

Gastro-oesophageal Reflux Disease in Adults

Reflux Disease



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This edition was updated by Associate Professor Geoffrey Hebbard, Director of Gastroenterology, The Royal Melbourne Hospital on behalf of the Digestive Health Foundation.

The Digestive Health Foundation of the Gastroenterological Society of Australia has prepared this document and every care has been taken in its compilation. The document is intended to be used as a guide only and not as an authoritative statement on every conceivable step or circumstance that may or could relate to the management of gastrooesophageal reflux disease in adults.

Clinicians should use this document as an aid in relation to gastrooesophageal reflux disease and not as a complete authoritative statement. Medical understanding of gastrooesophageal reflux is evolving. This document reflects this understanding as at February 2011 and may be subject to updating and review at a later date.

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1 GASTRO-OESOPHAGEAL REFLUX DISEASE

Terminology and the significance of Reflux

- Reflux of gastric contents into the oesophagus is a normal physiological event, occurring usually during the postprandial period.
- Gastro-oesophageal reflux disease occurs when reflux exposes the patient to the risk of physical complications, or symptoms lead to a significant impairment of wellbeing or quality of life.
- Clinically significant impairment of wellbeing (quality of life) usually occurs when symptoms are present on two or more days a week.
- Reflux disease carries the risk of reflux (peptic) oesophagitis and complications such as columnar-lined (Barrett's) oesophagus and oesophageal adenocarcinoma. However, the absolute risk of oesophageal cancer in an individual with reflux is small.
- Most patients with symptoms of Gastro-oesophageal reflux do not have endoscopically visible lesions. Only about one-third of patients with reflux disease have reflux oesophagitis as evidenced by endoscopically visible mucosal breaks (erosions or ulceration) or columnar-lined (Barrett's) oesophagus.

Epidemiology

- Reflux disease is common. Between 15-20% of adults experience heartburn at least once a week.
- Obesity (BMI $>30\text{kg/m}^2$), alcohol consumption (> 7 standard drinks a week) and a first-degree relative with heartburn increase the risk of having reflux symptoms.
- Patients with connective tissue diseases such as scleroderma, chronic respiratory diseases such as asthma and cystic fibrosis, institutionalised and intellectually handicapped people, and patients nursed in a supine position for prolonged periods are at increased risk of reflux disease and its complications.

Reflux disease is the most common cause of heartburn and indigestion in western society

Natural history

- In most patients, reflux disease is a chronic disorder. Mild symptoms may vary in intensity and occur only on some days. With increasing severity, symptoms tend to occur daily.
- Most patients will therefore require long term management, although this should be individualised to control the patient's symptoms and reduce the risk of complications.

Pathogenesis

- Gastro-oesophageal reflux disease occurs as a result of excessive exposure of the oesophagus to gastric contents. The most damaging components are acid and pepsin, although bile and pancreatic enzymes may contribute in some patients.
- The excessive exposure to gastric contents is largely the result of an increased frequency of acid reflux episodes, but impaired clearance of stomach contents from the oesophagus or impaired mucosal defences may also be an important factor in some patients.
- Under normal conditions, reflux is prevented by the tonic activity of the lower oesophageal sphincter (LOS), supported by the crural diaphragm. Reflux episodes occur primarily because of defective LOS function. The major event that leads to reflux is transient LOS relaxation. An important minority of reflux episodes occurs because of defective basal LOS pressure, often associated with hiatal hernia.
- A number of factors may aggravate reflux symptoms. These include dietary components such as fat, chocolate, caffeine and alcohol, as well as smoking and some drugs.
- Hiatal hernia is associated with reflux disease, however reflux disease may also be present without hiatal hernia, and the presence of a hiatal hernia does not necessarily mean that reflux disease is present or should be treated.

Clinical features

Symptoms directly related to reflux episodes and Symptoms caused by complications of reflux disease.

Symptoms may be broadly grouped into those which are directly related to reflux episodes, and those caused by complications of reflux disease.

Symptoms directly related to reflux episodes

• Heartburn

This is the hallmark symptom of reflux disease. It is characterised by a feeling of burning rising up from the stomach or lower chest towards the neck. It is typically provoked by meals, especially those containing fatty or highly spiced food or by bending, straining or lying down. It is usually eased or relieved by antacids.

• Regurgitation

This is the other characteristic symptom of reflux disease. Regurgitated material is usually re-swallowed but is sometimes so voluminous that it may be mistaken for 'vomiting'. Some patients may experience regurgitation as their predominant symptom, particularly if gastric acid secretion is suppressed.

• Waterbrash

Oesophageal acidification may cause such sudden and brisk stimulation of salivation that the patient's mouth fills with saliva. This may be associated with nausea.

• Atypical symptoms

Reflux may cause a number of other symptoms not easily identified as being due to reflux. These include angina-like chest pain, throat/voice changes, cough, asthma, excessive belching, dyspepsia and nausea. These symptoms are nonspecific and do not in themselves imply the presence of reflux, although it should be considered in the differential diagnosis.

Symptoms caused by complications of reflux disease

• Dysphagia

Dysphagia may be due either to inflammation, defective oesophageal peristalsis or heightened oesophageal sensitivity. Dysphagia that is associated with symptoms of bolus impaction is suggestive of a stricture or ring.

• Odynophagia (painful swallowing)

This is usually associated with severe oesophagitis but may also be due to excessive sensitivity of the oesophageal mucosa.

• Bleeding from oesophagitis

Haematemesis may be a presenting symptom but is rarely severe. Occasionally, iron deficiency may result from severe oesophagitis (however other causes must be excluded).

Symptoms of reflux disease

Typical	Atypical	Alarm
Heartburn Regurgitation	Cardiac-type chest pain Nausea Belching, bloating Hoarseness Throat symptoms Cough	Dysphagia Painful swallowing Haematemesis Weight loss

2 DIAGNOSIS

Symptoms

The diagnosis of reflux disease is primarily symptom based.

- In most patients, reflux disease has a characteristic symptom pattern. Heartburn is the cardinal symptom. However, this term is poorly understood by many patients and it is important to give a descriptive definition such as "a burning feeling rising up from the stomach or lower chest towards the neck". This approach has been found to identify more patients with reflux disease than the use of the term "heartburn" itself.
- There is substantial overlap between the symptoms of reflux disease and those of ulcer disease or functional dyspepsia. Approximately two-thirds of patients will also complain of upper abdominal pain or discomfort and about 40% of patients with Irritable Bowel Syndrome (IBS) also complain of reflux symptoms.
- Symptom severity is not a reliable guide to the severity of oesophagitis. Nevertheless, the presence of dysphagia, odynophagia, nocturnal choking, haematemesis or weight loss should alert the clinician to possible severe or complicated reflux disease or another diagnosis.

The history is the single most useful method for the diagnosis of reflux disease

Therapeutic trial

- A symptom-based diagnosis can be supplemented by the use of a therapeutic trial of high dose proton pump inhibitor for two to four weeks. This test has a sensitivity and specificity for reflux disease that is comparable to that of oesophageal pH monitoring and substantially superior to endoscopy.

A diagnosis based on symptoms can be aided by trial of treatment

Investigations: the role of endoscopy

When to investigate?

- It is inappropriate to investigate every patient with suspected reflux symptoms. Young patients who have longstanding mild, typical reflux symptoms and no alarm symptoms may be given a trial of therapy without investigation.

Investigations should be done when:

- the diagnosis is unclear because symptoms are either non-specific or atypical for reflux disease, or are 'mixed' with gastroduodenal symptoms such as the presence of epigastric pain.
- symptoms that persist or progress on therapy suggest severe or complicated oesophagitis is present; for example haematemesis, odynophagia, persistent dysphagia or weight loss
- other diagnoses seem possible, for example:
 - infective or drug-induced oesophagitis
 - oesophageal malignancy
 - gastroduodenal disorders
 - myocardial infarction or ischaemia.

Investigations are warranted if the diagnosis is unclear; symptoms persist or are refractory to treatment; complications are suspected or; alarm symptoms are present.

Which investigation?

- Endoscopy

Upper GI endoscopy is the investigation of first choice as it:

- is the most specific test for reflux oesophagitis (although not sensitive – see below)
- is the most accurate means of diagnosing other mucosal lesions such as infective oesophagitis, peptic ulcer disease, malignancy or other upper gut abnormalities that may be difficult to distinguish on history from reflux disease
- is the only effective way to grade oesophagitis, which has relevance to the choice of therapy and management of reflux disease (see below)
- is the most sensitive method for diagnosing columnar-lined or Barrett's oesophagus
- is useful for recognition and management of peptic stricture.

Approximately two thirds of patients with Gastro-oesophageal reflux disease are 'endoscopy negative' i.e. have no diagnostic oesophageal mucosal abnormalities

- However, endoscopy has a limited role in the diagnosis of reflux disease, as only approximately one third of patients with reflux symptoms have diagnostic endoscopic abnormalities. In these 'endoscopy negative' patients, distal oesophageal biopsies (which may demonstrate microscopic changes of oesophagitis in approximately 25% of cases/individuals/patients) are not recommended as routine practice, as this is a relatively expensive test that does not influence choice of therapy, which should be directed at symptom control. Potential roles for endoscopy are outlined in Table 1.
- In patients with alarm symptoms, endoscopy should be performed promptly, prior to empirical therapy. Early endoscopy is also indicated in patients with atypical symptoms or when symptoms fail to respond to initial therapy. Endoscopic reassessment should be performed within 6 months of anti-reflux surgery to exclude any new or unexpected pathology.

- The role of endoscopy in patients with longstanding 'medically controlled' Gastro-oesophageal reflux disease is less clear. Evidence suggests that symptomatic control equates to endoscopic healing (even in severe Los Angeles classification Grade C or D oesophagitis) so endoscopic assessment is only necessary if there is a relapse whilst on maximal or near maximal medical therapy. On the other hand, a 'once in a life-time' endoscopy in this subset of patients may be reasonable to assist discussions about long-term management and to exclude the potential complications of severe oesophagitis. There is, however, no convincing evidence that screening all patients with reflux for Barrett's oesophagus would be of benefit. Endoscopic surveillance in known Barrett's oesophagus is discussed in Section 4.

TABLE 1

Indications for early endoscopy:

- Alarm symptoms (including dysphagia, odynophagia, weight loss, haematemesis, anaemia)
- Diagnostic uncertainty such as mixed, non-specific or atypical symptoms
- Symptoms refractory to initial treatment
- Pre-operative assessment
- Provision of reassurance when verbal reassurance is inadequate.

Endoscopy may also be appropriate:

- For patients with long-standing frequent troublesome symptoms
- To tailor drug treatment
- To detect and manage Barrett's oesophagus.

Barium swallow and meal

- This is an inappropriate primary diagnostic test as it is insensitive and not specific for reflux disease.
- It may be useful however, to assess and plan management in patients with persistent dysphagia when a complicating stricture is suspected or for the assessment of large hiatal hernia.

24-hour ambulatory oesophageal pH monitoring

- This investigation tests the amount of exposure of the oesophagus to acid and whether symptoms are related to the occurrence of reflux.
- pH monitoring is useful in patients in whom the diagnosis and relationship between symptoms and reflux remains unclear despite a therapeutic trial of acid suppression and endoscopy.

3 MANAGEMENT

- As the severity of Gastro-oesophageal reflux disease varies significantly between patients, management needs to be individualised. The aims of management are to control symptoms (in the majority of patients) and to prevent complications (in a small but important minority).
- Although gastric acid secretion is normal and the cause of the disease is lower oesophageal sphincter dysfunction, the mainstay of treatment is acid suppression.
 - The proton pump inhibitors (PPI) are the most potent agents and are most effective if taken 30-60 minutes before food. Some PPIs are now available without prescription in Australia.
 - H2 receptor antagonists are less potent, but may have a more rapid onset of action. These are available over the counter, so are very accessible to patients.
 - Antacids have a rapid onset of action, but are ineffective in long-term management other than for mild intermittent or occasional breakthrough symptoms.
 - Prokinetic agents have little role in the management of reflux disease..

- Lifestyle measures have not been demonstrated to have significant effects in healing oesophagitis, however dietary changes (avoidance of precipitating foods), weight loss (reduction in weight in overweight or obese individuals), and nocturnal posture (elevation of the torso) may be useful in controlling symptoms in some patients. Patients should not be placed on unnecessarily restrictive diets.

Empirically treated patients

- In the group of patients where empirical treatment is commenced and who have an adequate therapeutic response indicating that reflux is the likely cause of their symptoms, it is appropriate to cease or reduce therapy and allow the patient to use acid suppression on an intermittent basis as required. It is likely that symptoms will return in 70% of cases, and patients will adjust the dose of medication to the severity and frequency of symptoms.
- Atypical symptoms (ENT, respiratory) often require a more prolonged/higher dose trial of therapy.

Patients who have undergone endoscopic assessment

- Patients with no oesophagitis or milder grades of oesophagitis at endoscopy (Los Angeles Grades A and B) can be treated in a similar manner to empirically treated patients, and 'stepped down' to the lowest level of acid suppression where symptoms are adequately controlled.
- Patients with severe oesophagitis (Los Angeles Grades C and D) should be treated with regular (standard dose) PPI on an ongoing basis to maintain mucosal healing. Initial healing and symptom relief are more rapid in these patients when treated with formulations of PPI that provide a greater degree of acid control.
- Patients with complications such as strictures will require endoscopic therapy (e.g. dilatation).

Risks of acid suppression and acid suppressive medication

- Long term acid suppression with PPIs has been associated with a slight increase in the rates of bacterial gastroenteritis, community acquired pneumonia, osteoporosis and hip fracture, as well as bacterial overgrowth of the small intestine and outbreaks of *Clostridium difficile* colitis in elderly patients in hospitals. The absolute risk of these complications is very low.
- The evidence for a clinically significant interaction with Clopidogrel is weak.
- There is a low incidence of interstitial nephritis with PPIs. However this should be considered in patients with a deterioration in renal function on PPI therapy.
- Patients on warfarin should have their INR checked following the introduction of acid suppressive medication, as with the commencement of any new medication.

Fundoplication

- Fundoplication is an effective treatment for Gastro-oesophageal reflux disease, and can be performed laparoscopically, but carries the small risks associated with laparoscopic abdominal surgery.
- Fundoplication is of particular value in patients whose symptoms cannot be controlled adequately by medical therapy, and may be considered in patients who wish to avoid long-term medication and are willing to accept the small risks involved.

Endoscopic therapies for gastro-oesophageal reflux disease

- A number of therapies that can be delivered endoscopically have been developed for the treatment of reflux disease. These include suturing devices, injection of inert substances, plication devices and devices that deliver radiofrequency energy to the Gastro-oesophageal junction.
- Experience with these techniques is relatively limited. They do not significantly reduce exposure of the distal oesophagus to acid, and many

have already been removed from the market because of lack of efficacy or complications (including death).

- These treatments should not be used by inexperienced operators or outside a program (e.g. a clinical trial) where complications can be easily reported.

Barretts Oesophagus

- Metaplasia of the lining of the lower oesophagus to an intestinal phenotype (Barrett's oesophagus) is related to Gastro-oesophageal reflux, and confers an increased risk of oesophageal adenocarcinoma.
- Although the relative risk is significantly increased, the absolute risk of an individual with Barrett's oesophagus developing adenocarcinoma of the oesophagus remains low (<2% lifetime risk), and very few patients with Barrett's oesophagus die of oesophageal adenocarcinoma.
- If Barrett's oesophagus is found at endoscopy, patients should be offered the opportunity to enroll into a screening program where regular biopsies are taken to assess for dysplasia or carcinoma, with appropriate follow-up management where required.





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