise have been performed. We commend this practice as a means of decreasing endoscopy. H pylori serology should be tested in dyspeptics under 45 whose symptoms are troublesome enough to be referred for endoscopy and who do not fall into the remaining categories listed below. Our recommendation here is based on early and limited data and full consensus has not been achieved. It requires the use and availability of an accurate serological assay whose sensitivity is high in the local population. Future guidelines will re-assess this recommendation.

GUIDELINES
The guidelines which follow combine the assumption of a requirement to protect resources, limit unnecessary risk and provide high quality care. Where strong evidence to support them is lacking consensus has been used.

1. INVESTIGATION
Waiting times for investigation should not exceed four weeks and ideally investigations should be available within two weeks. The best investigation for uncomplicated

A. Patients with dyspepsia in whom diagnostic endoscopy is appropriate.
1. Any dyspeptic patient with alarm symptoms or signs:
   Unintentional weight loss,
   Iron deficiency anaemia,
   Gastro-intestinal bleeding,
   Dysphagia* and odynophagia,
   Previous gastric surgery,
   Persistent vomiting,
   Epigastric mass,
   Suspicious barium meal,
   Previous gastric ulcer, NSAID use,
   Epigastric pain severe enough to hospitalise patient.
* A barium swallow should be considered as the first investigation in dysphagia.

2. Any patient over the age of 45 with recent onset dyspepsia.

3. Patients under the age of 45 with troublesome dyspepsia who are positive for Helicobacter Pylori on non-invasive testing.

B. Patients with dyspepsia in whom endoscopy is inappropriate.
1. Patients known to have duodenal ulcer who have responded symptomatically to treatment.

2. Patients under 45 asymptomatic after a single episode of dyspepsia.

3. Patients who have recently undergone a satisfactory endoscopy for the same symptoms.
dyspepsia is endoscopy. Double contrast barium radiology may be equally accurate, but does not allow for biopsies to be taken and is thus considered second best. At endoscopy, biopsy urease tests should be performed in all patients with ulcer in whom the H pylori status is not already known. Further assessment to identify NSAID and aspirin use, Crohns, lymphoma and other unusual causes of ulceration is necessary in such patients without evidence of H pylori.

TREATMENT BEFORE INVESTIGATION
It is acceptable to institute a single course of treatment with an anti-secretory agent for 2-4 weeks in patients under 45 with troublesome symptoms but without alarm symptoms. While this first empiric course of treatment is attempted it is recommended that blood is sent for Helicobacter pylori testing. Endoscopy is not recommended in such patients without evidence of H pylori and then should only be undertaken if the patient continues to be symptomatic.

Patients over 45 years of age with first onset dyspepsia should undergo investigation and if this cannot be provided promptly a 2-4 week treatment period before investigation may be acceptable.

TREATMENT

**MAJOR DIAGNOSES**

We recommend treatment of Helicobacter infection only for duodenal and gastric ulcer in line with consensus recommendations from other countries. Some authorities suggest treatment of Helicobacter pylori in all infected dyspeptics. At this time a consensus believes that there is insufficient evidence to justify this approach while accepting that future revisions could change these recommendations should evidence become clearer.

**DUODENAL ULCER**

*HP+ve duodenal ulcer:* 95% are associated with Helicobacter pylori and should receive treatment directed against this organism. We advise confirmation of Helicobacter infection by serology or urease testing before treatment, but accept that the prevalence of H pylori infection is so high that this may be considered unnecessary. We recognise that the best eradication regimen is not yet known but the present “best buy” regimens include:

**One week Triple Therapy:**

- Omeprazole 20mg BD (or lansoprazole 30mg BD), amoxycillin 500mg tds, metronidazole 400mg tds. Eradication rates 84 - 90%, well tolerated. (£20.12*)
- Omeprazole 20mg bd (or lansoprazole 30mg BD), clarithromycin 500mg bd, tinidazole 500mg bd (or metronidazole 400mg bd). Eradication rate around 90%, well tolerated. (£37.02*)
- Omeprazole 20mg bd (or lansoprazole 30mg bd), amoxycillin 1g bd and clarithromycin 500mg bd. Eradication rate around 90%, well tolerated. (£42 approx).

**Traditional Two Week Triple Therapy:**

- Oxytetracycline 500mg qds, metronidazole 400mg tds, tripotassium dicitrato bismuthate (bismuth chelate) 1 qds for 2 weeks. Eradication rate around 90%, poorly tolerated. (£18.11*)
- Dual therapies with a proton pump inhibitor plus either amoxycillin or clarithromycin or with ranitidine bismuth citrate plus clarithromycin while licensed for Helicobacter therapy are not more effective than the regimens above and are considerably more expensive. We do not recommend them.

**Follow-up:**

Asymptomatic patients
Repeat endoscopy is not needed. A urea breath test (ideally ¹³C) should be per-
DYSPEPSIA

<45y

NO ALARM SYMPTOMS OR SIGNS

H PYLORI SEROLOGY BY ELISA EMPIRICAL TREATMENT WITH ANTI SECRETORY AGENT

-VE

see treatment guidelines

+VE

ASYMPTOMATIC

WAIT TILL SYMPTOMATIC

>45y

ALARM SYMPTOMS OR SIGNS

SYMPTOMATIC

ENDOSCOPY
formed in all patients (one month or longer after the end of H pylori eradication treatment) if symptoms persist or recur. A urea breath test is also required in any patient whose ulcer had presented with complications and who would otherwise be given long-term anti-secretory treatment to prevent recurrence. If the result of the breath test is negative we recommend no further treatment. If the result is positive a second course of eradication therapy should be prescribed.

Symptomatic after initial symptom response
A urea breath test is indicated. If negative clinical re-evaluation is necessary and if positive repeat anti-helicobacter treatment.

HP-ve Duodenal Ulcer:
Antisecretory therapy; cimetidine 800mg noce is cheapest. Gastroenterological referral is advised if ulcers are not associated with NSAID. NSAID should be stopped if possible and if symptoms persist patients may need gastroenterological review. Long term treatment with antisecretory drugs or misoprostol should be considered in patients who cannot stop the NSAID.

2. EROSIVE DUODENITIS:
In the absence of alternative evidence we consider erosive duodenitis to be part of the spectrum of duodenal ulcer and advise treatment as in this condition.

3. GASTRIC ULCER
Helicobacter is present in about 70% and most of the remainder are associated with NSAIDs. Cytological smears and biopsies for histology should be taken and a urease test should be performed at endoscopy.

HP+ve Gastric ulcer:
Anti Helicobacter therapy as for duodenal ulcer followed by antisecretory therapy for two months. The reason for this latter recommendation is the lack of evidence that gastric ulcers heal as quickly after Helicobacter eradication alone. This recommendation would change if such evidence became available. Long term treatment with misoprostol should be considered in patients with proven ulcer who have to take NSAIDs.

HP-ve Gastric Ulcer:
Standard antisecretory therapy for two months. NSAIDs should be stopped if possible. Omeprazole 20mg daily is more effective than H2 antagonist if NSAID is continued. Long term treatment with misoprostol should be considered in patients with proven ulcer who can not stop the NSAID.

Follow-up of all cases of gastric ulcer:
Repeat endoscopy with biopsies is essential until complete epithelialisation. If ulcer remains unhealed for six months then surgery should be considered.

4. OESOPHAGITIS:
H pylori infection is no more likely to be associated with this condition than in the normal population. Patients should be informed of the association with obesity and heartburn. Weight loss is believed to be effective treatment in some though evidence is anecdotal. Propping up the head of the bed has been shown to be beneficial and patients should be given advice to avoid things which provoke symptoms amongst which bending, alcohol and fatty foods are prominent.

Treatment should provide symptom relief. 4 weeks is a reasonable starting course. Best relief is provided by proton pump inhibitors (omeprazole 20mg or lansoprazole 30mg) but many patients obtain adequate symptom control from antacids, raft preparations, H2 antagonists or prokinetic agents such as cisapride. Whatever therapy is chosen an attempt should always be made to titrate to the agent which provides symptomatic relief at the lowest cost with least influence on normal physiology.
**Follow-up:**
Repeated endoscopy is not justifiable except to check for healing of oesophageal ulcers, dilatation of strictures or when anaemia which is believed to be secondary to oesophagitis fails to resolve on treatment. The impact of endoscopic surveillance on the long term management and outcome of Barrett’s oesophagus remains to be determined. Some patients may need longer term treatment to maintain symptom relief. However, such prescriptions should be reviewed and attempts to titrate to simpler remedies should be made regularly.

5. MINOR ABNORMALITIES

**Non Erosive “Duodenitis” and “Gastritis”**
These conditions are often recorded following endoscopy but the correlation of endoscopic finding with either symptoms, or histological abnormality is poor. We do not recommend specific therapy in these conditions irrespective of Helicobacter pylori status. Symptomatic remedies can be tried until evidence suggests alternative specific treatments. Expensive anti-secretory treatment cannot be justified if cheaper alternatives work.

**No macroscopic mucosal abnormality [non-ulcer dyspepsia], non erosive reflux, hiatus hernia:**
The cause of symptoms in these patients, who account for a large proportion of those investigated, is usually unclear. It is likely that there are multiple factors involved including defective motility, H pylori infection and depression. Treatment is symptomatic but often ineffective. Research in this area has been hampered by poor definitions and the multifactorial nature of the problems. Thus the recommendations below are based on consensus.

a) Stop NSAIDs if possible and consider other drugs as provoking agents.
b) General reassurance may be sufficient.
c) Assess if symptoms are acid related by giving a short course (maximum 2 weeks) of a proton pump inhibitor in adequate dose (omeprazole 40mg or lansoprazole 30mg) then titrate to cheaper alternatives to complete a 4-6 week course if initial response good. If no initial response consider cisapride.
d) Evidence to support Helicobacter eradication in this group is conflicting. We do not recommend eradication therapy outside clinical therapeutic trials.
e) Investigation of the biliary tree by ultrasound should be considered.
f) Repeat investigations if serious symptoms develop (see table 1).

**POINTS FOR PURCHASERS**

**Resource Requirements**
1. General practitioners should have easy access to 13C Urea breath testing, and Helicobacter serology.
2. Easy and rapid access to endoscopy is a requirement for good practice and endoscopy units should be able to provide histology, urease testing and 13C breath tests.

Resources for the provision of this level of service should be available nationwide.

3. In some laboratories the facilities needed for full bacteriological assessment of Helicobacter sensitivity and resistance should be provided. One in each major city could provide a nationwide service.

**CONTROVERSY: THE NEED FOR FURTHER RESEARCH.**
These guidelines attempt to promote pragmatic managements based on existing evidence or consensus when evidence is lacking. Many clinical practices which are believed to be beneficial (financially and clinically) are presently empirical and are not based on sound evidence.
These include:

A. Serological screening of asymptomatic patients in an attempt to prevent gastric cancer.

B. Treating all infected symptomatic patients irrespective of diagnosis in an attempt to reduce prescribing and consultation costs.

C. Selective serological screening or Helicobacter eradication in patients on long-term anti-secretory agents.

There is a belief that such practices will reduce costs and provide clinical benefit. The frequency of significant side-effects, and of failure-related consultation is not known from general usage. If either of these is important such practices may increase costs. Clinical benefit is yet to be convincingly demonstrated. We have therefore adopted the stance of recommending practices for which convincing (albeit limited) evidence exists while awaiting other evidence. The guidance will be updated where appropriate as evidence accrues. In the meantime it is impossible to be prescriptive for large areas of dyspepsia management. Purchasers of healthcare research need to be aware of the deficiencies in our knowledge base and are advised to support research which will fill such gaps.

AUTHORSHIP

This guideline was prepared by members of the British Society of Gastroenterology, with valuable assistance from Dr R. Stevens, Primary Care Society for Gastroenterology, and approved by Council.

We plan that this guideline will be revised from time to time. Comments or suggestions for use in subsequent editions should be sent to: The Clinical Services and Standards Committee, British Society of Gastroenterology, 3 St Andrews Place, Regent’s Park, London NW1 4LB.

REFERENCES:

ADDENDUM

THE ROLE OF DOUBLE CONTRAST BARIUM MEALS

The preceding guidelines focused on the role of endoscopy and *H pylori* in the management of patients with dyspepsia. The role of the double contrast barium meal (DCBM) was not evaluated in these guidelines. The BSG does not wish the constraints placed upon the development of the guidelines as dismissing the role of the DCBM, which still has a very important part to play in the imaging of upper gastrointestinal disorders. DCBM and endoscopy are complimentary in nature rather than simple alternatives.

There are several obvious situations where the DCBM will be required, such as in dysphagia, motility disorders (particularly of the oesophagus), where endoscopy has failed and patient preference. Although DCBM does not demonstrate early mucosal inflammation well, it carries a high sensitivity for the diagnosis of carcinoma. It has particular strengths in the diagnosis of minor strictures, motility disorders, extrinsic and possible intramural abnormalities, as well as the diagnosis of malrotations, herniations and other structural abnormalities. In most centres the DCBM brings an economical advantage even with a small referral rate for subsequent endoscopy. In contrast to some endoscopic examinations, no sedation is required and the patients can return directly to the work place. Although barium radiology involves exposure to radiation, it does not carry the small, but significant morbidity and mortality of endoscopy. As with endoscopy or indeed any other subjective test the quality of the DCBM is very dependent upon the skill and experience of the operator.

The DCBM is therefore a reasonable alternative to endoscopy as the first line investigation of dyspepsia, and practice should depend on local expertise and availability. The indications would be the same as recommended for endoscopy in this document (NB: the DCBM does not provide a facility for biopsy). DCBM is preferable in patients with a contra-indication to endoscopy, patients with dysphagia in addition to dyspeptic symptoms, and patients in whom structural abnormalities are suspected. Endoscopy is to be preferred in patients with previous gastric surgery and where biopsy might be anticipated, such as for suspected malignancy and gastric ulcers. Any mass or stricture diagnosed on DCBM would require subsequent endoscopy for biopsy confirmation of its nature. Further research is required to define the role of the DCBM in the outpatient population, particularly in relation to non-invasive testing of *H pylori* status. At present the DCBM provides a complimentary and often appropriate supplementary or alternative examination in the management of dyspepsia and has a continuing role in the investigation of upper gastrointestinal disease.