

## Ulcers – A Microbial Infection?

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Peptic ulcers have long been associated with stress, spicy foods and alcohol consumption. It was thought that these agents caused excess acid production in the stomach leading to irritation of the lining of the stomach and small intestines with the formation of an ulcer. Over the last 15 years it has become clear that most ulcers are caused by a bacterial infection. Those not caused by infection are the result of anti-inflammatory drugs such as aspirin.

The microorganism that causes ulcers is a gram-negative, spiral or helical shaped bacterium called *Helicobacter pylori*. It took a long time for infection to be accepted as the cause of ulcers because the stomach was assumed to be sterile. The stomach contents are extremely acidic, with a pH of about 2. The combination of acid and digestive enzymes ensures that all food as well as most bacteria, fungi and viruses are killed and digested. The stomach was long thought to be sterile; thus, it was surprising to find that the characteristic helical shaped bacteria were thriving in tissue samples taken from the lining of the stomach of many people.

How does this organism survive the harsh chemical environment of the stomach? It actually does not grow in the stomach itself where the pH is very low, but instead takes up residence on the surface of the cells that line the stomach. These cells, called mucosal cells, produce a thick mucus layer that coats the lining of the stomach and protects the stomach itself from digestion. The bacteria grow under this layer of mucus. However, even this environment is quite acidic with a pH of about 4. In order to protect itself from this acidic environment, *Helicobacter pylori* neutralizes stomach acid by producing two basic compounds: bicarbonate and ammonia. The biochemical reaction that produces these compounds is the breakdown of urea [ $\text{CO}(\text{NH}_3)_2$ ], present in the stomach, by the action of the enzyme urease. Urease is made by *Helicobacter pylori* as it grows in the lining of the stomach.

The urease activity of *Helicobacter pylori* is used in a simple non-invasive diagnostic test called the breath test. Radioactive  $^{14}\text{C}$ -urea is swallowed by the patient. If there is *Helicobacter pylori* in the stomach, one of the products of the breakdown of  $^{14}\text{C}$ -urea will be  $^{14}\text{C}$ -bicarbonate.  $^{14}\text{C}$ -bicarbonate in the stomach travels to the blood, where it is then released into the lungs as  $^{14}\text{CO}_2$ . The patient breathes into a mylar balloon and the air in the balloon is tested for the presence of radioactive  $^{14}\text{CO}_2$ . This test takes only about 20 minutes and is quite sensitive. In addition to the breath test, there are also blood tests to detect antibodies to *Helicobacter pylori* as well as biopsies of stomach tissue that reveal the presence of the helical bacteria.

The exact mechanism by which infection causes ulcers is not known. Weakening of the mucosal lining by the infection may lead to irritation of the stomach wall by acid as well as by the infection itself. Ulcers may also result from the body's attempt to fight the infection as the immune response attacks the infection site. The treatment for ulcers addresses several aspects of the problem: the bacteria, the acid, and the stomach lining. Antibiotics such as metronidazole and tetracycline kill *Helicobacter pylori*. Drugs that block histamine production by the body and those that prevent the pumping of acid into the stomach help to lower acid production. Bismuth subsalicylate (present in Pepto-Bismol) helps to protect the stomach lining from acid. Treatment with two antibiotics and either bismuth or a drug to block acid production usually allows an ulcer to heal in about two weeks. Although this treatment is effective, there are often unpleasant side effects from the use of multiple drugs.

Although the first evidence that *Helicobacter pylori* causes ulcers came in 1982, and by 1994 was accepted by doctors and scientists at the National Institutes of Health, there are still skeptics in the medical community. *Helicobacter pylori* infection is very common in underdeveloped countries, but is also prevalent in the U.S. where about 20% of those under age 40 and 50% of those over age 60 have the organism. In about a third of these individuals the infection causes an ulcer. While it is not clear how the bacterium is transmitted, it is thought that it might be spread via water or food, or possibly directly between individuals in saliva by mouth-to-mouth contact.

Peptic ulcers are common and are a serious disease. With the discovery of the bacterial agent responsible for ulcers, we now have an effective treatment that should help to eliminate this disease. However, because all doctors are not aware of the advances in the diagnosis and treatment of ulcers, patients who have symptoms of an ulcer should request a test for *Helicobacter pylori*.