GASTRODUODENAL MOTOR PHYSIOLOGY

Based on electrophysiologic and functional characteristics, the stomach can be divided into two functional compartments. The proximal stomach (fundus and proximal third of the body) acts as a reservoir for recently ingested food, whereas the distal stomach grinds, mixes, and sieves food particles. The smooth muscle of the proximal stomach has a characteristic tonic contraction that allows for gastric accommodation, a process by which the fundus relaxes in response to incoming food and fluid, with little increase in intragastric pressure. In contrast, the distal stomach produces high-amplitude contractions originating from the pacemaker region in the midportion of the greater curvature.

Gastroduodenal motor events vary in response to fasting and food intake. During fasting, gastric motility is characterized by a pattern of phasic contractions known as the migrating motor complex (MMC). The MMC clears the stomach and small intestine of undigested food particles, mucus, and sloughed epithelial cells. The MMC begins in the stomach and migrates down the length of the small bowel with a combined duration of 84 to 112 minutes. Following a meal, irregular contractile activity propels the ingested material distally.

Gastric emptying of a mixed solid and liquid meal involves the coordinated actions of the distinct regions of the stomach with feedback from the small intestine. Although liquids empty from the stomach at a relatively linear rate, solids are propelled forward by gastric contractions toward the antrum, where particles are triturated by high-amplitude contractions. Once solids have been reduced in size to particles of 1 to 2 mm, they are emptied into the pylorus.

A variety of medications and foods that exert significant effects on gastroduodenal motility are described in Figure 36-1 (see Video 36-1). Agents that modify the lower esophageal sphincter and esophageal motility are explained in Chapter 36.

PEPTIC ULCER DISEASE

Definition and Epidemiology

Peptic ulcer disease (PUD) is a common clinical problem characterized by mucosal defects of the stomach or duodenum. The proteolytic enzyme pepsin and gastric acid were initially identified as key factors involved in their pathogenesis, leading to the concept of *no acid, no ulcer*. However, in the past two decades, factors other than acid and pepsin that contribute to the development of ulcers have been recognized. Men and women are at equal risk for developing PUD, and the overall lifetime risk is ~10%. Peptic ulcers are uncommon in children, but the risk increases with age. More than 70% of all ulcer cases occur in individuals between the ages of 25 and 64 years. Whereas the incidence of PUD is decreasing in younger age groups, more persons 65 years of age and older are developing ulcers. These trends are likely related to the overall decrease in the prevalence of *Helicobacter pylori* infection in the general population and the increasing use of NSAIDs by older persons. The most important risk factors for the development of peptic ulcers are infection with *H. pylori* and use of NSAIDs. If neither of these factors is present, an alternative cause must be sought, including hypersecretory states (e.g., Zollinger-Ellison syndrome [ZES]) or one of the other less common causes of ulcer disease such as Crohn disease, vascular insufficiency, viral infection, radiation therapy, and cancer chemotherapy. Although a significant number of environmental factors, including stress, personality type, occupation, alcohol consumption, and diet, have been linked to the development of ulcers, there is no convincing evidence suggesting that any of these factors by itself can cause PUD.

Pathology

By killing ingested bacteria and other microorganisms, gastric acid prevents the development of enteric colonization and ensures both efficient absorption of nutrients and prevention of systemic infections. Gastric acid is also an important factor in protein hydrolysis and digestion and, under various conditions, may play an etiologic role in inciting gastroduodenal mucosal injury. Postprandial gastric acid secretion is regulated primarily by increases in gastrin expression, which is controlled by a negative feedback loop wherein postprandial gastrin-mediated acid secretion stimulates the release of somatostatin from antral D cells. Somatostatin appears to act by a paracrine mechanism to inhibit further release of gastrin from G cells. Somatostatin produced by D cells in the gastric corpus and fundus may also directly inhibit acid secretion from parietal cells and may suppress histamine release from ECL cells. Although the presence of acid is necessary for the formation of ulcers, acid secretion is normal in nearly all patients with gastric ulcers and is increased in only one third of patients with duodenal ulcers. Therefore, acid is clearly not the only factor involved in the pathogenesis of peptic ulcers, and the balance between aggressive factors that act to injure the gastroduodenal mucosa and defensive factors that normally protect against corrosive agents is also important. When this delicate balance is disrupted for any reason, an ulcer may result.

In addition to the regulation of intragastric acidity, mechanisms involved in maintaining the protective mucosal barrier include mucus and HCO_3^- secretion, mucosal blood flow, cell restitution and repair, and changes in local immune factors. The mucosal defensive properties appear to be mediated to a large extent by endogenous prostaglandins, nitric oxide, and trefoil proteins. When the synthesis of these mediators is diminished, even normal rates of acid secretion may be sufficient to injure the mucosa.

Helicobacter pylori Infection

Helicobacter pylori (*H. pylori*) are curved, flagellated, gram-negative rods found only in gastric epithelium or in regions of gastric metaplasia. It is the most common worldwide cause of microbial infection, involving an estimated 50% of the world's population. *H. pylori* organisms clearly cause histologic gastritis and are found in 50% to 95% of patients with gastroduodenal ulcers. However, only a minority of patients with *H. pylori* gastritis develop peptic ulcer disease (PUD) or gastric cancer. In the Western world, there is a clear age-related prevalence of *H. pylori* infection in healthy individuals, increasing from 10% in those younger than 30 years to 60% in those older than 60 years. The mode of transmission appears to be by the fecal-oral route. Improvements in sanitation and standards of living appear to