A Bug That Can Dig a Hole in the Stomach!
The Discovery that Revolutionized the Treatment of Peptic Ulcer
Nobel Prize in Physiology or Medicine 2005

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Barry J Marshall and J Robin Warren from Australia received the Nobel Prize for their discovery of the role of the bacterium *Helicobacter pylori* in gastritis and peptic ulcer. Their findings challenged the prevailing dogma about peptic ulcer. Thanks to their pioneering work, peptic ulcer is no longer a chronic, frequently disabling condition, but a disease that can be cured by a short regimen of antibiotics and acid secretion inhibitors.

What is an Ulcer?

Gastric secretion is highly acidic, which is essential for the digestive process. Epithelial cells that line the stomach and duodenum (proximal part of intestine) are protected from this acidic secretion. An imbalance between the acid secreting mechanism and the protective mechanism causes inflammation of the gastric mucosal epithelium, a condition which is known as ‘gastritis’ that can progress to form ‘peptic ulcer’. Ulcer is an erosion of the epithelial layer. The term peptic ulcer includes both gastric and duodenal ulcer.

Peptic Ulcer: Paradigm Revised

Before their pioneering discovery, the etiology of peptic ulcer was obscure. Stress, alcohol, tobacco and spicy foods were considered to be causative factors. Treatment mainly involved antacids, H2 receptor blockers like ranitidine and proton pump inhibitors like omeprazole. But the relapse rate after such treatment was very high. Surgical intervention for complications like bleeding peptic ulcers was quite common. After the discovery of
the role of *H. pylori* in peptic ulcer, antibiotics like clarithromycin that act against these bacteria were included in the treatment regimen. This revolutionized the treatment of peptic ulcer. The frequency of relapse dramatically came down and surgical interventions became rare. This discovery of Marshall and Warren has transformed our understanding of the microbiology and pathology of the human stomach. “No acid, no ulcer”, a calcified dictum which had prevailed before, disappeared.

**Discovery of an Unexpected Bug**

On the 12th of June 1979 (his 40th birthday), Robin Warren, a pathologist, made an important observation that curved bacteria are present in gastric biopsies. After examination of many gastric biopsy specimens he noticed that the curved bacteria were always associated with specimens that showed signs of inflammation and that their number correlated with the degree of inflammation. Barry Marshall joined Robin Warren in 1981. Together, they studied stomach biopsy samples from several peptic ulcer patients and found these bacteria in more than 85% of cases. They were unable to find such bacteria in healthy specimens. Although there were earlier reports of the presence of such bacteria in the stomach, no one had previously associated them with any pathological condition.

Interestingly, Marshall found an article about gastric ulcer healing property of bismuth. They went ahead to test the antibacterial activity of bismuth against these newly identified bacteria trying to link the presence of these bugs to ulcers and gastritis. For this, bacteria had to be cultured. They tried different selective growth media but without any success for more than a year. Every time they incubated only for 48 hours. But one Easter weekend, Marshall left the plates for six days. This time they could see growth. They could see many corkscrew shaped bacteria under the microscope. They also observed that bismuth can kill these bacteria. But just isolation of bacteria from the specimen was not sufficient to convince the scientific community about its role in peptic ulcer. Reputed journals rejected their