

A historical perspective of *Helicobacter* gastroduodenitis and its complications

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The discovery of *Helicobacter pylori* was one of the most notable in gastroenterology – and indeed medicine. The century before Marshall and Warren's discovery is peppered with isolated accounts of spiral-shaped bacteria in the stomach. The discovery of *H. pylori*, and the recognition of its importance, came about as a consequence of combined clinical, pathological and microbiological work. The discovery has transformed the treatment of peptic ulcers and other related diseases.

Key words: antibiotic resistance; gastric cancer; *Helicobacter pylori*; MALT lymphoma; peptic ulcer disease; treatment.

INTRODUCTION

The discovery of *Helicobacter pylori* (*H. pylori*) is one of the most significant landmarks in gastroenterology. The organism is associated with a wide range of gastroduodenal pathology, ranging from peptic ulcer disease to gastric cancer. In the past few years, many of the issues concerning *H. pylori* have been clarified. Epidemiological studies have suggested new associations, and further insights into the pathogenesis have been gained by investigating the virulence of the bacterium and the host response to it. Significant improvements have been made in treatment regimes. The modern era of *Helicobacter* study began in earnest in the early 1980s with Warren and Marshall's Nobel-prize-winning discovery. However, throughout the preceding century

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a number of researchers had very nearly discovered this elusive micro-organism and uncovered its role in gastroduodenal disease.

HELICOBACTER PYLORI: A HISTORY

The *H. pylori* bacterium has been present for at least 3000 years. Traces are present in faecal specimens from mummified human remains from the Andean area of South America.¹ The presence of gastric spirochaetal organisms was first documented by Bizzozero, an Italian pathologist at the end of the nineteenth century (Table 1).^{2,3} Bizzozero described spiral bacteria in the canine stomach. He presented his discovery at a meeting of the Turin Medical Academy in March 1892 in his own commentary:⁴

'Even more exciting are certain spirilli I found constantly in the dog's stomach and that, in addition to being numerous in the mucus layer that covers the mucosa, penetrate into the gland lumen of both pylorus and fundus, and sometimes reach the bottom of glands.'

Spiral bacteria were demonstrated for the first time in the human stomach in 1906.⁵ This initial report concerned patients with gastric carcinoma. Nine years later, spiral micro-organisms in the stomachs of patients with gastric and duodenal ulceration were reported.⁶ It was felt, however, that these organisms were contaminants from the oral cavity.

Table 1. Key dates in the history of *Helicobacter pylori*.

Year	Key dates in the history of <i>H. pylori</i>
1893	Gastric spiral bacteria are reported for the first time in the stomachs of dogs ²
1906	Spirochaetes are demonstrated in the human stomach
1924	Urease activity in the stomach is reported ¹²
1950	Urease in patients with gastric ulceration neutralises gastric acid via the production of ammonia
1975	Gastric spirochaetes and gastritis present in 80% of gastric ulcers
1976	Multi-step cascade of gastric carcinogenesis proposed by Correa
1983	Campylobacter-like organisms associated with gastritis and possibly peptic ulceration
1985	Temporal relationship between acquisition of <i>H. pylori</i> infection and development of gastritis
1987	Eradication of <i>H. pylori</i> leads to long-term cure of duodenal ulceration
1989	The genus ' <i>Helicobacter</i> ' is suggested
1993	Eurogast Study Group correlates <i>H. pylori</i> infection and gastric cancer mortality
1993	Regression of low-grade MALT lymphoma after eradication of <i>H. pylori</i>
1994	<i>H. pylori</i> classified as a grade I (definite) carcinogen
1994	The infection should be eradicated in patients with peptic ulcers
1996	MACH 1 study: omeprazole triple therapies produce high eradication rates
1997	Maastricht consensus report on the management of <i>H. pylori</i> infection
1999	MACH 2 study: susceptibility testing
2001	Gastric cancer develops only in individuals infected with <i>H. pylori</i>
2002	Second Maastricht consensus report on the management of <i>H. pylori</i> infection
2005	Serum pepsinogen is a good predictive marker for the development of gastric cancer
2005	Nobel Prize
2006	Third Maastricht consensus report on the management of <i>H. pylori</i> infection

Table modified from ref. 3.

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