Case-based learning: dyspepsia in adults

Module summary

This case-based module will guide you through the latest evidence in the diagnosis and management of dyspepsia in adults. This module was developed with Dr Mark Follows and it reflects his views and opinions – it does not represent the views and opinions of RB.

Learning objectives

This module will update you on:

- The diagnosis of dyspepsia
- Management of dyspepsia in primary care
- Dealing with ‘non-responders’
- Determining which patients need referral for endoscopy and specialist referral

Dyspepsia in adults

The British Society of Gastroenterology defines dyspepsia as ‘a group of symptoms that alert doctors to consider disease of the upper gastrointestinal tract’ and states that ‘dyspepsia itself is not a diagnosis’. Symptoms include heartburn, regurgitation, epigastric pain, nausea, bloating and fullness.

When considering dyspepsia, it can be helpful to think of it as three separate conditions:

- **Reflux type** – heartburn and regurgitation
- **Ulcer type** – epigastric pain
- **Dysmotility type** – nausea, bloating and fullness

Most patients who present with these symptoms will have little in the way of pathology to account for them, but some may have a more serious disease, including cancer. The aim of this case-based learning module is to enhance your knowledge and confidence to manage these patients and to recognise who and when to refer.

Reference

Case history 1 – Mr A

Mr A is a 35-year-old office worker who has come to see you because of increasing symptoms of heartburn and regurgitation after meals and at bedtime, that have worsened since he gained 4 kg after moving from a manual job. He smokes 15 cigarettes a day and drinks 28 units of alcohol per week. He has no problems with his swallowing and is otherwise well. He has been taking simple antacids, but these only relieve his symptoms for a short while. He doesn’t take any other medications.

Which of the following would you do? Tick all that apply

A. Give lifestyle advice (correct)
B. Advise taking an alginate or antacid/alginate combination (correct)
C. Prescribe a proton pump inhibitor (PPI) (incorrect)
D. Test for Helicobacter pylori (H. pylori) (incorrect)
E. Refer for an upper GI endoscopy (incorrect)

Patients presenting with new symptoms of dyspepsia should be managed in a stepwise fashion in accordance with NICE dyspepsia guideline CG184, flowchart 4.3.1 ‘Flowchart for the interventions for uninvestigated dyspepsia’.¹ This man has symptoms of uncomplicated reflux-type dyspepsia (heartburn and regurgitation), which is likely to have been brought on by weight gain and aggravated by smoking and alcohol. Lifestyle advice should be given to address weight loss, stopping smoking, reducing alcohol consumption, not eating late and raising the head of the bed.¹ Alginites are very helpful in reflux disease as they form an anti-reflux barrier, as well as helping to neutralise acid if they also contain antacids, and should be tried before prescribing a PPI as part of lifestyle advice. Food entering the stomach stimulates acid production and an area of unbuffered acid can accumulate in the proximal stomach in a ‘pocket’.²

Alginates colocalise with the acid pocket and suppress reflux,\(^2\) relieving heartburn and regurgitation. \(H.\) \textit{pylori} plays no part in causing or aggravating reflux-type dyspepsia and therefore testing is not required in such patients (more on this issue later). Endoscopy should only be considered at this stage if the patient has an alarm symptom that raises the possibility of cancer (see list below),\(^3\) or if there is some other concern, such as patient anxiety regarding the diagnosis.

- Offer direct-to-test endoscopy within 2 weeks for patients:
  - With dysphagia
  - >55 years old with weight loss plus:
    - Upper abdominal pain
    - Reflux
    - Dyspepsia
- Consider non-urgent direct-to-test endoscopy for people with:
  - Haematemesis
  - Treatment-resistant dyspepsia
  - Upper abdominal pain and low haemoglobin
  - Raised platelet count plus:
    - Nausea and/or vomiting
    - Weight loss
    - Reflux and/or dyspepsia
    - Upper abdominal pain
  - Nausea or vomiting plus:
    - Weight loss
    - Reflux
    - Dyspepsia
    - Upper abdominal pain
- 2-week wait referral for patients with upper abdominal mass suspicious of a cancer

**Key takeaways**

- Patients with uncomplicated reflux-type dyspepsia should be managed in a stepwise fashion in accordance with NICE dyspepsia guideline CG184.\(^1\)
- Lifestyle and alginate, antacid and combination interventions should precede initiation of PPI therapy.\(^1\)
- \(H.\) \textit{pylori} testing is not warranted in patients with reflux-type dyspepsia.
- Endoscopy should be considered in patients with alarm symptoms that raise the possibility of cancer.\(^3\)
References


Case history 1 (continued) – Mr A

Mr A returns to see you 4 weeks later. He has managed to lose 2 kg and has reduced his alcohol intake by half. He finds that alginate helps for a time but he is still getting troublesome heartburn 3–4 times a week.

Which of the following would you prescribe?

A. Ranitidine 150 mg twice daily
B. Low-dose PPI once daily for 4 weeks
C. Full-dose PPI as required
D. Full-dose PPI once daily for 4 weeks (correct answer)
E. Full-dose PPI twice daily for 4 weeks

The NICE full guideline CG184 advises treating the patient with a full-dose PPI once daily for 4 weeks. Low-dose PPI is used for maintenance or when trying to step down the patient from higher doses. Higher-dose PPI is used post-endoscopy to treat severe reflux oesophagitis and heal gastric ulcers, as part of H. pylori treatment regimens, and can be used in patients with severe reflux-type dyspepsia who get breakthrough symptoms late in the day. The table below gives details of the various PPIs and their doses for severe oesophagitis.1

<table>
<thead>
<tr>
<th>PPI</th>
<th>Low dose (on-demand dose)</th>
<th>Full/standard dose</th>
<th>Double dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esomeprazole</td>
<td>(20 mg* OD)</td>
<td>(40 mg* OD)</td>
<td>40 mg BD*</td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>15 mg OD</td>
<td>30 mg</td>
<td>30 mg BD</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>(20 mg* OD)</td>
<td>(40 mg* OD)</td>
<td>(40 mg* BD)</td>
</tr>
<tr>
<td>Pantoprazole</td>
<td>20 mg OD</td>
<td>40 mg</td>
<td>40 mg BD</td>
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</tbody>
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<table>
<thead>
<tr>
<th>Rabeprazole</th>
<th>10 mg OD</th>
<th>20 mg OD</th>
<th>20 mg BD</th>
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</table>

* Change from the 2004 dose, specifically for severe oesophagitis, agreed by the GDG during the update of CG17

‡ Off-label dose for GORD.

**Key takeaways**

- NICE CG184 advises treating patients with uninvestigated dyspepsia with full-dose PPI once daily for 4 weeks.¹
- People who need long-term management of dyspepsia symptoms should be offered an annual review of their condition and treatment.¹

**Reference**


**Case history 1 (continued) – Mr A**

Mr A comes back to see you after 6 additional weeks. He was symptom-free taking his full-dose PPI but found that his heartburn returned within a few days of stopping the medication. He has come to see you to get another prescription. What do you do?

A. Refer him for an endoscopy
B. Issue him another prescription at the same dose
C. Issue him another prescription but at a lower dose (correct)
D. Issue him another prescription at a higher dose
E. Give him a different PPI at an equivalent dose
F. Give him an alginate

This is a very common scenario that results in a lot of patients being referred for a needless endoscopy. Gastric acid production from the parietal cells is regulated by a complex feedback process. Acid suppression stimulates the G cells in the antrum to increase gastrin production to stimulate the parietal cells. Once the patient stops their PPI, acid production resumes, but the high gastrin levels cause a rebound hyperacidity that can result in a transient increase in heartburn symptoms.¹ This is not an indication to refer for endoscopy. The NICE dyspepsia guideline CG184, section 4.3 and flowchart CG17 ‘Interventions for uninvestigated dyspepsia’ advises that patients can be treated with repeat courses of PPIs but at the lowest dose to control their symptoms, including on a PRN basis.¹

**Key takeaways**

- Patients stopping PPI may experience rebound hyperacidity resulting in a transient increase in heartburn symptoms.
• Patients requiring intervention for uninvestigated dyspepsia should be treated with repeat courses of PPI, at the lowest dose necessary to control symptoms.
• Rebound hyperacidity, on its own, is not an indication to refer patients for endoscopy.

Reference

Case history 1 (continued) – Mr A

Mr A comes back to see you for his annual physical examination after 40 additional weeks. He has been symptom-free taking a low-dose PPI, but would like to stop taking medication. What do you do?

A. Issue him another prescription at the same low dose
B. Suggest a step-down approach to stopping PPI use, which may include certain alginates to control rebound symptoms (correct)
C. Stop treatment with PPI
D. Give him an alginate

It is recommended that patients have an annual medication review. These patients can be instructed that they should seek medical advice if their symptoms change or they develop new symptoms, which might then require endoscopy. In patients who are not experiencing symptoms, this is an opportunity to consider a stepwise approach to reducing their use of prescribed medication (unless there is an underlying condition or comedication that would indicate continuing current treatment), by using the effective lowest dose, by trying therapy ‘as needed’ or by returning to self-treatment with antacid and/or alginate therapy. It is worth remembering that certain alginates are licensed to be used to control heartburn symptoms when patients are taking a concurrent PPI or have recently stopped a PPI, which is especially useful after meals.

Key takeaways
• Annual polypharmacy medication reviews are recommended for patients on long-term therapies including PPIs.
• If symptoms change or patients develop new symptoms, endoscopy may be warranted.
• In patients that are symptom-free, a step-down approach to stopping PPI use may be considered.
• It is important to educate patients on potential rebound heartburn symptoms, as well as PRN management strategies.
Reference


Case history 2 – Ms Q

Ms Q is a 43-year-old office worker who was previously diagnosed with dyspepsia and has come to see you because of increasing symptoms of heartburn and regurgitation after meals and at bedtime, despite being highly compliant on PPI therapy (once-daily omeprazole 20 mg). She has had hypertension for the past 2 years, which is well controlled with a calcium channel blocker. She is a non-smoker who has reduced alcohol intake to about 6 units of alcohol a week after her initial diagnosis with GORD 1 year ago, but has gained about 3 kg, which she struggles to keep off.

What do you do?

A. Refer for an endoscopy
B. Issue her another prescription at the equivalent dose
C. Issue her another prescription, twice daily (correct)
D. Give her a different PPI at the equivalent dose
E. Give her an alginate as add-on therapy (correct)

Symptoms of GORD can be refractory, with an estimated 10–40% of patients having incomplete or no response to standard therapy. In patients such as this, it may be important to determine whether the patient still has reflux. Since this patient is compliant, it may be worth considering twice-daily PPI therapy before considering any additional studies such as endoscopy referral or reflux studies, which would be appropriate for a patient that was already receiving twice-daily PPI therapy. An alginate can also be considered as add-on therapy to protect the oesophageal mucosa. The symptoms may also be the result of oesophageal sensitivity, which may be further addressed by using pain modulators. This patient should have a yearly medication review and be instructed to return if she develops any new symptoms.

Key takeaways

- Symptoms of GORD can be refractory in patients.
- Consider the whole patient when determining an appropriate course of treatment to ascertain whether it is in fact reflux.
- Alterations to medication, including twice-daily PPI therapy, or add-on therapy with alginate may be appropriate.
- Consider additional endoscopy and reflux studies, if necessary.
References


Case history 3 – Mr C

Mr C is a 52-year-old smoker. He has suffered with heartburn for over 5 years, initially only getting symptoms if he ate late or after alcohol, but recently he has noted heartburn at other times as well. He is slightly overweight, is otherwise fit and well, and has no alarm symptoms. His friend takes a PPI for his heartburn and he thought a similar approach might work for him. He has come to see if you would prescribe some for him.

Which of the following would you do? Tick all that apply.

A. Give lifestyle advice (correct)
B. Advise use of a OTC alginate (correct)
C. Prescribe a full-dose PPI (incorrect)
D. Refer for an endoscopy (correct)
E. Test for H. pylori (incorrect)

The NICE guideline CG184, ‘Gastro-oesophageal reflux disease and dyspepsia in adults, 2014’, states: ‘Do not routinely offer endoscopy to diagnose Barrett’s oesophagus, but consider it if the person has GORD. Discuss the person’s preferences and their individual risk factors (for example, long duration of symptoms, increasing frequency of symptoms, previous oesophagitis, previous hiatus hernia, oesophageal stricture or oesophageal ulcers, or male gender).’

Based on this patient’s long duration of symptoms and increasing frequency of symptoms, it is clear that this man could be at risk of Barrett’s oesophagus and being a smoker also increases his risk of upper GI malignancy. This gentleman could be offered an upper GI endoscopy prior to starting him on a PPI. He could use regular doses of an alginate to help his symptoms until he has had his endoscopy. Equally alginates can be used in the 2-week washout period for patients who are required to stop their PPI prior to H. pylori faecal antigen testing or prior to an upper GI endoscopy. Lifestyle advice would include smoking cessation advice and weight management. H. pylori testing is not required in the primary care setting and is likely to be done at the time of the endoscopy.

Key takeaways

- Age, history of disease, worsening of symptoms of GORD and previous smoking history may support a referral for endoscopy to determine presence of Barrett’s oesophagus or upper GI malignancy.
- Endoscopy should not be done in patients who are currently receiving a PPI, rather it should be done prior to initiating PPI therapy, or after a 2-week washout period.

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• Symptoms of GORD including symptoms of rebound reflux can be managed with alginates prior to endoscopy during this washout period.

Reference


Case history 3 (continued) – Mr C

Mr C has been for his endoscopy and was found to have a 4 cm sliding hiatus hernia, a 3 cm-long suspected Barrett’s segment and grade A oesophagitis above that. He was given a 2-week supply of high-dose PPI by the hospital and told to see his GP for his results. Unfortunately, you don’t have any further information regarding the histology and the patient is due to run out of medication.

What do you do?

A. Refuse to prescribe any further PPI until you have received the histology results
B. Continue the patient on high-dose PPI long term
C. Continue the patient on full-dose PPI long term (correct)
D. Continue the patient on low-dose PPI long term
E. Offer full-dose PPI to be taken as required

Barrett’s oesophagus is an endoscopic and histological diagnosis. The biopsies confirm the presence of columnar metaplasia and intestinal metaplasia within the oesophagus and also look for evidence of dysplasia and neoplasia. This man should be prescribed full-dose PPI long term, which will heal his oesophagitis, prevent his Barrett’s segment from progressing and reduce the risk of developing dysplastic and neoplastic change within it. The existing Barrett’s will not revert to the native squamous mucosa so he will require endoscopic surveillance,\(^1\) the interval being determined by the histological findings. He should have a yearly medication review and be instructed to return if he develops any new symptoms, such as increased heartburn or dysphagia, in which case he should be referred for an urgent endoscopy.\(^2\)

Key takeaways

• Barrett’s oesophagus is diagnosed using both endoscopic and histologic assessments. Histologic assessment allows confirmation of metaplasia and can assess presence of neoplasia.
• Full-dose long-term use of PPI is appropriate in some circumstances, including a diagnosis of Barrett’s oesophagus
• A yearly medication review is appropriate for patients, as well as monitoring for the development of any new symptoms.

References

Miss D is a 28-year-old lady from Eastern Europe. She has developed upper abdominal pain and nausea over the past 2 months. She is not aware of anyone else in the family having ‘stomach problems’ and she is otherwise well. She hasn’t been vomiting or had black stools.

What would you do next?

A. Give *H. pylori* eradication therapy without testing first
B. Prescribe full-dose PPI once daily for 4 weeks
C. Test for *H. pylori* and then start full-dose PPI before the result is available (correct)
D. Test for *H. pylori* and await the result before starting treatment
E. Refer for an endoscopy

This lady has ulcer-type dyspepsia. Unlike for patients with reflux-type dyspepsia, it is important to exclude *H. pylori* in such patients, irrespective of whether or not they have taken medication that can cause dyspepsia. The prevalence of *H. pylori* has fallen significantly and in some areas is as low as 15%.\(^1\) However, this is not the case in people born in poorer countries, where it can be over 50%.\(^2\) The non-invasive options for testing for *H. pylori* are faecal antigen testing, carbon-13 urea breath tests and a locally validated, laboratory-based serology test.\(^3\) Patients must either be PPI-naive or have had a 2-week wash-out period before faecal antigen or breath testing can be done.\(^3\) In the case of this PPI-naive patient, she could be offered a prescription for full-dose PPI to commence as soon as she had done her stool sample but before the result is available.

**Key takeaways**

- Testing for *H. pylori* is important in patients with ulcer-type dyspepsia.
- Some common tests for *H. pylori*, such as the faecal antigen or breath tests, require a patient to be PPI-naive or have a 2-week wash-out period before testing can be done.

**References**


3. National Institute for Health and Care Excellence. Dyspepsia and gastro-oesophageal reflux disease: investigation and management of dyspepsia, symptoms suggestive of gastro-oesophageal reflux disease, or both. Full clinical guideline 184, 2014. Available at:
Case history 4 – Miss D

Unsurprisingly, this lady’s *H. pylori* test is positive. You now want to prescribe her with eradication therapy but you note she developed a rash the last time she was given flucloxacillin. She had a course of clarithromycin 6 months ago for a respiratory tract infection without any problems.

Which of the following regimens could you offer? Tick those that apply.

A. PPI + clarithromycin + metronidazole BD for 7 days  
B. PPI + bismuth + metronidazole + tetracycline BD for 7 days (correct)  
C. PPI + amoxicillin + metronidazole BD for 7 days  
D. PPI + amoxicillin + tetracycline + levofloxacin for 7 days

There are two issues to contend with in prescribing *H. pylori* eradication therapy for this lady. First, she is allergic to penicillin and second, she has had recent exposure to clarithromycin, which can result in antibiotic resistance. This means that amoxicillin and clarithromycin should be avoided.¹

Post-eradication testing should not be carried out routinely and only if the patients have ongoing symptoms using a carbon-13 urea breath test. Serology remains positive for life so cannot be used for post-eradication testing.

*H. pylori* eradication therapy¹

- First line
  - PPI + amoxicillin + clarithromycin/metronidazole BD for 7 days
- If allergic to penicillin
  - PPI + clarithromycin + metronidazole BD for 7 days
- If allergic to penicillin and had previous exposure to clarithromycin
  - PPI + bismuth + metronidazole + tetracycline BD for 7 days
- Second line: if patients still have symptoms, repeat triple therapy using the opposite of clarithromycin/metronidazole to previous regimen
  - If had both clarithromycin and metronidazole previously, use
    - PPI + amoxicillin + tetracycline/quinolone for 7 days
  - If allergic to penicillin (and has not had previous exposure to a quinolone)
    - PPI + metronidazole + levofloxacin BD for 7 days
  - If allergic to penicillin and has had previous exposure to a quinolone
    - PPI + bismuth + metronidazole + tetracycline for 7 days

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Key takeaways

- It is important to understand the patient’s antibiotic allergy and treatment history before initiating eradication therapy for H. pylori.
- Post-eradication testing is generally only required in the presence of ongoing symptoms using a breath test.
- PPI therapy is appropriate to use for management of symptoms during eradication therapy.

Reference


Case history 5 – Mrs B

Mrs B is a 50-year-old lady who has a troublesome cough. She has never smoked and is otherwise fit and well. She has been treated with inhalers for suspected asthma, with no benefit, and her chest X-ray is normal. On further questioning, she admits to having heartburn several times a week.

What would you do?

A. Refer to ENT
B. Prescribe full-dose PPI once daily for 4 weeks
C. Advise the patient to take an appropriately licensed alginate (either prescribed or purchased over the counter) (correct)
D. Refer for an endoscopy

This lady appears to be suffering from a reflux-related cough. This is a common extra-oesophageal manifestation of reflux-type dyspepsia and can occur even when the patient experiences mild heartburn and/or regurgitation. Patients with so called ‘laryngo-pharyngeal reflux’ (LPR) can develop respiratory and ENT symptoms such as cough and hoarse voice. As part of the consultation, ask about relevant red flag and alarm symptoms such as hoarse voice, smoking, dysphagia, and refer to ENT or for endoscopy only if there are concerns about cancer. Lifestyle advice should be given, as with any patient with reflux-type dyspepsia. While PPIs are often used, their efficacy for treatment of LPR is somewhat equivocal with some studies demonstrating an improvement in laryngeal symptoms after PPI therapy but others not. In a prospective randomised pilot study, appropriately licensed liquid alginate formulations have been shown to be effective at relieving the signs and symptoms of LPR.

Key takeaways

- Laryngo-pharyngeal reflux can involve ENT and respiratory symptoms, including cough, and may be more challenging to manage with PPI therapy.
- Alginate formulations have been shown to be effective in managing LPR.
References


Case history 5 (continued) – Mrs B

Instead of being treated with an alginate, Mrs B received a 4-week trial of high-dose PPI and returned to see you as planned. Her heartburn is 75% better but her cough persists. What would you do next? Tick all that apply.

A. Refer to ENT
B. Refer for an endoscopy
C. Continue the high-dose PPI (correct)
D. Advise the patient to take an over-the-counter alginate (correct)
E. Start ranitidine 300 mg nocte

PPIs are very effective at suppressing acid production from the parietal cells in the stomach. If acid is responsible for causing a patient’s reflux symptoms, then these drugs will help them immensely. Mrs B has not fully responded to high-dose PPI, which may lead one to wonder what is going on.

An estimated 10–40% of patients with typical reflux-type dyspepsia will not fully respond to standard-dose PPIs. During an episode of reflux, stomach contents (refluxate) enter the oesophagus. This acidic refluxate also contains recently ingested food residue, pepsin (the stomach’s proteolytic enzyme) and duodenal refluxate, in particular bile salts and bile acids. It is these non-acid components that can continue to cause symptoms despite high-dose acid suppression. Also, not all symptoms of reflux are attributable to liquid being regurgitated. Gaseous reflux occurs when people belch, resulting in an aerosol of acid, pepsin and bile being expelled up the oesophagus and into the larynx, pharynx, nasal passages and mouth, which can cause extra-oesophageal symptoms as outlined previously.

Alginates can have a role in managing patients with PPI-resistant reflux-type dyspepsia and in treating LPR. The anti-reflux raft that forms on top of the stomach contents prevents both liquid and gaseous reflux and traps pepsin and bile. Patients could take 10–20 ml of an appropriately licensed alginate 20 minutes after meals and at bedtime.

Pepsin is active in an acid environment, so high-dose acid suppression is still necessary to help partial PPI responders and patients with LPR, even if acid is not fully to blame for their symptoms. Patients could persist with high-dose PPI and alginate for at least 2 months when treating refractory reflux and LPR.

Ultimately, if patients don’t respond to this regimen, a referral to a gastroenterologist would be advisable for an endoscopy and (more importantly) oesophageal physiology studies.
Key takeaways

- While effective at suppressing acid production in the stomach, in an estimated 10–40% of patients PPIs may not be completely effective in reducing reflux-like dyspepsia. Pepsin and duodenal refluxate can also contribute to symptoms of dyspepsia.
- Liquid and gaseous reflux can impact extra-oesophageal symptoms of dyspepsia.
- Alginate formulations can form a raft on top of stomach contents preventing both liquid and gaseous reflux.
- Referral to a gastroenterologist for endoscopy and oesophageal physiology studies is appropriate in patients with persistent symptoms despite treatment.

Reference