ADVANCES IN UPPER GI DISORDERS

Current Developments in the Management of Upper GI Disorders

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Does Treatment of *Helicobacter pylori* Infection Pose a Risk to Patients With GERD?

Nimish Vakil, MD
Clinical Adjunct Professor
Department of Medicine
University of Wisconsin School of Medicine and Public Health
Madison, Wisconsin

G&H Are there any specific groups of patients with gastroesophageal reflux disease that should be tested for *Helicobacter pylori* infection?

NV There are two groups of patients that should be considered for testing. The first group includes all patients who have a history of peptic ulcer disease, who have a family history of gastric cancer, and who come from countries with a high prevalence of gastric cancer, such as China, Taiwan, Japan, and some countries in South America. In the United States, non-White immigrants have a higher risk of gastric cancer compared with non-Hispanic White males, with Korean American men aged 50 years or older having the highest risk. The patients in the first group have something in their history that puts them at risk of serious complications of *H pylori* infection, which is a clear indication for intervention.

> Once *H pylori* infection is found, treatment should always be offered to the patient.

A second group that should be considered for testing includes all patients who are going to be on long-term proton pump inhibitor (PPI) therapy for gastroesophageal reflux disease (GERD). In infected individuals, PPI therapy can lead to progression of chronic gastritis and to atrophy, and eradicating *H pylori* can prevent this progression. The evidence comes from a randomized controlled trial (RCT) comparing GERD patients treated with omeprazole vs fundoplication. Among *H pylori*–positive patients on omeprazole, atrophic gastritis developed in 18 of 59 patients (31%) over 5 years compared with none among fundoplication patients who did not receive acid suppression ($P<.001$). Among *H pylori*–negative patients, only 2 of 46 (4%) developed atrophy on omeprazole. The patients in this second group have none of the factors present in the first group of patients. Whether to test patients in this second group is an individual decision for practitioners in joint decision-making with patients. The decision depends on patient preference and the risk for gastric cancer in the individual.

G&H If a patient with GERD is found to have *H pylori* infection, should it always be treated?

NV Once *H pylori* infection is found, treatment should always be offered to the patient. *H pylori* infection is a cause of gastric cancer and of gastric mucosa-associated lymphoid tissue lymphoma, and eradicating the organism substantially reduces the risk. Gastric cancer is the fifth most common cause of cancer death, and approximately 30,300 new cases are diagnosed each year in the United States, with a 5-year survival rate of only 32% to 36%. A meta-analysis in 2025 (11 RCTs) confirmed reduced gastric cancer risk in infected individuals with *H pylori* eradication (relative risk, 0.64; 95% CI, 0.48-0.84).

I think this question emphasizes that by performing the test, one is committing to offering treatment if the test is positive. When a patient tests positive for *H pylori,* it is not ethical to identify a potential carcinogen and then not offer the patient a treatment. Regardless of the GERD issue, the health care practitioner is obligated to offer the

patient treatment for prevention of gastric cancer. Unfortunately, it has been shown that there are patients who have been tested and after testing positive have not been offered treatment for *H pylori.*

G&H Does the presence of GERD influence the choice of treatment for *H pylori* infection?

NV The presence of GERD should not affect the choice of antibiotic treatment. Practical considerations include cost, prevalence of antimicrobial resistance in the community, and patient-specific factors such as drug allergies.

In the United States, high levels of acid suppression are used with *H pylori* treatment to concentrate the drugs. GERD treatment is augmented during *H pylori* treatment, for example, by doubling the dose of a PPI in a patient who is on a single dose. Otherwise, the 2-week antibiotic course does not impact a patient's GERD treatment.

G&H Does eradication of *H pylori* affect GERD symptom severity?

NV Several studies have shown no change in GERD symptoms after eradication of *H pylori* in patients who are on PPI therapy in standard doses for treatment of GERD, whereas other studies have shown mild symptom worsening particularly in those on low-dose PPI therapy. The effects may vary according to the degree and location of gastritis caused by *H pylori* and its effect on acid secretion. For example, patients with antral predominant gastritis and increased acid secretion may have benefit in GERD symptoms after eradication therapy, whereas those with corpus predominant gastritis and decreased acid secretion may report a small increase in symptoms after acid secretion is restored to normal. A recent meta-analysis found that there was moderate heterogeneity in the studies evaluating the development of GERD after *H pylori* eradication. Risk estimates for worsening of GERD after eradication therapy derived from RCTs did not reach statistical significance.

It is important to recognize that many studies reporting an increase in symptoms of heartburn after eradication of *H pylori* are from Asia, where very low doses of PPI therapy (as low as 10 mg of omeprazole) are used, which is not a common practice in Western populations.

G&H Is there consensus on treatment of *H pylori* infection in GERD?

NV The Taipei Global Consensus II published in 2025 concluded that there is no concern for an increased risk of GERD or esophageal adenocarcinoma (EAC) after *H pylori* eradication. Eradication is advised for GERD patients on long-term acid suppression, as it may reduce corpus predominant gastritis and limit atrophic progression, although evidence for histologic reversal of atrophy that has already developed remains limited.

G&H How do you explain the apparent negative association between *H pylori* infection and Barrett esophagus/EAC that is seen in some countries?

NV In population-based studies, there is a negative association between Barrett esophagus, when comparing infected individuals to population controls (odds ratio [OR], 0.44), but this negative association disappears when comparing to GERD controls (OR, 0.96), confirming that GERD is the primary mediator of risk. Multiple studies also show an inverse relationship with EAC but not with squamous cell cancer, again suggesting a reflux-based mechanism. Initially, it was thought that the protective effect of *H pylori* infection was from a reduction in acid secretion caused by infection-induced gastric atrophy; however, case-control studies from Finland and Sweden suggest that the protective effect is unrelated to atrophy. Patients infected with *CagA*-positive strains have the greatest benefit. The mechanism is unknown but may involve changes in the microbiome at the GE junction, changes in ghrelin levels, and activation of a neuro-immunologic cholinergic anti-inflammatory pathway by *H pylori* infection.

There are significant beneficial effects of eradication in preventing peptic ulcer disease and gastric cancer.

A question that many clinicians and patients have is whether eradication therapy is associated with an increased risk of developing esophageal cancer. A large Nordic cohort study of over 660,000 patients who received *H pylori* eradication treatment found no increased risk of EAC; in fact, the risk decreased over time after treatment (standardized incidence ratio, 0.73 at 11-24 years posttreatment).

G&H How would you advise nonspecialists and primary care providers who might be reluctant to treat the infection in these circumstances?

NV As I mentioned, there are no significant harmful effects of *H pylori* eradication with regard to EAC and minor effects on reflux disease symptoms. There are significant beneficial effects of eradication in preventing peptic ulcer disease and gastric cancer. It is important to remember that the United States is projected to have over 30,000 new gastric cancer cases, compared with an estimated 7000 to 8000 new EAC cases annually. The magnitude of gastric cancer is much greater than that of EAC.

Any reluctance could reflect a continued influence effect, which is when people continue to rely on misinformation even after it has been corrected. The sensationalist story (that getting rid of *H pylori* might worsen the gut or cause esophageal cancer) tends to permeate through the community and linger in the memory, whereas more sober, thoughtful evaluations, which subsequently follow the sensationalist story, often do not have the same impact as the original story.

G&H What future research is needed on this topic?

NV The negative association between *H pylori* infection and Barrett esophagus/EAC in population-based studies remains a subject of interest. Understanding the mechanism may offer a novel approach to treat both reflux disease and perhaps prevent the development of Barrett esophagus.

Disclosures

Dr Vakil has received stock options from ISOThrive.

Suggested Reading

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