# Rationale for a *Helicobacter pylori* Test and Treatment Strategy in Gastroesophageal Reflux Disease

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**KEYWORDS**

• *H pylori* • GERD • Proton pump inhibitors • Intestinal metaplasia • Gastric atrophy

**KEY POINTS**

- Proton pump inhibitors worsen corpus gastritis in patients infected with *Helicobacter pylori* and increase the rate of progression to intestinal metaplasia, both of which are precursor lesions for cancer.
- In animal models of gastric cancer, progression to gastric cancer can be demonstrated in infected animals that are treated with proton pump inhibitors.
- Eradicating *H pylori* prevents the progression to intestinal metaplasia and atrophy and should be offered to infected patients who are about to commence long-term proton pump inhibitor therapy, especially in countries and populations in which the incidence of gastric cancer is high.

## INTRODUCTION

*Helicobacter pylori* infection causes a chronic gastritis that progresses to atrophy and intestinal metaplasia in a proportion of cases. Gastric atrophy and intestinal metaplasia are precursor lesions for gastric cancer. Eradication of *H pylori* infection can reverse atrophy, but intestinal metaplasia has not been reversible in most human studies. There is a great deal of interest in understanding the mechanisms for progression from chronic gastritis to atrophy and intestinal metaplasia. Identifying risk factors for the progression of atrophy is important in clinical practice because it offers a way to prevent gastric cancer. One risk factor that has been identified is the administration of proton pump inhibitors (PPIs) to patients infected with *H pylori* infection. In this article,

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the data on the risk of administering PPIs to patients with *H pylori* infection and the rationale for eradicating *H pylori* before initiating long-term PPI therapy are reviewed.

## THE EFFECT OF PROTON PUMP INHIBITOR TREATMENT ON CHRONIC *HELICOBACTER PYLORI*–RELATED GASTRITIS

In 1996, Kuipers and colleagues[1] studied 2 cohorts of patients, one from Sweden treated with fundoplication for reflux disease and the other from the Netherlands who were treated with omeprazole 20 mg or 40 mg for gastroesophageal reflux disease (GERD). Both cohorts were followed for an average of 5 years. Patients in the fundoplication group did not receive acid inhibitory therapy over the course of the study. Histology was performed at baseline in the fundoplication group and histology and serology for *H pylori* were performed in the PPI therapy group. In the fundoplication group, there were 31 patients infected with *H pylori* at baseline, and none developed atrophic gastritis over the follow-up period. In the cohort of 59 *H pylori*–infected patients treated with omeprazole, corpus gastritis increased significantly from 59% to 81%. Atrophic gastritis increased from 0% at baseline to 4%, representing an annual increase of 0.8% in the prevalence of atrophy. Intestinal metaplasia did not develop in any of the patients. In patients who were not infected with *H pylori*, there was no progression to atrophy in either of the cohorts.

In another study, in 230 patients with GERD treated long term with omeprazole, 4.7% of the patients with moderate to severe gastritis who were infected with *H pylori* developed gastric atrophy. In contrast, only 0.7% of *H pylori*–negative subjects who had moderate to severe gastritis at baseline developed gastric atrophy.[2]

## THE EFFECT OF *HELICOBACTER PYLORI* ERADICATION ON CHRONIC GASTRITIS AND ATROPHY RELATED TO *HELICOBACTER PYLORI* INFECTION

A randomized controlled trial evaluated the effect of *H pylori* eradication in patients with GERD who had been treated with PPIs for 12 months or longer. Two hundred thirty-one patients infected with *H pylori* were randomized to omeprazole or omeprazole triple therapy.[3] There was significant corpus gastritis at baseline in 50% of cases, and it remained unchanged at 1 and 2 years. In contrast, in the triple therapy group, moderate to severe gastritis was present at baseline in 55% of patients and decreased significantly to 4% and 5% at 1 and 2 years, respectively. Atrophy of the glands in the corpus was present in 24% of patients in the omeprazole group and remained unchanged at 1 and 2 years. In the triple therapy group, corpus glandular atrophy declined significantly with eradication from 27% at baseline to 19% and 14% at 1 and 2 years, respectively. When patients with moderate and severe atrophy were considered separately, the results were striking. Moderate to severe atrophy declined from 15% to 3% at 1 year and 5% at 2 years. These studies show an improvement in an intermediate marker on the progression to gastric cancer but do not prove that cancer can be prevented by eradication therapy. Long-term studies in humans to prove the hypothesis that cancer can be prevented have many challenges, including the prolonged duration of follow-up required and the ethics of not offering eradication therapy to controls. Animal models offer a potential solution to these challenges.

## GASTRITIS AND ADENOCARCINOMA IN MONGOLIAN GERBILS

Mongolian gerbils infected with *H pylori* are a model for gastric cancer. The lesions created by *H pylori* are similar to the lesions produced in human gastric mucosa. In an experimental study, young Mongolian gerbils were infected with *H pylori* 1 month