



CLINICAL FOCUS

Peptic Ulcer

Approximately 10% of people in the United States will develop **peptic ulcers** during their lifetime. Peptic ulcers are caused when the gastric juices (acid and pepsin) digest the mucosal lining of the GI tract. Approximately 80% of peptic ulcers occur on the duodenal side of the pyloric sphincter, but peptic ulcers can also occur in the stomach (gastric ulcers) or esophagus (esophageal ulcers).

Nearly all peptic ulcers are due to infection by a specific bacterium, *Helicobacter pylori*. *H. pylori* is also linked to gastritis and gastric cancer. Because stress, diet, smoking, and alcohol cause excess acid secretion in the stomach, for years it was accepted that these lifestyle patterns were responsible for ulcers. Although they can contribute to ulcers, it is now clear that the root cause is *H. pylori*.

The presence of bacteria in the stomach mucosa was first discovered in 1892, but the finding was met with severe skepticism because it was believed that bacteria could not survive in the acidic stomach environment. In 1982, an Australian doctor, Barry Marshall, was finally able to culture an unusual bacterium, *H. pylori*, from stomach biopsies. To prove his belief that

this bacterium could cause gastritis and ulcers, Marshall did something that no one should do at home. He drank a solution of *H. pylori* and subsequently developed gastric inflammation. Luckily, antibiotic treatment was able to cure him. In 2005, along with his colleague, Dr. Robin Warren, he received the Nobel Prize in Physiology or Medicine for his discovery.

Antibiotic treatment to eradicate *H. pylori* is the best therapy for ulcers. A combination of antibiotics and antacids cures 95% of gastric and 74% of duodenal ulcers within 2 months, with less than a 10% recurrence rate. In contrast, the previous conventional treatment with antacids yields only temporary relief, with about 90% recurrence rates within a year. Other treatments involve drugs that prevent histamine-stimulated acid secretion or that directly inhibit the proton pumps that secrete the acid. Such treatments are effective only for short-term relief, not for long-term treatment. These acid-blocking drugs, however, are effective agents in the treatment of **gastroesophageal reflux disease (GERD)** caused by acid reflux from the stomach. GERD is commonly known as heartburn.

Most bacteria cannot survive in the stomach. Hence, *H. pylori* is one of the most pervasive of human pathogens because it inhabits a niche without competition. It is estimated that well over half of the world's population is infected with *H. pylori*. The infection rate in the United States is about 1% per year of age—for example, 30% of all 30-year-olds are infected. In developing countries, nearly all people over age 25 are infected. This may contribute to the high rates of stomach cancer in some of those countries. Analyses of the *H. pylori* DNA sequences from various ethnic and geographic populations suggest that *H. pylori* infection has been present in humans for over 150,000 years, yet most people do not display the symptoms of *H. pylori* infection. Only about 15%–20% show gastric problems attributed to *H. pylori*. What triggers the bacterial infection to become symptomatic is a major unanswered question. It seems likely that both *H. pylori* infection and conditions that elevate acid secretion or damage the stomach wall, such as stress or the excessive ingestion of alcohol or aspirin, contribute to the development of an ulcer.



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Intestinal Disorders

INFLAMMATORY BOWEL DISEASE

Enteritis is inflammation of the intestine, and **colitis** is inflammation of the colon. Both can result from an infection, chemical irritation, or unknown cause. **Inflammatory bowel disease (IBD)** is the general name given to either Crohn disease (regional enteritis) or ulcerative colitis. IBD occurs at a rate in Europe and North America of approximately 4 to 8 new cases per 100,000 people per year, which is much higher than in Asia and Africa. Males and females are affected about equally. IBD is of unknown cause, but infectious, autoimmune, and hereditary factors have been implicated. **Crohn disease** involves localized inflammatory degeneration, which may occur anywhere along the digestive tract but most commonly involves the distal ileum and proximal colon. The degeneration involves the entire thickness of the digestive tract wall. The intestinal wall often becomes thickened, constricting the lumen, with ulcerations and fissures in the damaged areas. The disease causes diarrhea, abdominal pain, fever, and weight loss. Treatment centers around anti-inflammatory drugs, but other treatments, including the avoidance of foods that increase symptoms and even surgery, are used. **Ulcerative colitis** is limited to the mucosa of the large intestine and rectum. The involved mucosa exhibits inflammation, including edema, vascular congestion, hemorrhage, and the accumulation of plasma cells, lymphocytes, neutrophils, and eosinophils. Patients may experience abdominal pain, fever, malaise, fatigue, and weight loss, as well as diarrhea and hemorrhage. In rare cases, severe diarrhea and hemorrhage require transfusions. Treatment includes the use of anti-inflammatory drugs and, in some cases, the avoidance of foods that increase symptoms.

IRRITABLE BOWEL SYNDROME

Irritable bowel syndrome (IBS), also called spastic colon, is a disorder of unknown cause in which intestinal mobility is abnormal. The disorder accounts for over half of all referrals to gastroenterologists. Male and female children are affected equally, but women are affected twice as often as men. IBS patients

experience abdominal pain mainly in the left-lower quadrant, especially after eating. They also have alternating bouts of constipation and diarrhea. There is no specific histopathology in the digestive tracts of IBS patients. There are no anatomical abnormalities, no indication of infection, and no sign of metabolic causes. Patients with IBS appear to exhibit greater than normal levels of psychological stress or depression and show increased contractions of the esophagus and small intestine during times of stress. There is a high familial incidence. Some patients present with a history of traumatic events, such as physical or sexual abuse. Treatments include psychiatric counseling and stress management, diets with increased fiber and limited gas-producing foods, and loose clothing. In some patients, drugs that reduce parasympathetic stimulation of the digestive system are useful.

MALABSORPTION SYNDROME

Malabsorption syndrome (sprue) is a spectrum of disorders of the small intestine that results in abnormal nutrient absorption. One type of malabsorption, called **celiac disease**, or **gluten-sensitive enteropathy**, results from an immune response to gluten, which is present in certain types of grains and involves the destruction of newly formed epithelial cells in the intestinal glands. These cells fail to migrate to the villi surface, the villi become blunted, and the surface area decreases. As a result, the intestinal epithelium is less capable of absorbing nutrients. Another type of malabsorption, **tropical malabsorption**, is apparently caused by bacteria, although no specific bacterium has been identified.

COLON CANCER

Colon cancer is the second leading cause of cancer-related deaths in the United States; it accounts for 55,000 deaths a year. Susceptibility to colon cancer can be familial; however, a correlation exists between colon cancer and lifestyle factors, including diets low in fiber and high in fat and red or processed meats.

A gene for colon cancer may be present in as many as 1 in 200 people, making colon cancer

one of the most common inherited diseases. Eleven different genes have been associated with colon cancer. One group of those genes is involved in cell regulation—that is, keeping cell growth in check. The second group is required for genetic stability. As a result of mutations in the second group, there are wholesale errors and mutations throughout the genome. Such genetic instability has been identified in at least 15% of sporadic (not occurring in families) colon cancer. Screening for colon cancer includes testing the stool for blood content and performing a colonoscopy, which allows physicians to see into the colon.

CONSTIPATION

Constipation is the slow movement of feces through the large intestine. The feces often become dry and hard because of increased fluid absorption during the extended time they are retained in the large intestine. In the United States, 2.5 million doctor visits occur each year from people complaining of constipation, and \$400 million is spent each year on laxatives.

Constipation often results after a prolonged time of inhibiting normal defecation reflexes. A change in habits, such as travel, dehydration, depression, disease, metabolic disturbances, certain medications, pregnancy, or dependency on laxatives, can cause constipation. Irritable bowel syndrome can also cause constipation. Constipation can also occur with diabetes, kidney failure, colon nerve damage, or spinal cord injuries or as the result of an obstructed bowel. Of greatest concern, the obstruction could be caused by colon cancer. Chronic constipation can result from the slow movement of feces through the entire colon, in just the distal part (descending colon and rectum), or in just the rectum. Interestingly, in one large study of people who claimed to be suffering from chronic constipation, one-third were found to have normal movement of feces through the large intestine. Defecation frequency was often normal. Many of those people were suffering from psychological distress, anxiety, or depression and just thought they had abnormal defecation frequencies.