

Managing heartburn, undifferentiated dyspepsia and functional dyspepsia in general practice

Heartburn, undifferentiated dyspepsia and functional dyspepsia are common. Management requires an individually tailored combination of lifestyle modification and drug treatment.

Key Adviser
Professor Gil Barbezat



Dyspepsia is a range of symptoms which may indicate significant organic disease but most people with dyspepsia have no underlying pathology and do not seek medical advice

Heartburn is a burning sensation rising from the epigastrium toward the neck.

Dyspepsia is pain or discomfort located in the epigastrium. Associated symptoms may include fullness after meals, bloating, belching, early satiety, anorexia, nausea and vomiting. The symptoms of dyspepsia may be episodic, recurrent or chronic and whilst many symptoms are associated with food this is not always the case.

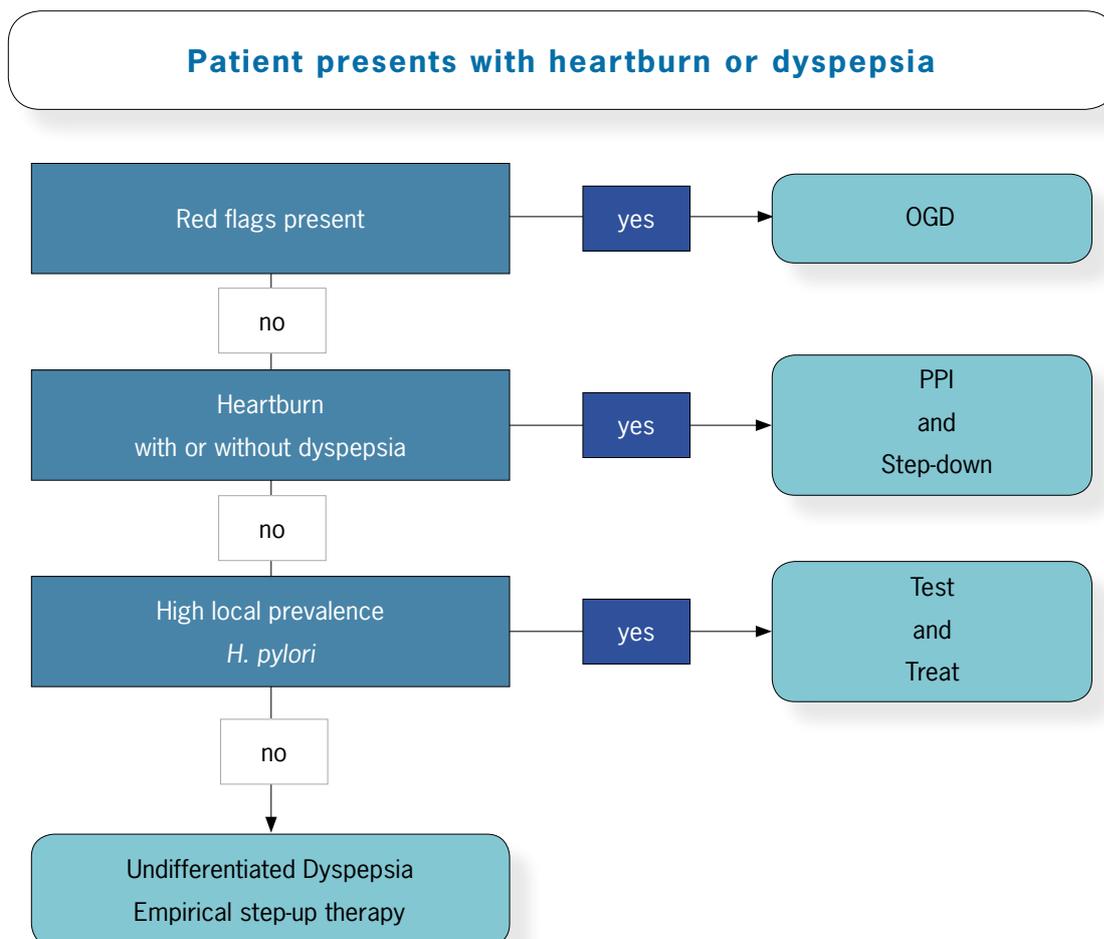
Undifferentiated dyspepsia is dyspepsia that has not been investigated. In a person at low risk of underlying pathology this can be managed empirically without further investigation.

Functional dyspepsia is dyspepsia, which has been investigated and no underlying pathology found.

The management of dyspepsia associated with underlying pathology, e.g peptic ulceration or use of NSAIDs is not discussed in this article.

Key Points

- Red flags are indications for oesophago-gastro-duodenoscopy (OGD)
- People with heartburn or undifferentiated or functional dyspepsia often benefit from modification of lifestyle and drug therapies
- If heartburn is part of the symptom complex, treat initially as gastro-oesophageal reflux disease (GORD) with a proton pump inhibitor (PPI) and step down therapy
- If drug treatment for undifferentiated or functional dyspepsia without heartburn is required an H₂-receptor antagonist (H2RA) is the drug of choice
- In areas of moderate to high prevalence of *H. pylori* consider the need for a test and treat approach
- After the initial control of symptoms encourage people to step down to the lowest effective dose and/or treat symptoms intermittently 'on-demand'
- Review your patients with chronic dyspepsia annually for the appearance of alarm signals and use of aggravating drugs
- Review all patients for on-going requirement for pharmacotherapy, especially PPIs



First check for red flags of significant organic disease

A number of features in the initial history or examination of people with dyspepsia or heartburn increase the likelihood of significant organic disease. These red flags are detailed in Table 1. Red flags are indications for further investigation with OGD. In some cases, such as bleeding or severe dysphagia, this needs to be done immediately.

When there is less urgency, people need to be off PPIs or H2RAs for two weeks prior to OGD as these can mask signs of organic disease. Antacids may be continued.

Table 1: Red Flags

(Adapted from NZGG and Prodigy Guidance^{1,2})

The following increase the likelihood of significant organic disease:

- | | |
|---|---|
| - Aged 50–55 years or older at first presentation | - Chronic gastrointestinal bleeding |
| - Aged 40–45 years or older at first presentation for people of Māori, Pacific Island or Asian descent* | - Unexplained weight loss |
| - Family history of gastric cancer with onset age <50 years | - Difficulty in swallowing |
| - Severe or persistent dyspepsia | - Persistent or protracted vomiting |
| - Previous peptic ulcer disease, particularly if complicated | - Iron deficiency anaemia |
| - Ingestion of NSAIDs including aspirin (check OTC use) particularly those at increased risk | - Palpable abdominal mass |
| | - Coughing spells or nocturnal aspiration |
- *Gastric cancer tends to occur a decade earlier in these people

recognise

For some a PPI is critical, while for others more cost effective options can be introduced as part of treatment review.

Heartburn with or without dyspepsia is usually caused by GORD and step-down PPI therapy is indicated

In the absence of red flags the presence of heartburn with or without dyspepsia is the single most important feature determining management.

Heartburn with or without dyspepsia is usually related to lower esophageal dysfunction and the presence of GORD. This often follows a large meal or is related to obesity; people with a BMI of 25 or above are at much greater risk of getting GORD. Heartburn needs to be differentiated from other causes of similar symptoms such as cardiac disease.

GORD is appropriately managed empirically by lifestyle measures (Table 2) with or without a step down drug regimen. The following step down programme usually in 4–8 week steps is appropriate for most patients (adapted from NZGG, 2004).¹

Step 1 Full-dose PPI (omeprazole 20 mg or lansoprazole 30 mg daily)

Step 2 Half-dose PPI

Step 3 H2RA (famotidine 20–40 mg, ranitidine 150–300 mg twice daily)

Step 4 antacids/alginate

If there is no response to full dose PPI after three months double the dose. Trial this for 3–6 months and review. If the person fails to respond, or if symptoms recur within one month after the end of treatment, consider OGD rather than long-term empiric treatment.

Table 2: GORD is appropriately managed empirically by lifestyle measures

Heartburn or dyspepsia is often due to or worsened by lifestyle factors. Modification of these factors may reduce or resolve symptoms without the need for drug treatment or allow the use of lower drug doses or intermittent therapy when symptoms worsen.

- Offer simple lifestyle advice; including healthy eating, weight reduction, smoking cessation and limiting alcohol intake.
- Advise avoidance of trigger factors if these are known to aggravate symptoms. These may include, bending, alcohol, chocolate, spicy food, fatty food and smoking.
- If people have reflux symptoms, weight control, eating smaller meals, avoiding fat and not eating before going to bed are often helpful.

(Adapted from Prodigy Guidance)²

People with heartburn can often step-down to intermittent therapy taken either in response to heartburn or when lifestyle indiscretions make it likely. Up to 20% can stop medication without recurrence of symptoms.

Dyspepsia without heartburn

How common is dyspepsia?

Dyspepsia is extremely common with a prevalence of 23–41 % in OECD countries. Most people with dyspepsia do not seek advice about it from their GPs and often accept symptoms as part of their lifestyle and dietary habits. This explains the widespread availability and purchase of over the counter (OTC) antacids, H2RAs (e.g. ranitidine) and PPIs in some countries.

It has been estimated that only 25% of people with symptoms of dyspepsia actually seek medical advice³ but because it is so common dyspepsia accounts for between 2% and 7% of visits to GPs.

Who gets dyspepsia?

Dyspepsia can occur at any age but in older people it is more likely to be associated with organic diseases such as peptic ulcer or gastric cancer. NSAIDs are a major cause of dyspepsia and peptic ulcer and are more frequently prescribed in people over 65, who are more susceptible to complications. It should be noted that low dose aspirin is associated with dyspepsia and increased risk of peptic ulceration.

There are no accurate figures linking the prevalence of dyspepsia with ethnicity in New Zealand. However, *H. pylori* infection which is associated with peptic ulceration is more common among Māori and Pacific Island people.

Initial management of undifferentiated dyspepsia without heartburn

(Adapted from NZGG, 2004)¹

When a person with dyspepsia presents for the first time there are two important issues to consider:

- Is there a significant underlying pathology?
and
- Why has the person decided to present with the problem at this time?

A reasonable approach is to:

- If there are red flags (Table 1), refer to a specialist for OGD
- Review lifestyle factors (Table 2)
- Review use of antacids and H2RAs as this may guide drug treatment if this is necessary
- Review intake of other medicines, including OTC, especially NSAIDs but also calcium antagonists, corticosteroids, nitrates, bisphosphonates and theophylline
- In areas with high prevalence of *H. pylori*, test for *H. pylori*
- If *H. pylori* testing is not indicated or is negative treat as undifferentiated dyspepsia
- If there is no response to initial treatment after a reasonable trial period of 4–12 weeks refer for OGD

review

If you are initiating therapy for new patients or if you are reviewing patients who suffer from dyspepsia, Gutreaction resources could be helpful.

Test and treat for *H. pylori* in areas of high prevalence

If a person has no red flags but there is a high (> 30%) local prevalence of *H. pylori* it is worth testing for *H. pylori*.

The best tests for this are the *H. pylori* faecal antigen and the breath test. Both are available in NZ but the faecal antigen test is a lot cheaper, funded and more readily available. Patients should be off PPIs for two weeks before both of these tests. The sensitivity and specificity of both tests (about 95%) is very much better than serology. In clinical use, serology has a sensitivity and specificity ranging from 68–80%, although in some research studies can reach the 90–95% level.

The quality of serology depends on the matching of the local *H. pylori* with the commercial kit used for the assay and very few are actually validated for local consumption. Although serology is cheap and convenient it is no longer regarded as the test of choice.

People, for whom *H. pylori* testing is either not indicated or is negative, can be treated empirically as undifferentiated dyspepsia, as long as they have no red flags.

For undifferentiated dyspepsia step up therapy until symptoms are controlled and then step down or treat intermittently

The use of antacids, alginates and over the counter H2RAs are effective for many people with intermittent mild symptoms of dyspepsia. However many people do not seek medical advice and become chronic users of OTC antacids and H2RAs. Many of these people will benefit from advice on lifestyle modification or a trial of full dose drug therapy.

The preferred drug treatment for undifferentiated dyspepsia is contentious due to inconsistent study design and interpretation of the literature. A vast majority of clinical trials show a placebo response of about 40%, and some even higher⁴, making any effects of drug treatment difficult to measure.

Another major problem is that many studies do not differentiate between two distinct patient groups, those with heartburn with or without dyspepsia, and those with dyspepsia alone. This is important, as heartburn is predominantly due to reflux of acid into the oesophagus, but dyspepsia without heartburn is often related to reduced GI motility and other factors. This distinction significantly affects the success of the various drug treatments available and has failed to be taken into account in some international guidelines.

Overall, prokinetics appear to be the most effective drugs for functional dyspepsia. This supports the theory that this condition is most often due to a motility disorder rather than over-secretion of acid. The two main prokinetics used in clinical trials were cisapride and domperidone. Cisapride is no longer available and there have been recent concerns about cardiotoxicity associated with domperidone. There is insufficient evidence to support the widespread use of metoclopramide for functional dyspepsia and there is a risk of extrapyramidal effects with this drug.

In practice, drug choice is usually between a PPI and an H2RA because of the adverse effects of prokinetics.

NNT for drugs used in management of dyspepsia without heartburn:

- **Prokinetics (domperidone): NNT = 2.8**
- **H2RAs: NNT = 5.9**
- **PPIs: NNT = 11.1**

These figures are based on a Cochrane review in which people presenting primarily with heartburn were excluded.⁵ The most recent Cochrane Review⁴ did not find any conclusive evidence of superiority of either agent in the treatment of functional dyspepsia and the authors concluded that H2RAs might still be the drugs of choice in this condition on the grounds of cost.

The standard doses of H2RAs are famotidine 20 mg BD and ranitidine 150 mg BD. These doses can be doubled for severe disease.

If H2RAs do not control symptoms it is appropriate to step-up to PPIs until symptoms are under control and then to step-down again.

Functional dyspepsia is managed as for undifferentiated dyspepsia

Functional dyspepsia accounts for 45% of dyspepsia diagnosis on OGD

Functional dyspepsia is the most common diagnosis after OGD accounting for approximately 45% of cases. It refers to people with symptoms and a normal OGD (i.e. exclusion of peptic ulcer, oesophagitis and malignancy).

Other diagnoses include; oesophagitis 29%; duodenitis 3%; gastric ulcer 4–9%; duodenal ulcer 6–9%; cancer of stomach or oesophagus 0.3–2%. Erosive duodenitis and gastric erosions are considered to be part of the spectrum of peptic ulcer disease.

The role of hyperacidity in functional dyspepsia?

Although antisecretory drugs are used extensively in the treatment of functional dyspepsia, there is little evidence that excess acid secretion is involved in the aetiology of this condition.⁴ The cause of functional dyspepsia is multifactorial so acid suppression with PPIs or H2RAs is not always helpful in treatment. The reason why antisecretory drugs are sometimes effective is not clearly understood but it may in part relate to the fact that a significant number of people have acid reflux symptoms associated with their dyspepsia.

Management of Functional Dyspepsia without heartburn (adapted from NZGG, 2004)¹

It is important to provide reassurance that there is no underlying organic pathology. Encourage lifestyle changes such as diet, weight control, smoking cessation and alcohol moderation and manage in the same way as undifferentiated dyspepsia.



reduce

Gutreaction resources are designed to provide support to practices. They include a patient and practice toolkits.

DO YOU PRESCRIBE PAROXETINE?

The brand of subsidised paroxetine hydrochloride 20 mg tablets is changing from Aropax to Loxamine.

Timelines for this change are as follows:

- From April 1 2007 Loxamine will be available fully subsidised without the need for endorsement and Aropax will be available fully subsidised by endorsement (as it is now)
- From June 1 2007 the endorsement for full subsidy for Aropax will be removed and patients may have to pay a part-charge
- From September 1 2007 Loxamine will remain fully subsidised and Aropax will be delisted from the Pharmaceutical Schedule

Bpac has developed an education programme to support this brand change.

The resources available include information on the bioequivalence of Loxamine and Aropax, the latest research on patients perceptions of brand changing and generic drugs, practical advice for counselling patients and patient information.

To access these resources follow the link on the bpac home page

www.bpac.org.nz

Table 3: Summary of empiric drug treatment

Heartburn with or without dyspepsia

- Start with PPI and step-down and/or revert to intermittent use

Undifferentiated or functional dyspepsia but no heartburn

- If OTC antacids, alginates or H2RAs have been used prior to consultation, check these have been taken regularly and at full dose. If not, regular full dose treatment in combination with lifestyle modification, may be effective
- In areas of high prevalence for *H. pylori* test and treat
- Otherwise step-up therapy until symptoms under control
- When symptoms are under control step-down therapy to the lowest effective dose and/or intermittent use. This applies to H2RAs and PPIs
- If previous dyspepsia symptoms recur one– six months after stopping treatment, re-evaluate the person for red flags, taking in to account timing of relapse and severity of symptoms
- If previous dyspepsia symptoms recur after six months with no red flags, repeat empiric therapy

Review and reduce

- Review patients who have been taking acid suppression (PPI or H2RA) treatment for more than six weeks
- Check for lifestyle factors such as stress or drugs such as NSAIDs which may be contributing to the problem
- Reduce the dose of PPI or H2RA and assess symptom response. Some patients may only require intermittent treatment when they have symptoms and in this case an H2RA may give more rapid relief than a PPI
- Up to 20% of patients can stop therapy with recurrence of symptoms but need to be warned that stopping PPIs may lead to transient recurrence of symptoms. Slow withdrawal may be better

References

1. NZGG. New Zealand Guidelines Group Dyspepsia Guidelines, 2004
2. Prodigy Guidance. Dyspepsia – Proven non ulcer dyspepsia (July 2005) <http://snipurl.com/1cee7>
3. Jones R, Lydeard S. Prevalance of dyspepsia in the community. BMJ 1989;298:30-2
4. Moayyedi P, Soo S, Deeks J, Delaney B, Innes M, Forman D. Pharmacological interventions for non-ulcer dyspepsia. Cochrane Database of Systematic Reviews: 2006 Issue 4 John Wiley & Sons, Ltd Chichester, UK DOI: 0.1002/14651858.CD001960.pub3
5. Soo S, Moayyedi P, Deeks J et al. Pharmacological interventions for non-ulcer dyspepsia. The Cochrane Library, Issue 2, 2000



Are you interested?

Please tick the box on the journal resource request form.

www.gutreaction.co.nz

Resources will be launched May 2007 and supplied in advance.

This campaign supports recommended prescribing practice which is set out in the New Zealand Guidelines and aims to promote the responsible use of medications for this particular therapy area.