

Helicobacter Pylori

Helicobacter pylori is a motile, Gram-negative, curved or spiral bacillus. It was originally named *Campylobacter pyloridis*. It was then renamed *C. pylori* and later *H. pylori*, as its structure became better identified.

Pathogenesis

The full genetic code of *H. pylori* is now known.^[1] Specific genotypes are associated with severe morbidity. The most prevalent genotypes in patients with peptic ulcerations are *vacA*-positive and *cagA*-positive.^[2]

The presence of *vacA*, *cagA* and other strains of *H. pylori* is strongly associated with intestinal-type gastric cancer.^[3]

Prevalence

- The prevalence of *H. pylori* in many areas of the UK is lower than 15% and continues to fall.^[4]
- A Belgian study found the lowest prevalence in residents of Western European origin and the highest prevalence in those of North African origin.^[5]
- As a general rule, the prevalence of *H. pylori* increases with age.^[6]
- Globally, more than 50% of all people are infected.^[7]

Sequelae of Helicobacter pylori infection

More than 50% of the world's population are infected with *H. pylori*, so infection is not invariably associated with disease.^[7] However, it is present in almost all cases of duodenal ulcer and most cases of gastric ulcer. The recognition of the association between *H. pylori* infection and peptic ulcer disease was a major breakthrough in gastroenterology. Peptic ulcer is rare without either *H. pylori* or non-steroidal anti-inflammatory drugs (NSAIDs).^[8] There has been some debate about whether *H. pylori* is a cause of duodenal ulcer or whether the two are simply associated. There is a considerable weight of evidence supporting the latter, including the finding that a high proportion of children who have duodenal ulcer disease test positive for *H. pylori*.^[9]

H. pylori-positive patients have at least a six-fold greater risk of developing gastric adenocarcinoma than do those without infection.^[10]

Gastric mucosa-associated lymphoid tissue (MALT) lymphoma is a rare but interesting condition in that eradication of *H. pylori* causes clinical regression of the lymphoma in 75% of cases.^[11] In the remaining 25%, there appears to be translocation of genes with oncogenic properties.^[12]

The association between *H. pylori* infection and gastro-oesophageal reflux disease remains controversial. In fact some studies suggest that there is an inverse relationship and that its presence may confer a protective effect against reflux oesophagitis.^[13]

Presenting features

H. pylori infection may be asymptomatic - as above.

There may be symptoms of peptic ulcer disease (dyspepsia) - eg, fullness, bloating, early satiety and nausea.

Assessment^[14] ^[15]

Alarm signs like weight loss, vomiting, haematemesis, anaemia or dysphagia at any age require urgent referral for endoscopy.

Patients aged 55 years and older with unexplained and persistent recent-onset dyspepsia alone should also have endoscopy.

- Review medications for possible causes of dyspepsia - eg, calcium antagonists, nitrates, theophyllines, bisphosphonates, corticosteroids and NSAIDs. In patients requiring referral, suspend NSAID use. Consider the possibility of cardiac or biliary disease as part of the differential diagnosis.
- **Either** empirical treatment for four weeks with a full-dose proton pump inhibitor (PPI) **or** testing for and treating *H. pylori* may be employed. Current evidence offers no guidance on preference.
- A two-week washout period following PPI use is necessary before testing for *H. pylori* with a breath test or a stool antigen test.
- If there is failure to resolve, or relapse on stopping acid suppression, evidence suggests testing and treating *H. pylori* if the test is positive.
- *H. pylori* eradication therapy without testing first is not recommended and is likely to be very wasteful of resources, especially as this is likely to cause some dilemma if the patient returns with symptoms.^[16]
- Eradication of *H. pylori* in patients who are about to start NSAIDs substantially reduces the risk of endoscopic and complicated ulcers.^[17]

Testing for Helicobacter pylori

Non-invasive testing is useful only if it will alter the subsequent management of the patient. The National Institute for Health and Care Excellence (NICE) offers advice on which test to use:^[14]

- ¹³C urea breath tests or stool antigen tests are the recommended way of testing for *H. pylori*, although laboratory-based serology can be used if locally validated. Stop antisecretories or bismuth two weeks before the test.
- The breath test is the only currently validated method for assessing eradication in primary care.

Treatment

Offer eradication therapy to all patients with positive tests for *H. pylori*.

There are several regimes. There is probably no difference between the various PPIs available, provided that they are used at the equivalent dose and this is a matter of personal choice.

The following is based on the recommendations of NICE.^[14] ^[18]

Recommended first-line regimes

These are optimum regimes on current evidence:

- A seven-day course of PPI plus either amoxicillin 1 g and either clarithromycin 500 mg or metronidazole 400 mg - all three given twice a day.
- Choose the treatment regime with the lowest acquisition cost and take into account previous exposure to clarithromycin or metronidazole.
- For people allergic to penicillin use a PPI, clarithromycin and metronidazole - all twice a day for seven days.
- For people allergic to penicillin who have previously been exposed to clarithromycin, use a PPI, metronidazole, tetracycline and bismuth.

Second-line *H. pylori* eradication regimes

- For people who do not respond to first-line therapy, offer a PPI, amoxicillin and either clarithromycin or metronidazole (whichever was not used first-line).
- For people who have had previous exposure to clarithromycin and metronidazole, offer a seven-day, twice-daily course of treatment with a quinolone or tetracycline (whichever has the lowest acquisition cost).
- For people who are allergic to penicillin and who have not had previous exposure to a quinolone, offer a seven-day, twice-daily course of a PPI, and either metronidazole or levofloxacin.
- For people who are allergic to penicillin and who have had previous exposure to a quinolone, offer a PPI, amoxicillin, bismuth, metronidazole and tetracycline.

Treatment failures

If there is failure of treatment, this is usually due to poor compliance or to antibiotic resistance:

- If there was poor compliance, a more tolerable regime may be required. Abdominal discomfort and diarrhoea are very common but the patient should be encouraged to persist to achieve eradication.
- Resistance can even develop during treatment, especially with a single antibiotic.
- Metronidazole and clarithromycin are the antibiotics most implicated in resistance; resistance rates vary across the UK.^[19]

Antibiotic resistance

It would be reasonable to have local protocols based upon local patterns of antibiotic resistance.^[20] Resistance to metronidazole (in particular) is highly variable.

- The Health Protection Agency reports that the prevalence of *H. pylori* antibiotic resistance varies within the UK depending on location. It is around 20-63% for metronidazole and 4.4-11% for clarithromycin.^[19]
- Metronidazole resistance is low in rural areas within the UK but can be as high as 65% in urban areas with large immigrant populations.^[20]
- Amoxicillin resistance is rare but does occur.
- Resistance can be acquired during treatment.

Patients who are not cured with two consecutive treatments, including clarithromycin and metronidazole, will have at least single and usually double resistance. No standard third-line therapy exists, although isolated studies have reported success with a PPI, bismuth subcitrate, tetracycline and metronidazole.^[21] Seek specialist advice if second-line therapy fails. European guidelines recommend culture before treatment based on the microbial antibiotic sensitivity in such circumstances.^[22]

Benefits of treatment^[23]

- There is definitive evidence that eradicating *H. pylori* improves remission rates for gastric and duodenal ulcers and is superior and more cost-effective than maintenance acid suppressive therapy in preventing duodenal ulcer.
- One study found that *H. pylori* eradication was more successful in decreasing recurrent gastroduodenal ulcer bleeding than ulcer healing treatment alone.
- *H. pylori* eradication is beneficial in patients with dyspepsia who have been identified as *H. pylori*-positive but have not had an endoscopy ('test and treat').^[14]
- *H. pylori* eradication has been proposed as first-line treatment for infected patients with stage I low-grade gastric MALT lymphoma.
- The evidence concerning the protective effect of *H. pylori* against gastric carcinoma is complex but the consensus is that it should be eradicated as soon as possible and best before pre-cancerous lesions are present.
- Re-infection rates are variable. One study reported a re-infection rate of 1.8%. Developed countries had lower re-infection rates compared with those of developing countries.^[24]

Follow-up^[14]

- In dyspepsia it is only necessary to check for *H. pylori* eradication in patients whose symptoms return.
- Patients with peptic ulcer should have a re-test (gastric or duodenal) six to eight weeks after beginning treatment.
- Serology can remain positive for up to one year after eradication.
- If the patient was taking NSAIDs it will be necessary to discuss further management.
- Low-dose misoprostol is less effective than acid suppression.

See separate [Peptic Ulcer Disease](#) article for details concerning the management of non-healing ulcers.

Prevention

- Studies suggest that probiotics and lactobacilli reduce the activity of *H. pylori*.^[25]
- It is generally advocated that *H. pylori* testing should be driven purely to confirm an infection as the cause of disease and then to eradicate it.
- The risk:benefit ratio of *H. pylori* eradication in asymptomatic patients requires further evaluation. A large trial of Asian patients provided moderate evidence that eradication reduced the risk of gastric carcinoma but studies of patients from other ethnic communities are required.^[26]
- *H. pylori* infection has been implicated in the aetiology of coronary heart disease but this has recently been refuted.^[27] Likewise, evidence linking [cirrhosis](#), gastroduodenal ulcers and *H. pylori* is lacking.^[28]

There is also ongoing work to produce a vaccine against the organism.^[29]

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