

# Clinical spectrum of *H. pylori* related gastrointestinal disorders-an overview

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*Helicobacter pylori* (*H. pylori*) infection is a gastric infection that is recognized as the main cause of chronic gastritis, peptic ulcer disease, and gastric cancer including MALT (mucosa-associated lymphoid tissue) lymphoma. *H. pylori* infection correlates inversely to socioeconomic conditions, with infection rates in developed countries with around 10%-20%, while rates in developing countries with 80%–90%. Once *H. pylori* infection occurred, the infection almost persists for life long unless antibiotic therapy is administered. Most infected individuals experience asymptomatic gastritis, although recurrent gastroduodenal ulceration may occur in 10%–15% of the infected population. The incidence of gastric cancer is approximately 1% of infected individuals developing adenocarcinoma and gastric MALT lymphoma. *H. pylori* is the major trigger for a sequence of changes in the gastric mucosa, progressing from inflammation to superficial gastritis, chronic atrophic gastritis, intestinal metaplasia, dysplasia, and finally carcinoma. A recent study has suggested that the presence of *H. pylori* is necessary for the development of noncardia gastric cancer.

## **The *H. pylori* and association with gastroesophageal reflux disease (GERD)**

*H. pylori* has a profound impact on the gastric mucosa and to a lesser extent on gastrin, somatostatin, and gastric acid secretion. GERD is the result of an increased esophageal exposure to gastric acid. Gastric acid secretion is the key factor in the relationship between *H. pylori* and GERD. In patients who develop chronic atrophic gastritis as a consequence of *H. pylori* infection, gastric acid secretion decreased and acid would no longer appear to be produced in a critical amount for the induction of GERD. *H. pylori* induces an antrum predominant gastritis with increased gastric acid secretion. This is also reflected in the different association of antrum predominant gastritis with duodenal ulcer and pangastritis with gastric ulcer. Antrum predominant gastritis is also the usual phenotype in GERD patients infected with *H. pylori*. In patients with atrophic gastritis reported increased acid production following *H. pylori* eradication and induction of GERD in a subset of patients. From these pathophysiological considerations the risk for GERD development following eradication seems to be low and is restricted to patients with atrophic gastritis in whom acid secretion recovers and meets with the premise of an abnormal gastroesophageal reflux barrier.

### **The *H. pylori* and association with dyspepsia**

Dyspepsia can be defined as persistent or recurrent pain or discomfort localized to the upper abdomen. A substantial proportion of patients who present for diagnostic evaluation for dyspepsia are not found to have evidence of chronic ulcer, reflux esophagitis and malignancy. The pathogenesis of functional dyspepsia remains uncertain, although abnormalities of visceral perception, motor dysfunction, and gastritis or duodenitis have been considered. Approximately 50% of patients with dyspepsia have *H. pylori* gastritis. To establish that *H. pylori* is a causal factor requires evidence that infection precedes the development of symptoms and that symptoms are abolished by eradication of the infection. In acute ingestion studies, two volunteers who ingested *H. pylori* developed epigastric pain, nausea, anorexia, early satiety and belching. The best evidence of a possible role of *H. pylori* in functional dyspepsia may come from studies of eradication therapy. Long-term effect of *H. pylori* eradication, all patients had early improvement in symptoms. However, those with persistent *H. pylori* infection had relapses of dyspepsia at 1 year.

### **The *H. pylori* and association with duodenal ulcer**

*H. pylori* infection is the most common cause of duodenal ulcer disease. Possible explanations are difference in host, in social, dietary or other environmental factors, in the strain of *H. pylori*, or both host and bacterial factor. Host factors include genetic susceptibility to *H. pylori* infection, excess gastric acid secretion. Potential *H. pylori* virulence factors include Cag A protein and the vacuolating cytotoxin. Eradication of *H. pylori* enhances duodenal ulcer healing and greatly reduces the ulcer relapse rate.

### **The *H. pylori* and association with gastric ulcer**

Many people have *H. pylori* infection, but only a small amount of infected individuals have peptic ulcer. Gastritis is more persistent and severe in gastric ulcer patients than in duodenal ulcer; however, it seems that the effect of eradication therapy of *H. pylori* in gastric ulcer is similar. Successful eradication of *H. pylori* infection resulted in both better ulcer healing and a reduced ulcer relapse rate than in *H. pylori* positive patients without eradication patients.

### **Association of *H. pylori* infection with gastric carcinoma**

A prospective study found that 37% of infected Mongolian gerbils developed adenocarcinoma and several developed carcinoids during 62 Weeks. Most other experiments have required additional carcinogens, such as N-methyl-N-nitrosourea or N-methyl-Nnitro-N-nitrosguanidine, to demonstrate potentiation of a carcinogenic effect by *H. pylori*. Most of studies suggest that *H. pylori* can trigger carcinogenesis. It seems *H. pylori* triggers a proliferative response in the epithelium, perhaps related to the delivery of CagA into the epithelial cells, whereas components of *H. pylori* such as CagA and VacA cause

increased apoptosis to balance the proliferative effect. Although these events are not necessarily carcinogenic, the associated inflammation, reactive oxygen species, nitric oxide, HCl, and ammonia may generate known carcinogens, such as nitrosodimethylamine.

### **Extradigestive manifestations of *Helicobacter pylori* infection**

Chronic *H. pylori* infection localized in the stomach, could be involved in the pathogenesis of some extradigestive diseases, such as short stature in children, anemia, or coronary and liver diseases. As peculiar *H. pylori* cytotoxic strains may induce a local chronic release of cytokines, or vasoactive or procoagulant substances by the immune cells in susceptible subjects, several studies have been designed to assess a role of *H. pylori* infection in some extragastric idiopathic diseases. However, as *H. pylori* eradication often leads to the disappearance of or an improvement in some extradigestive pathologies, further well designed in vitro, epidemiological, and controlled intervention studies are needed.