HOW WE MANAGE THE DYSPEPTIC PATIENT WITH *HELICOBACTER PYLORI* 'INFECTION'

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'THE GOOD, THE BAD AND THE UGLY?'

All *H. pylori* are ugly and some are pathogenic, and therefore bad for our patients - we shall describe how we deal with these; however, some strains are undoubtedly harmless and may even be beneficial.

Dyspepsia refers to upper abdominal discomfort or pain. It can be associated with other symptoms such as heartburn, early satiety, bloating, nausea, vomiting and anorexia. Dyspepsia suggests peptic ulcer problems but it should be noted that peptic ulcer disease is only found in 20% of those referred for investigation. Several other causes should be considered, the most common of which is non-ulcer dyspepsia (Table 1). This diagnosis is reached after excluding all other causes of dyspepsia and it accounts for 50% of patients who have undergone investigation.[1]

TABLE 1
Common causes of dyspepsia.

- Peptic ulcer disease
- Non-ulcer dyspepsia
- Biliary tract disease
- Gastro-oesophageal reflux disease
- Gastric carcinoma
- Pancreatitis
- Pancreatic carcinoma

The discovery of *Helicobacter pylori* has radically changed the treatment of peptic ulcer disease, which has progressed from radical gastric surgery to nerve sectioning and, penultimately, to pharmacologically-elegant life-long drug blockade of acid production. Now it is a disease that can be successfully cured in a week:[2] all this in three decades, which is a spectacular example of medical progress. *H. pylori* infection is associated with at least 90% of duodenal ulcers and 70% of gastric ulcers, NSAIDs and other modes of injury or inflammation being responsible for the rest.[1] The eradication of *H. pylori* leads to successful healing and prevents recurrence of ulceration.

H. pylori is not only a risk factor for peptic ulcer disease, it is also an established risk factor for the development of gastric adenocarcinoma; this has lead to a suggestion that population-wide eradication of *H. pylori* should be considered.[3] However, only certain types of *H. pylori* predispose to gastric adenocarcinoma,[4] and it has also been shown that the same type of *H. pylori* that predisposes to gastric adenocarcinoma is absent in adenocarcinoma of the oesophagus or of the gastric cardia, and may exert a protective role.[5] Other evidence has also emerged suggesting that being *H. pylori*-positive protects against gastro-oesophageal reflux disease.[6-8] On the basis of this, our practice is to look for *H. pylori* only when there is a case for eradicating the organism in an individual patient.

HOW WE INVESTIGATE THE DYSPEPTIC PATIENT

We investigate as follows:

- All patients under the age of 45 years, with typical symptoms of peptic ulcer, should have their *H. pylori* status established by non-invasive means (either by serology or by carbon breath testing).
- Patients under the age of 45 years with alarm symptoms or signs, or an atypical medical history, should be referred for endoscopy (Table 2).
- All patients over the age of 45 years with new onset dyspepsia should be referred for endoscopy.
- In patients that are referred for endoscopy, the *H. pylori* status should be established in those who have erosive gastritis or duodenitis, gastric or duodenal ulcers, previous gastric surgery, a past history of peptic ulcer disease, gastric adenocarcinoma or B-cell MALToma (Mucosa-Associated Lymphoid Tissue Lymphoma).[9-13]

Our approach of eradicating *H. pylori* in those who are under 45 years with no alarm symptoms, without undertaking an endoscopic investigation, is not accepted by everyone. Others recommend that all who are *H. pylori*-positive should have an endoscopy before eradication

TABLE 2
Alarm symptoms and signs, and relevant past medical history which suggest the need for endoscopy.

- Unintentional weight loss
- Dysphagia
- Odynophagia
- Persistent vomiting
- Haematemesis/melaena
- Iron deficiency
- Epigastric mass
- Previous gastric surgery
- Non-steroidal anti-inflammatory drug use

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therapy, and eradication therapy should only be prescribed if there are endoscopic indications.[10-11] The rationale for this approach is that most *H. pylori*-positive individuals will not have endoscopic evidence of peptic ulcer disease. We believe that treating all *H. pylori*-positive individuals under 45 years with eradication therapy has benefits because in this way (1) demands on endoscopy services are lessened, and (2) the risk of missing a patient with quiescent peptic ulcer disease, who would benefit from eradication therapy, is reduced.

There are four methods of diagnosing *H. pylori* infection. Two are based on the organism having the enzyme urease which hydrolyses urea to ammonium hydroxide and carbon dioxide. Serology and the various breath tests are non-invasive, the others utilise endoscopic biopsies.

The 'CLO test' uses an endoscopic biopsy from the gastric antrum which is placed in a medium. If *H. pylori* is present, the alkaline ammonium hydroxide produced changes the colour of the medium from yellow to red. However, the medium must be incubated at 37°C for 24 hours before the colour change is read. The urea breath test uses ^{13}C- or ^{14}C-labelled urea. In those who are infected with *H. pylori*, labelled carbon dioxide is released into the expired air and measured using mass spectrometry (for ^{13}C) or a scintillation counter (for ^{14}C).

Serology can also be used to assess the *H. pylori* status. It is a cheap, easy and effective way of assessment but unfortunately it cannot be used to provide a prompt assessment of the response to eradication therapy.

Histology is also utilised in the detection of *H. pylori* and is regarded as the gold standard. *H. pylori* induces an acute and chronic inflammation of the gastric mucosa. Neutrophils and chronic inflammatory cells are seen and the Helicobacter organisms are often observed in the same specimen. The bacteria are best seen in the gastric antrum. However, recent therapy with acid suppression or antibiotics causes migration of Helicobacter to the gastric fundus and body, and in these circumstances biopsies should be obtained from the gastric body and fundus.

TO WHOM WE OFFER *H. PYLORI* ERADICATION THERAPY

We would give eradication therapy to the following:

- Those patients under 45 years who have typical symptoms of peptic ulcer disease, with no alarm symptoms and who are positive for *H. pylori* on non-invasive testing.
- Patients who after endoscopy are found to be *H. pylori*-positive and who have one or more of the following features: gastric or duodenal erosions, gastric or duodenal ulceration, previous gastric surgery or a past history of peptic ulcer disease, gastric carcinoma, B-cell MALToma.[9-13]

The recent guidelines in the *Maastricht Report* recommend that eradication therapy is also given to individuals having a first-degree relative with gastric carcinoma but the evidence for this is equivocal.[13] The guidelines also recommend that eradication therapy be prescribed for those who are or will be on long-term acid suppression for gastro-oesophageal reflux disease. The rationale behind this is that acid suppression may hasten the progression of *H. pylori* atrophic gastritis which is believed to be a stage in the pathogenesis of *H. pylori*-induced gastric adenocarcinoma. This hypothesis is controversial.

WHAT ERADICATION THERAPY WOULD WE USE?

Depending on the individual's past history of sensitivity and exposure to antibiotics, we would use one of the following regimens:

- Omeprazole 20 mg bd, amoxycillin 500 mg tds, metronidazole 400 mg tds.
- Omeprazole 20 mg bd, amoxycillin 1 g bd, clarithromycin 500 mg bd.
- Omeprazole 20 mg bd, clarithromycin 500 mg bd, metronidazole 400 mg tds.

  N.B. Lansoprazole 30 mg bd may be used instead of omeprazole 20 mg bd.

In general we would use omeprazole, amoxycillin and metronidazole as first-line therapy, as in our area they are effective and it is the least expensive regimen.

PATIENTS WHO REQUIRE FOLLOW-UP

We would follow up the following groups of patients, using the outlined methods:

- All patients with a gastric ulcer should undergo a repeat endoscopy to ensure the healing of the ulcer and at the same time establish efficacy of the eradication therapy.
- All patients with a complicated duodenal ulcer (i.e. those who have had a bleeding or a perforated duodenal ulcer) should have the efficacy of eradication established using a carbon breath test.
- Patients with persistent symptoms following a completed course of eradication therapy should have a carbon breath test.[11-13] Patients should have completed the eradication therapy for one month and not been on acid suppression therapy for one month before undertaking the carbon breath test.

The *H. pylori* status can be assessed (at gastroscopy) using either a CLO test or a biopsy. The CLO test, if positive, indicates persistent infection. However, the sensitivity of the test is affected by the prior use of antibiotics and acid suppressants. If a patient has been on either in the month prior to endoscopy, we recommend that biopsies be taken from both the gastric body and fundus for histological assessment of *H. pylori* status.

THE MANAGEMENT OF FAILED ERADICATION THERAPY

If eradication therapy had failed, it could be due to either poor patient compliance or *H. pylori* resistance to the antibiotics. We would then undertake one of two courses of action:

- If the patient is not known to be allergic to its components, we would prescribe an alternative triple therapy regimen.
- If the above course of action is not possible, we prescribe a quadruple therapy regimen comprising tetracycline 500 mg qds, metronidazole 400 mg tds, tripotassium dicitratobismuthate 120 mg qds and omeprazole

20 mg bd for 14 days.
- If there are recurrent failures of eradication therapy consideration is given to long-term acid suppression with an H_2 antagonist.

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