Helicobacter pylori: to treat or not to treat

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Whether to treat Helicobacter pylori *infection is a common problem for GPs. Benefits from successful treatment are yet to be unequivocally determined in patients other than those with a current or past history of peptic ulceration or those in whom the rare gastric MALT lymphoma has been diagnosed.*

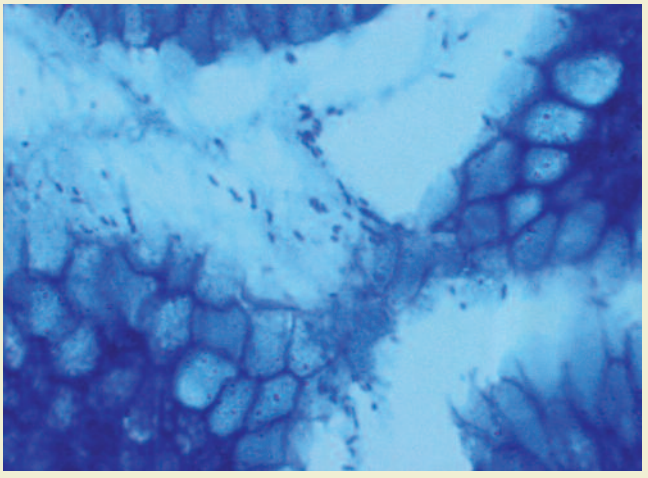

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Figure. Gastric biopsy from a patient with a chronic duodenal ulcer, showing numerous *Helicobacter pylori*.

The prevalence of infection with *Helicobacter pylori* varies widely. In Australia, up to 40% of the population is infected, while in some developing countries this figure is greater than 90%. In most cases, infection is acquired in childhood, probably through faecal–oral spread. The success of a course of eradication therapy (typically triple therapy) can be established by a urea breath test or, in the case of a gastric ulcer or a complicated (e.g. bleeding) duodenal ulcer, by histology or a rapid urease test performed on gastric biopsies taken at follow up gastroscopy to assess healing. Once successfully treated, re-infection is rare.

H. pylori is now accepted as the main cause of peptic ulcers. It is also involved in the pathogenesis of gastric adenocarcinoma and the rare gastric mucosa associated lymphoid tissue (MALT) lymphoma. Most patients infected with the bacterium, however, remain asymptomatic. Why only some people develop clinical manifestations of disease is probably related to both host factors and bacterial genotype – the cagA and vacA genotypes, for example, are known to be the more virulent *H. pylori* strains. In spite of this, debate exists as to which infected patients should be treated.

Proponents of the dictum 'the only good *H. pylori* is a dead one' believe that eradication therapy should be given to all those infected. Antagonists of widespread treatment argue that treating *H. pylori* on a large scale would increase antibiotic resistance, making it more difficult to treat infection in those in whom therapy is definitely indicated. Furthermore, widespread treatment would generate significant costs and side effects, such as antibiotic associated colitis and anaphylaxis, which can lead to significant morbidity. Finally, it is possible that *H. pylori* has some, as yet to be proven, health benefit.

H. pylori and gastrointestinal disease

Peptic ulcer disease

H. pylori is responsible for approximately 90% of duodenal ulcers and 70% of gastric ulcers, and infection with this organism carries a lifetime risk of developing an ulcer in the order of 20% (Figure). The other major cause of peptic ulceration is NSAIDs, including aspirin. Current evidence suggests that these drugs have a synergistic effect with *H. pylori*, further increasing the risk of developing a peptic ulcer. Additional risk factors for peptic ulcer disease include the use of selective serotonin reuptake inhibitors, smoking and a family history.

Present evidence dictates that anyone found to have a peptic ulcer or a past history of a gastric or duodenal ulcer should, if infected with *H. pylori*, be prescribed a course of therapy aimed at eradicating this bacterium. Whether those who are infected and are taking NSAIDs should be similarly treated remains to be determined, although recent studies support this approach. There is no evidence yet that therapy to eradicate *H. pylori* should be prescribed merely to reduce a person's lifetime risk of developing an ulcer.

Gastro-oesophageal reflux disease

H. pylori is not a risk factor for gastro-oesophageal reflux disease (GORD), and some studies have even suggested that it may actually protect against the condition. Therefore, successfully treating *H. pylori* may potentially precipitate or aggravate GORD. Concerns that the efficacy of acid suppressants such as proton pump inhibitors may be impaired in the presence of *H. pylori*, and that the use of these agents in patients infected with the organism may be associated with the more rapid development of gastric atrophy, have yet to be proven.

Nonulcer dyspepsia

Despite many studies, a definite link between *H. pylori* infection and functional dyspepsia remains to be demonstrated, and accordingly, symptoms generally do not improve following treatment to eradicate the organism. While a 'test and treat' policy is often recommended in young dyspeptic patients in the absence of alarm symptoms such as dysphagia, anorexia and weight loss, a

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significant proportion of those who improve probably have undiagnosed ulcers. In addition, treating *H. pylori* is rarely of benefit in patients with dyspepsia who have not been endoscoped because most of this group have GORD or functional dyspepsia.

Gastric cancer

H. pylori has been classified as a class 1 carcinogen by the World Health Organization. As yet, however, it is not known whether eradicating this organism definitely reduces the risk of developing stomach cancer since other variables, such as a family history of stomach cancer and dietary and environmental factors, are involved. Also, it is not yet possible to conclude that eradicating infection in someone with a family history of gastric cancer will subsequently eliminate their chance of developing this disease. It is notable that the incidence of gastric cancer in Africa is low in spite of a high prevalence of infection with *H. pylori*. In addition, the incidence of stomach cancer started to fall in Western society before the discovery of *H. pylori*, although this may be due to improved living standards as poor hygiene is associated with an increased prevalence of the bacterium.

Gastric MALT lymphoma

Primary gastric mucosa associated lymphoid tissue (MALT) lymphoma is a rare disorder that in most cases is associated with *H. pylori* infection. Resolution of low grade disease often occurs following eradication of the organism. Surgery and chemotherapy may also be necessary with more severe disease.

Gastritis

Infection with *H. pylori* universally causes gastritis but in the vast majority of patients the gastritis is asymptomatic. While eradicating *H. pylori* in these patients may potentially reduce the risk of developing an ulcer or gastric cancer, the significant costs and side effects of the treatment need to be balanced against the possible benefits.

H. pylori and nongastrointestinal disease

Infection with *H. pylori* has been implicated in the pathogenesis of a number of disorders unrelated to the gastrointestinal tract. These include coronary artery disease, unexplained iron deficiency anaemia, thrombocytopenia, sudden infant death syndrome, growth retardation and migraine headaches. However, there is no convincing evidence that *H. pylori* is the cause of these conditions.

So who should we treat?

Without doubt, those with a current or past history of a peptic ulcer who are infected with *H. pylori* should be prescribed a course of eradication therapy as successful treatment will reduce recurrence to less than 5% per year. (Available triple therapy combinations are Klacid HP 7 and Losec HP 7; both are combinations of omeprazole, amoxycillin and clarithromycin). Current evidence suggests that patients with concurrent NSAID usage should also be treated. In the case of MALT lymphomas, low grade lesions may be cured and the course of high grade ones modified with anti-*H. pylori* treatment, although long term clinical follow up is still required.

In patients with GORD, there is no role for *H. pylori* eradication therapy. Apart from potentially precipitating or aggravating symptoms in established GORD, there is some evidence that treating *H. pylori* may increase the risk of developing oesophageal adenocarcinoma. Although it is not uncommon for patients with GORD to feel better following a course of triple therapy, the symptomatic improvement in most cases results from the acid suppressant (usually a proton pump inhibitor) present in these combination therapies.

While it is tempting to propose that appropriate treatment for *H. pylori* may reduce the risk of developing gastric cancer, particularly where there is a family history of this condition, clear-cut evidence in this regard is lacking. Hopefully the true benefit of *H. pylori* therapy in this group will soon become apparent from ongoing studies.

Although gastritis is a universal finding in those infected with *H. pylori*, in itself it does not cause symptoms. Therefore, there is no symptomatic gain from treating this group with eradication therapy. Similarly, there is no proven advantage in prescribing anti-*H. pylori* therapy for those with nonulcer or functional dyspepsia. However, some of these patients will achieve symptom relief through treatment of an undiagnosed ulcer or GORD with the acid suppressant agent present in combination therapies.

Conclusion

The only patients to definitely benefit from *H. pylori* eradication are those with a current or past history of peptic ulceration and those in whom the rare gastric MALT lymphoma has been diagnosed. In all others, a gain from treatment is yet to be unequivocally determined. MT

Further reading

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