Treatment of gastro-oesophageal reflux disease in adults & children

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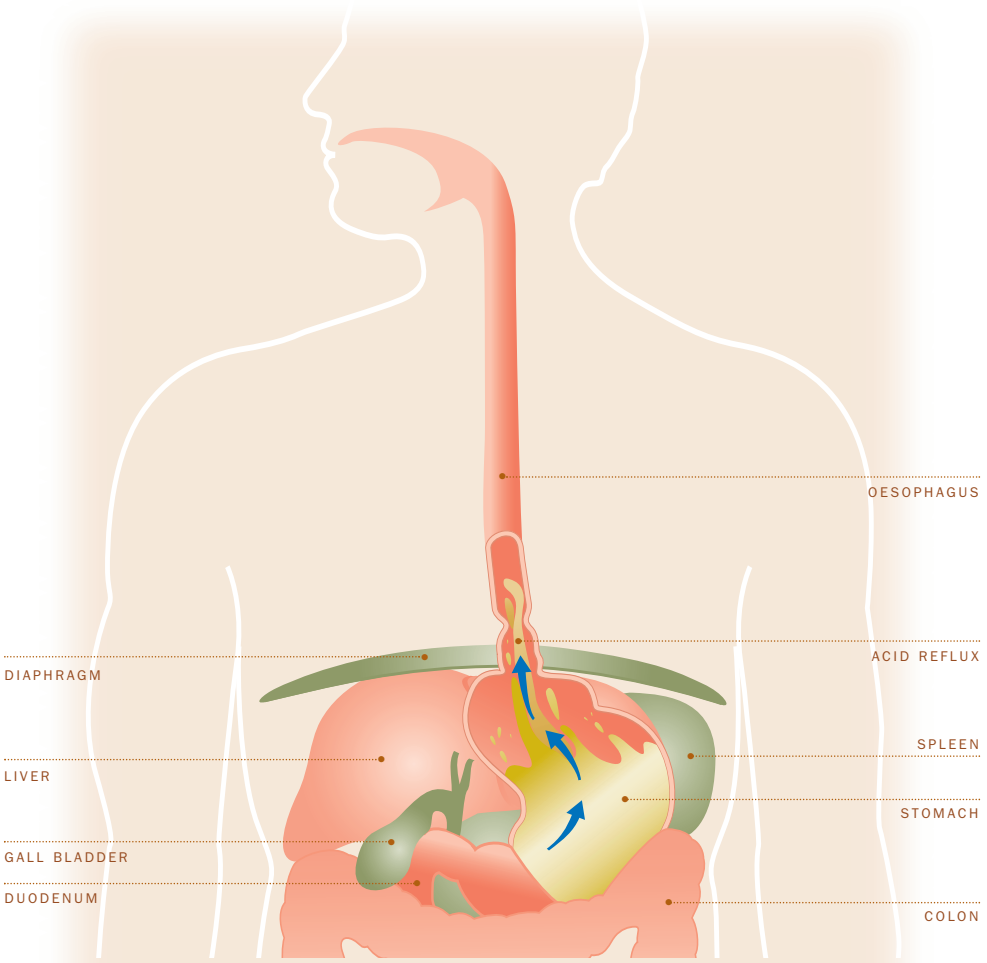
What is gastro-oesophageal reflux disease? (GORD)



GORD is usually associated with excessive exposure of the oesophagus to gastric acid.

Acid reflux occurs through a relatively incompetent lower oesophageal sphincter that is commonly associated with hiatus hernia. Under normal circumstances acid reflux is prevented by the contraction of the lower oesophageal sphincter together with muscular activity within the lower oesophagus which clears the refluxed contents back to the stomach.

The role of hiatus hernia

The lower oesophageal sphincter between the oesophagus and the stomach is normally supported by the diaphragm. If the diaphragm is weakened, the stomach moves up into the chest reducing the effectiveness of the lower oesophageal sphincter and allowing acid and gastric contents to escape upwards into the oesophagus, resulting in heartburn.

Those with higher acid secretion may develop symptoms, whereas those who have lower acid secretion will not. Many people with hiatus hernia have no symptoms and require no treatment because it does not interfere with the function of the lower oesophageal sphincter.

Heartburn in the Australian community

The Gut Foundation carried out two telephone newspoll surveys of 1,200 respondents (over a six-year interval) in the Australian community.

Summary

- 22% experienced heartburn at least once a month.
- There was a trend for more women to be affected than men, with more severe heartburn occurring in older women.
- Of the total sample, 47% had symptoms of less than 5 years duration; 15% had experienced symptoms for more than 20 years.
- Half the respondents found heartburn affected their ability to eat and drink normally.
- 44% had nocturnal problems.
- Less than 20% used prescription medications.
- 25% did not use any medications.
- Only 12% of full time workers use medications compared with 28% of those not in the work force.

- Individuals blamed a combination of factors including:

Stress
Smoking
Pregnancy
Coffee
Alcohol
Food allergy
Overeating
Rich and greasy foods

Symptoms

A] Those related to reflux

Heartburn is the key symptom of GORD. Acid in the oesophagus causes a burning sensation rising upwards behind the breastbone towards the neck, and maybe especially provoked by heavy meals, bending or straining. It occurs as frequently however, in upright subjects.

Regurgitation. Regurgitated gastric contents are sometimes so large that they rise up into the larynx and are associated with a bitter taste in the mouth. In some subjects with hiatus hernia, regurgitation is the primary problem and dominates heartburn as a symptom.

B] Symptoms caused by complications

Dysphagia is usually confined to difficulty in swallowing solids such as meat, bread and pastry. It is primarily due to ulceration associated with inflammation and narrowing either by oedema or fibrous stricture of the lower oesophagus. The first presentation can sometimes be by food bolus obstruction.

Odynophagia (painful swallowing)
It is a less common symptom, due to associated ulceration in the distal oesophagus and may occur with solids or liquids, either hot or cold.

Unusual complications include:

- Exacerbation of asthma.
- Hoarseness.
- Erosive dental disease.
- Sinusitis.

Should **bleeding** result from ulceration in the oesophagus it may present as hematemesis, melaena or iron deficiency anaemia.

C] Associated dysmotility

Abnormal neuromuscular function of the oesophagus or the stomach may produce a different set of additional symptoms which include dysphagia for solids and this may be associated with a choking sensation in the pharynx together with recurrent cough. There may also be symptoms of fullness, early satiety, bloating and burping and these occur particularly following a meal.

Alarm associations

Difficult or painful swallowing

Weight loss

Repeated vomiting or vomiting blood

Taking medications that may cause heartburn, such as aspirin or arthritis tablets, tetracycline or biphosphonate supplements

Exercise (could it be angina).

Management of GORD

Heartburn is a universal experience. For those whose heartburn is trivial, intermittent, or related to obvious precipitants, symptomatic therapy only is required. Reflux oesophagitis is primarily a clinical diagnosis based on history.

A careful history should:

Check for the cardiac features in the history; if present arrange stress test or other appropriate investigation.

Determine if symptoms are typical.

Check for alarm symptoms of bleeding, dysphagia, anaemia and vomiting.

Check lifestyle precipitants including alcohol consumption, cigarette smoking, obesity, and NSAID ingestion.

Patients with alarm symptoms require immediate investigation.

Patients with **mild symptoms** and correctable lifestyle factors require advice and symptomatic therapy including H_2 Receptor Antagonists or antacid therapy with review in one month.

Patients with **moderate or severe heartburn** regardless of whether there are reversible lifestyle factors, should receive a trial of a proton pump inhibitor with review at one month. If symptoms persist which require ongoing PPI therapy, referral for endoscopy is advisable because such therapy may need to be **life-long.**

If **Barrett's Oesophagus** is present then high dose PPI's should be prescribed on a long-term basis and the patient entered into a surveillance program. Depending on local expertise, consideration for endoscopic ablation may be advised.

All PPI's are comparable in terms of effectiveness. Some have more rapid onset of action. This may make them suitable for "on-demand" therapy, but in this situation H_2RA's may also be effective.

Helicobacter *pylori* status will be determined at the time of endoscopy and the bacteria should be eliminated if present. If endoscopy shows no ulceration then the minimum therapy which controls symptoms is appropriate.

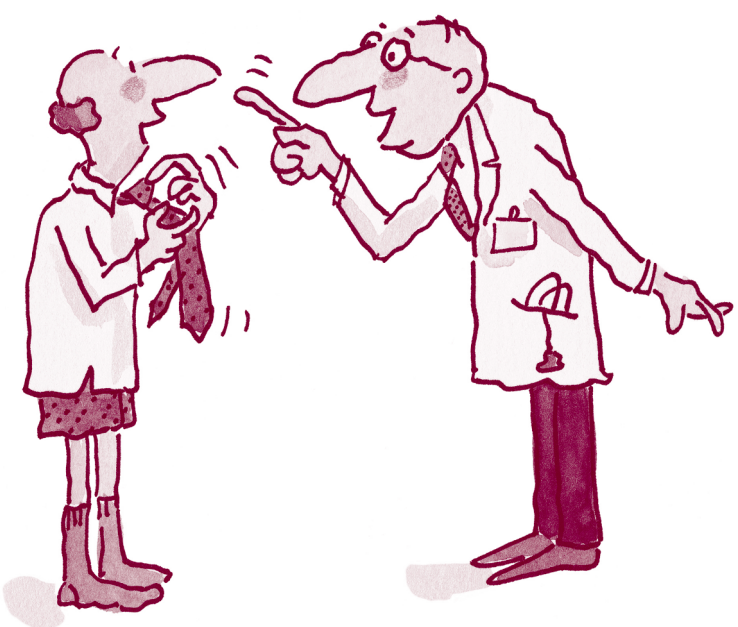
If significant ulceration is present in the lower oesophagus then life-long continuous PPI's should be prescribed.

Helicobacter *pylori* eradication in GORD

While some controversy still exists about whether or not GORD is exacerbated following successful helicobacter *pylori* eradication, consensus is moving towards the concept that it has no influence on such symptoms. Helicobacter *pylori* eradication therefore warrants therapy on its own merits particularly in terms of eliminating one risk factor for subsequent gastric cancer and minimisation of the risk in developing peptic ulceration with concurrent use of aspirin, NSAIDs or coxibs.

Other investigations

If dysmotility is suspected, then a video barium swallow with marshmallows may delineate the underlying muscular abnormality.



Heartburn

no alarm symptoms

alarm symptoms

moderate–severe symptoms

R_x PPI for 1 month

review 2 months

symptoms recur

endoscopy

mild symptoms

correct lifestyle factors and give advice re: H_2RA+/– antacids

no or minimal ulceration

minimum R_x to control symptoms program H_2RA or PPI

significant ulceration

life-long PPI [or consider surgery]

Barrett's Oesophagus

high dose PPI surveillance

endoscopy

Medical treatment of GORD

The objectives are:

1] **To achieve** symptomatic relief.

2] **Reduce the risk** of complications and improve quality of life.

3] **Heal** oesophageal ulceration.

Non–medication interventions

i] **Lifestyle modifications**

As surveys have indicated, individuals blame a combination of lifestyle factors as the cause of their heartburn. These need to be addressed and will vary between such individuals. In general, avoidance of high fat diets, excessive coffee and alcohol and other caffeine containing drinks together with stopping smoking is important.

ii] **Elevation of the bed head**

As reflux episodes occur as frequently while upright as when prone, elevation of the bed head has little to offer in terms of therapeutic response, particularly since the advent of proton pump inhibitor therapies.

iii] **Weight loss**

There is equally little evidence that weight loss will result in the improvement of symptoms unless there is avoidance of the particular lifestyle factors that precipitate episodes of acid reflux. There are however other major health benefits from weight reduction.

iv] **Drugs/medication**

Medications that might exacerbate reflux disease include anticholinergic drugs, antidepressants such as amitriptyline, aspirin, non-steroid inflammatory drugs, coxibs, tetracycline, slow release potassium and biphosphonates for treatment of osteoporosis. Prescription of alternatives may be required.

Acid suppression

If symptoms are mild or an endoscopy has shown a normal oesophagus or minimal inflammation, then it would be appropriate to begin with H_2 Receptor Antagonist therapy either once or twice daily.

If symptoms are inadequately controlled, then **“step up” therapy** becomes mandatory, with the use of proton pump inhibitors. It must be recognised that once this level of therapy is reached, treatment is likely to be lifelong and therefore endoscopy prior to embarking on such therapy is mandatory.

If symptom control is achieved with normal doses of PPI’s then there is a virtue in determining if a smaller dose of PPI will achieve the same effect as **“step down” therapy**.

If this is unsuccessful then reversion to normal dose therapy is required.

In general terms, intermittent or every second or third day therapy with PPI's is largely unsuccessful because of the time taken to achieve acid inhibition, although intermittent therapy with an H_2RA is frequently helpful due to the rapid response in terms of acid control. The latter however, is only useful in mild disease.

Persistence of retrosternal pain despite adequate therapy

The advent of powerful proton pump inhibitors has made 24 hour ambulatory pH monitoring less relevant. In those whose symptoms don't respond to high dose PPI therapy, other factors should be considered:

- Could it be cardiac ischaemia?
- Is there a musculo-skeletal contribution (Tietze's syndrome) associated with tenderness over the costochondral junctions and frequently thoracic back pain?
- Could it be dysmotility?

Surgical treatment of GORD

The traditional anti-reflux surgery is now done laparoscopically. Although there are prospects for endoscopic day only procedures, at this time they remain relatively experimental.

The major indication for surgery is for **volume reflux** where gastric contents reflux into the mouth without significant heartburn as the symptoms of **acid reflux** are almost universally controlled with acid suppression. If a patient has volume reflux, a prokinetic agent may be a useful prerequisite to considering fundoplication, particularly if there is any suggestion of dysmotility. However, the presence of established dysmotility remains an almost certain contraindication to fundoplication.

Anti-reflux surgery for heartburn has no place for patients who have failed to respond to acid inhibition.

It should also be recognised that some years after initially successful fundoplication, acid reflux may recur and warrant acid suppression.

After fundoplication patients in general will be unable to burp and may initially have mild dysphagia.

Barrett's Oesophagus

Barrett's Oesophagus is present when the normal squamous mucosa of the lower oesophagus is replaced by columnar epithelium, which contains intestinal metaplasia. At endoscopy columnar mucosa will appear with a salmon pink colour which is quite distinct from the normal lighter coloured squamous mucosa. However it is necessary to take biopsies and have them examined by an experienced pathologist to determine if intestinal metaplasia is present, since fundic and cardiac mucosa has the same appearance at endoscopy.

The recent development of high resolution and magnification endoscopy has improved the ability to detect abnormal mucosa and to target biopsies.

Chromo-endoscopy using either vital dyes, which are taken up by the tissues or surface agents which allow easier definition of mucosal patterns have also been advocated. The combination of magnification and chromo-endoscopy is currently advocated but has not been proven to be of benefit in the detection of Barrett's Oesophagus or the targeting of biopsies to detect the presence of dysplasia.

Presentation of Barrett's Oesophagus

Many, but no means all patients with Barrett's Oesophagus will have a long history of significant heartburn. The sequence of development in Barrett's Oesophagus is thought to be that gastroesophageal reflux causes oesophageal ulceration and subsequent replacement of normal squamous lining by columnar epithelium containing intestinal metaplasia. There is some evidence that control of reflux ulceration will prevent the development of Barrett's Oesophagus.

Significance of Barrett's Oesophagus

Barrett's patients with intestinal metaplasia in their lower oesophagus have an increased risk of developing oesophageal cancer. Progression to cancer will go through a series of dysplastic changes. Mild dysplasia may progress but equally is frequently noted to disappear. Once severe dysplasia is present and this has been confirmed by a second expert pathologist, then a significant proportion of patients will already have developed carcinoma of the oesophagus even if not visually apparent. Further, there is a high likelihood of invasive carcinoma developing within the next few years.

Treatment of Barrett's Oesophagus

As there is evidence that control of reflux oesophageal ulceration will prevent progression to Barrett's, it is therefore important that patients take a proton pump inhibitor indefinitely to ensure ulceration remains healed.

Once Barrett's Oesophagus has developed there is no evidence that surgical fundoplication or treatment with proton pump inhibitors will eliminate the intestinal metaplasia. Surgery and medical therapy may reduce the length of Barrett's mucosa.

Surveillance program

In those with no dysplasia endoscopic surveillance on a two yearly basis is advised.

When mild dysplasia develops, a 6–12 monthly review is advocated.

Once definite high-grade dysplasia is established then esophagectomy is advised.

Because of the magnitude of this operation clinicians and pathologists involved need to be absolutely certain that definite high-grade dysplasia exists.

Endoscopic mucosal ablation in Barrett's Oesophagus

A variety of techniques have been used to ablate Barrett's mucosa with or without the presence of dysplasia. These include thermal destruction of tissue with lasers, argon plasma coagulation, heater probes, cryotherapy, laser photodynamic therapy and endoscopic mucosal resection.
All these methods suffer from one or more of the following complications:

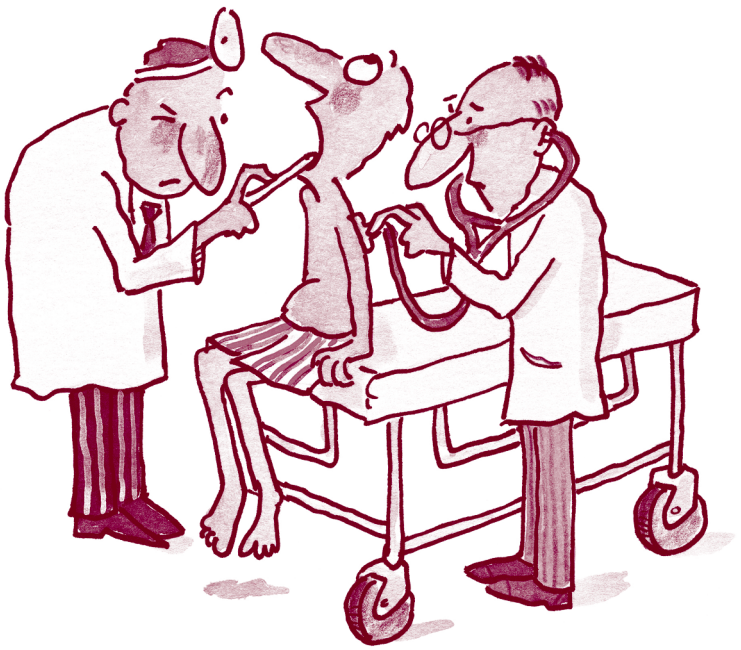
- Oesophageal perforation.
- Incomplete removal of mucosa containing intestinal metaplasia.
- "Burying" islands of intestinal metaplastic mucosa beneath regrowth of squamous epithelium.
- Failure to detect and therefore treat appropriately, already present adenocarcinoma.
- Oesophageal stricture formation.

There is as yet no clear and convincing evidence that eradication of Barrett's mucosa by these techniques is cost-effective and improves survival.

Endoscopic treatment of localised high-grade dysplasia

Patients with diffuse dysplastic changes are best referred for surgery. However, for patients who are not fit for surgical resection, or where surgical resection is not acceptable to the patient, then localised areas of high-grade dysplasia can be resected using the technique of endoscopic mucosal resection.

Endoscopic ultrasound should be used to confirm that the lesion has not penetrated into the muscle layers of the oesophagus. The lesion is then elevated on a saline cushion and removed by one of several endoscopic mucosal resection techniques.



Evaluation & management

gastro-oesophageal reflux in infants and children

Gastro-oesophageal reflux (GOR) is defined as the passage of gastric contents into the oesophagus due to spontaneous relaxation of the lower oesophageal sphincter, whereas **gastro-oesophageal reflux disease (GORD)** describes the symptoms consequent upon the associated oesophagitis. Both are very common events in infants and children.

The important features in management of these conditions are:

- Differentiating GOR from GORD.
- Excluding other potential causes of symptoms.
- Using appropriate investigations and management options.

Vomiting and GOR/GORD

GOR may be seen as a physiological event in most (if not all) healthy infants, and improves spontaneously in the majority of instances. Defining when this becomes “pathological” is vital. In addition, it is important to remember that “all that vomits is not reflux”. A differential to be considered should include conditions such as infections (eg. UTI), overfeeding, and structural abnormalities. Eosinophilic (or allergic) oesophagitis also may be present with symptoms of GORD.

Diagnostic approaches

In most cases history and physical examination provide the diagnosis of GOR and management can then be initiated.

Diagnostic approaches include imaging studies, oesophageal pH monitoring, oesophagoscopy and biopsy, nuclear medicine scans, and empiric medical therapy.

Treatment options

A number of management options including diet changes, positioning and lifestyle changes are relatively simple. These options may be all that is required in physiological GOR, and can be considered first.

Acid-suppression therapy with histamine receptor antagonists (HRA's) or proton pump inhibitors (PPI's) forms the cornerstone to management of GORD because of prompt symptom relief and mucosal healing. Initial therapy can entail ranitidine at appropriate doses. PPI's provide enhanced acid suppression, superior symptom control and healing. Antacids may be used for short-term symptom relief, but should not be considered as long-term therapy because the other agents provide more convenient and safer options.

Prokinetic agents have limited roles in children with GOR/GORD. Of the agents previously used there is most evidence favouring cisapride. Unfortunately, this is no longer available.

There is no clear evidence to support the use of other prokinetic agents for GOR and other prokinetics such as metoclopramide may have additional side effects.

Surgical treatment is required for some infants and children with GOR/GORD. Case series illustrate generally favourable outcomes. The potential risks, benefits and costs of successful prolonged medical therapy versus fundoplication have not been well studied in infants or children.

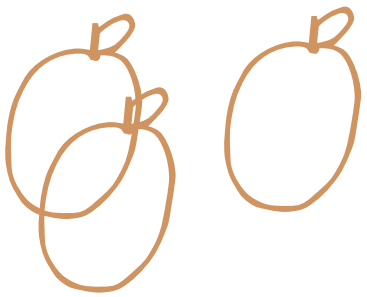
Evaluation and management

The infant with recurrent vomiting

A thorough history and exam is usually sufficient, when there are no alarm symptoms present, to establish whether or not this is physiological reflux. In most of these infants, who are otherwise thriving, reassurance and guidance are all that is required. Thickening of formulae or a brief trial of hypo-allergenic formulae may be indicated. A barium study is not always required, but should be undertaken with any suggestion of obstruction, or if symptoms become severe or prolonged. Other diagnostic tests should only be considered if there are complications (such as severe irritability or failure to gain weight).

The infant with vomiting and poor weight gain

These children should be investigated to determine the cause of the vomiting. Tests should include a barium study and urine culture. Management should begin with food thickening and increasing caloric intake. Acid suppression, prokinetics and assisted feeding may all be required.



The vomiting infant with irritability

Differentials should include food intolerance, UTI and neurological conditions. These children are often difficult to manage.

The child with recurrent vomiting and regurgitation

In otherwise normal children, who present with this symptom after 2 years of age, management options include upper endoscopy and acid suppression therapy.

Heartburn in the child or adolescent

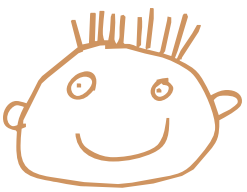
May be due to simple acid reflux, as in adults. Lifestyle changes and possibly a trial of an H_2RA are recommended. If symptoms persist, patients should be referred for endoscopy.

Dysphagia/odynophagia Endoscopy may be the best initial diagnostic test as the symptoms indicate oesophagitis. Barium study may also be required to exclude structural abnormality.

When oesophagitis is demonstrated initial options include lifestyle changes although acid suppression may be required.

Respiratory associations with GOR

Some children with recurrent respiratory conditions (eg. Recurrent pneumonia, difficult to control asthma) may have underlying GOR contributing to respiratory disease. An oesophageal pH study may demonstrate increased acid exposure and patients may then respond to prolonged acid suppression. Hoarseness and sore throat may be related to GOR in some individuals.



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