Barry Marshall and Robin Warren: 
**H. pylori in Peptic ulcer**

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Robin Warren (1937-) a pathologist from Perth, Australia, first observed small curved bacteria in stomach of gastric ulcer patients (1979). Young Barry Marshall (1951-) a clinical fellow, became interested in Warren’s findings. They initiated a study of gastric biopsies in 100 patients of acid peptic disease (1981). Spiral shaped bacteria in the lining of stomach were found by bacteriologist in 1875 but were eventually forgotten as they could not be stained or cultured by available methods. This resulted in a firm belief that no bacterium could survive in acidic pH of human stomach. Warren and Marshall first reported “unidentified curved bacilli on gastric epithelium in active chronic gastritis” in June 1983. These bacteria were always present beneath gastric mucosa, close to the site of inflammation, possibly explaining how they might be protected from gastric acid. After several attempts, Marshall succeeded in cultivating hitherto unknown bacterial species, calling it *Campylobacter jejuni*.

The duo first published their full paper in June 1984, referring to *Campylobacter jejuni* as probably etiologically related to antral gastritis and peptic ulceration. The bacterium was later placed in its own genus *Helicobacter pylori*. During the next 10 years, medical world was skeptical at the idea of peptic ulcer being an infectious disease, and refused to let go the age old notion of treating DU by combating gastric acid secretion by H2 receptor antagonists and PPIs. Obtaining the organism in pure culture was only one step. Strict “Koch’s postulate” had to be satisfied for confirmation. Effective therapeutic response to antibiotics and immunological studies can be considered a substitute for these postulates.

In an attempt to demonstrate the cause by the most direct means, Marshall and Warren reported an “Attempt to fulfill Koch’s postulates for pyloric Campylobacter” in 1985. A normal volunteer, after swallowing pure culture of *C. pyloritidis* developed a mild illness with histologically proven syndrome of acute Campylobacter gastritis, lasting for 14 days. However, because it involved only a single subject (Marshall himself!), it was far from conclusive. Potent inhibitors of acid production resulted in complete healing of endoscopy proven duodenal ulcers in 95% of cases. Problem was relapses after initial successful treatment. If temporary acid suppressants were coupled with antibacterial regimen, recurrence rate dropped 5-10 %. Thomas Broody invented the first triple drug therapy for treatment of DU (1987).

Due to the very nature of the illness it took several years for double blind trials over a long period (12 to 36 months) to establish the effectiveness of the regimen. After Marshall’s 1992 trial, three more large studies were published. This finally convinced the academic medical world about the causative nature of *H. pylori* in PUD. The entire process took about 10 years. Robin Warren also helped develop a convenient diagnostic test (14C-Urea breath-test) for detecting *H. pylori* in ulcer patients. Marshall and Warren were awarded the Nobel Prize in Physiology and Medicine in 2005.