

## CHAPTER

# 27

# Alterations in Gastrointestinal Function

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**G**astrointestinal disorders are not cited as the leading cause of death in the United States, nor do they receive the same publicity as heart disease and cancer. However, according to government reports, digestive diseases rank third in the total economic burden of illness, resulting in considerable human suffering, personal expenditures for treatment, lost working hours, and a drain on the nation's economy. It has been estimated that 60 to 70 million Americans have digestive disease.<sup>1</sup> Even more important is the fact that proper nutrition or a change in health practices could prevent or minimize many of these disorders.

## DISORDERS OF THE ESOPHAGUS

The esophagus is a tube that connects the oropharynx with the stomach. It lies posterior to the trachea and larynx and extends through the mediastinum, intersecting the diaphragm at the level of the 11th thoracic vertebra. The esophagus functions primarily as a conduit for passage of food from the pharynx to the stomach, and the structure of its wall is designed for this purpose: the smooth muscle layers provide the peristaltic movements needed to move food along its length, and the epithelial layer secretes mucus, which protects its surface and aids in lubricating food.

### Dysphagia

The act of swallowing depends on the coordinated action of the tongue and pharynx. These structures are innervated by cranial nerves V, IX, X, and XII. *Dysphagia* refers to difficulty in swallowing. If swallowing is painful, it is referred to as *odynophagia*. Dysphagia can result from altered nerve function or from disorders that produce narrowing of the esophagus. Lesions of the central nervous system (CNS), such as a stroke, often involve

the cranial nerves that control swallowing. Strictures and cancer of the esophagus and strictures resulting from scarring can reduce the size of the esophageal lumen and make swallowing difficult. Scleroderma, an autoimmune disease that causes fibrous replacement of tissues in the muscularis layer of the gastrointestinal tract, is another important cause of dysphagia.<sup>2</sup> Persons with dysphagia usually report choking, coughing, or an abnormal sensation of food sticking in the back of the throat or upper chest when they swallow.

In a condition called *achalasia*, the lower esophageal sphincter fails to relax; food that has been swallowed has difficulty passing into the stomach, and the esophagus above the lower esophageal sphincter becomes enlarged. One or several meals may lodge in the esophagus and pass slowly into the stomach. There is danger of aspiration of esophageal contents into the lungs when the person lies down.

### Esophageal Diverticulum

A diverticulum of the esophagus is an outpouching of the esophageal wall caused by a weakness of the muscularis layer. An esophageal diverticulum tends to retain food. Reports that the food stops before it reaches the stomach are common, as are reports of gurgling, belching, coughing, and foul-smelling breath. The trapped food may cause esophagitis and ulceration. Because the condition usually is progressive, correction of the defect requires surgical intervention.

### Gastroesophageal Reflux Disease

The term *reflux* refers to backward or return movement. In the context of gastroesophageal reflux, it refers to the backward movement of gastric contents into the esophagus, a condition that causes heartburn. Often referred to as *gastroesophageal reflux disease* (GERD), it probably is the most common disorder originating in the gastrointestinal tract. Most persons experience heartburn occasionally as a result of reflux. Such symptoms usually occur soon after eating, are short lived, and seldom cause more serious problems. However, for some persons, persistent heartburn can represent reflux disease with esophagitis.

The lower esophageal sphincter regulates the flow of food from the esophagus into the stomach. Both internal and external mechanisms function in maintaining the antireflux function of the lower esophageal sphincter.<sup>3,4</sup> Relaxation of the lower esophageal sphincter is a brain stem reflex that is mediated by the vagus nerve in response to a number of afferent stimuli. Transient relaxation with reflux is common after meals. Gastric distension and meals high in fat increase the frequency of relaxation. Refluxed material normally is returned to the stomach by secondary peristaltic waves in the esophagus, with swallowed saliva neutralizing and washing away the refluxed acid.

GERD is thought to be associated with a weak or incompetent lower esophageal sphincter that allows reflux to occur, the irritant effects of the refluxate, and decreased clearance of the refluxed acid from the esophagus after it has occurred.<sup>5,6</sup> Delayed gastric emptying also may contribute to reflux by increasing gastric volume and pressure with greater chance for reflux. Esophageal mucosal injury is related to the destructive nature of the refluxate and the amount of time it is

in contact with mucosa. Acidic gastric fluids (pH < 4.0) are particularly damaging. There is controversy regarding the importance of hiatal hernia (*i.e.*, herniation of the stomach through an enlarged hiatus in the diaphragm) in the pathogenesis of reflux disease. Small hiatal hernias are common and considered to be of no significance in asymptomatic people. However, in cases of severe erosive esophagitis where gastroesophageal reflux and large hiatal hernia coexist, the hernia may retard esophageal acid clearance and contribute to the disorder.<sup>3,5</sup>

Reflux esophagitis involves mucosal injury to the esophagus, hyperemia, and inflammation. The most common symptom of gastroesophageal reflux is heartburn. It frequently is severe, occurring 30 to 60 minutes after eating. It often is made worse by bending at the waist and recumbency and usually is relieved by sitting upright. The severity of heartburn is not indicative of the extent of mucosal injury; only a small percentage of people who report heartburn have mucosal injury. Often, the heartburn occurs during the night. Antacids give prompt, although transient relief. Other symptoms include belching and chest pain. The pain usually is located in the epigastric or retrosternal area and often radiates to the throat, shoulder, or back. Because of its location, the pain may be confused with angina. The reflux of gastric contents also may produce respiratory symptoms such as wheezing, chronic cough, and hoarseness. There is considerable evidence linking gastroesophageal reflux with bronchial asthma.<sup>7</sup> The proposed mechanisms of reflux-associated asthma and chronic cough include aspiration, laryngeal injury, and vagal-mediated bronchospasm.

Persistent gastroesophageal reflux produces a cycle of mucosal damage that predisposes to strictures and a condition called *Barrett's esophagus*. Strictures are caused by a combination of scar tissue, spasm, and edema. They produce narrowing of the esophagus and can cause dysphagia. Barrett's esophagus is characterized by a reparative process in which the squamous mucosa that normally lines the esophagus gradually is replaced by columnar epithelium resembling that in the stomach or intestines.<sup>5,6</sup> It is associated with increased risk for development of esophageal cancer.

The diagnosis of gastroesophageal reflux depends on a history of reflux symptoms and selective use of diagnostic methods, including radiographic studies using a contrast medium such as barium, esophagoscopy, and ambulatory esophageal pH monitoring.<sup>8</sup>

The treatment of gastroesophageal reflux usually focuses on conservative measures. These measures include avoidance of positions and conditions that increase gastric reflux.<sup>8</sup> Avoidance of large meals and foods that reduce lower esophageal sphincter tone (*e.g.*, caffeine, fats, chocolate), alcohol, and smoking is recommended. Sleeping with the head elevated helps to prevent reflux during the night. Weight loss usually is recommended in overweight people.

Antacids or a combination of antacids and alginic acid also are recommended for mild disease. Alginic acid produces a foam when it comes in contact with gastric acid; if reflux occurs, the foam, rather than acid, rises into the esophagus. Histamine type 2 receptor-blocking drugs, which inhibit gastric acid production, often are recommended when additional treatment is needed. Proton pump inhibitors, which block the final pathway for acid secretion, may be used for persons who

continue to have daytime symptoms, recurrent strictures, or large esophageal ulcerations. Surgical treatment may be indicated in some people.



### Gastroesophageal Reflux in Children

Gastroesophageal reflux is a common problem in infants. The small reservoir capacity of an infant's esophagus coupled with frequent spontaneous reductions in sphincter pressure contributes to reflux. Regurgitation of at least one episode a day occurs in as many as half of infants 0 to 3 months of age. By 6 months of age it becomes less frequent, and it abates by 2 years of age as the child assumes a more upright posture and eats solid foods.<sup>9,10</sup> Although many infants have minor degrees of reflux, complications occur in 1 of every 300 to 500 children.<sup>9,10</sup> The condition occurs more frequently in children with cerebral palsy, Down's syndrome, and other causes of developmental delay.

In most cases, infants with simple reflux are thriving and healthy, and symptoms resolve between 9 and 24 months of age. Pathologic reflux is classified into three categories: (1) regurgitation and malnutrition, (2) esophagitis, and (3) respiratory problems. Symptoms of esophagitis include evidence of pain when swallowing, hematemesis, anemia caused by esophageal bleeding, heartburn, irritability, and sudden or inconsolable crying. Parents often report feeding problems in their infants.<sup>9</sup> These infants often are irritable and demonstrate early satiety. Sometimes the problems progress to actual resistance to feeding. Tilting of the head to one side and arching of the back may be noted in children with severe reflux. The head positioning is thought to represent an attempt to protect the airway or reduce the pain-associated reflux. Sometimes regurgitation is associated with dental caries and recurrent otalgia. The ear pain is thought to occur through referral from the vagus nerve in the esophagus to the ear. A variety of respiratory symptoms are caused by damage to the respiratory mucosa when gastric reflux enters the esophagus. Reflux may cause laryngospasm, apnea, and bradycardia. A relationship between reflux and acute life-threatening events or sudden infant death syndrome has been proposed. However, the association remains a matter of controversy, and the linkage may be coincidental.<sup>9,10</sup>

Rumination is the repetitive gagging, regurgitation, mouth-ing, and reswallowing of regurgitated material. Although the cause of the disorder is unknown, it often is associated with mental retardation or altered interaction with the environment (*e.g.*, lack of stimulation in newborn intensive care units or because of altered relationships with caregivers). As with pure reflux, rumination may produce severe esophagitis with signs of iron deficiency anemia, failure to thrive, and head tilting.<sup>10</sup>

Diagnosis of gastroesophageal reflux in infants and children often is based on parental and clinical observations. The diagnosis may be confirmed by esophageal pH probe studies or barium fluoroscopic esophagography. In severe cases, esophagoscopy may be used to demonstrate reflux and obtain a biopsy.

Various treatment methods are available for infants and children with gastroesophageal reflux. Small, frequent feedings are recommended because of the association between gastric volume and transient relaxation of the esophagus. Thickening an infant's feedings with cereal tends to decrease the volume of

reflux, decrease crying and energy expenditure, and increase the calorie density of the formula.<sup>9,10</sup> In infants, positioning on the left side seems to decrease reflux. In older infants and children, raising the head of the bed and keeping the child upright may help. Medications usually are not added to the treatment regimen until pathologic reflux has been documented by diagnostic testing.

### Cancer of the Esophagus

Carcinoma of the esophagus accounts for approximately 6% of all gastrointestinal cancers. This disease is more common in persons older than 50 years, with a male-to-female ratio of approximately 2:1.<sup>11</sup>

There are two types of esophageal cancers: squamous cell and adenocarcinomas. Fewer than 50% of esophageal tumors are squamous cell cancers. These cancers are associated more commonly with dietary and environmental influences.<sup>11,12</sup> Most squamous cell cancers in the United States and Europe are attributable to alcohol and tobacco use. Adenocarcinomas, which typically arise from Barrett's esophagus, account for more than 50% of esophageal cancers. The incidence of this type of cancer appears to be increasing. Adenocarcinomas typically are located in the distal esophagus and may invade the adjacent upper part of the stomach. Endoscopic surveillance in people with Barrett's esophagus may detect adenocarcinoma at an earlier stage, when it is more amenable to curative surgical resection.<sup>12</sup>

Dysphagia is by far the most frequent complaint of persons with esophageal cancer. It is apparent first with ingestion of bulky food, later with soft food, and finally with liquids. Unfortunately, it is a late manifestation of the disease. Weight loss, anorexia, fatigue, and pain on swallowing also may occur.

Treatment includes surgical resection, which provides a means of cure when done in early disease and palliation when done in late disease. Irradiation is used as a palliative treatment. Chemotherapy sometimes is used before surgery to decrease the size of the tumor, and it may be used along with irradiation and surgery in an effort to increase survival.<sup>12</sup>

The prognosis for persons with cancer of the esophagus, although poor, has improved. However, even with modern forms of therapy, the long-term survival is limited because, in many cases, the disease has already metastasized by the time the diagnosis is made.

**In summary,** the esophagus is a tube that connects the oropharynx with the stomach; it functions primarily as a conduit for passage of food from the pharynx to the stomach. Dysphagia refers to difficulty in swallowing; it can result from altered nerve function or from disorders that produce narrowing of the esophagus. A diverticulum of the esophagus is an outpouching of the esophageal wall caused by a weakness of the muscularis layer.

Gastrointestinal reflux refers to the backward movement of gastric contents into the esophagus, a condition that causes heartburn. Although most persons experience occasional esophageal reflux and heartburn, persistent reflux can cause esophagitis. Gastroesophageal reflux is a common problem in infants. Reflux commonly corrects itself with age, and symptoms abate in most children by 2 years of age.

Although many infants have minor degrees of reflux, some infants and small children have significant reflux that interferes with feeding, causes esophagitis, and results in respiratory symptoms and other complications.

Carcinoma of the esophagus, which accounts for 6% of all cancers, is more common in persons older than 50 years, and the male-to-female ratio is approximately 2:1. There are two types of esophageal cancer: squamous cell and adenocarcinoma. Most squamous cell cancers are attributable to alcohol and tobacco use, whereas adenocarcinomas are more closely linked to esophageal reflux and Barrett's esophagus.

## DISORDERS OF THE STOMACH

The stomach is a reservoir for contents entering the digestive tract. While in the stomach, food is churned and mixed with hydrochloric acid and pepsin before being released into the small intestine. Normally, the mucosal surface of the stomach provides a barrier that protects it from the hydrochloric acid and pepsin contained in gastric secretions. Disorders of the stomach include gastritis, peptic ulcer, and gastric carcinoma.

### Gastric Mucosal Barrier

The stomach lining usually is impermeable to the acid it secretes, a property that allows the stomach to contain acid and pepsin without having its wall digested. Several factors contribute to the protection of the gastric mucosa, including an impermeable epithelial cell surface covering, mechanisms for the selective transport of hydrogen and bicarbonate ions, and the characteristics of gastric mucus.<sup>13</sup> These mechanisms are collectively referred to as the *gastric mucosal barrier*.

### KEY CONCEPTS

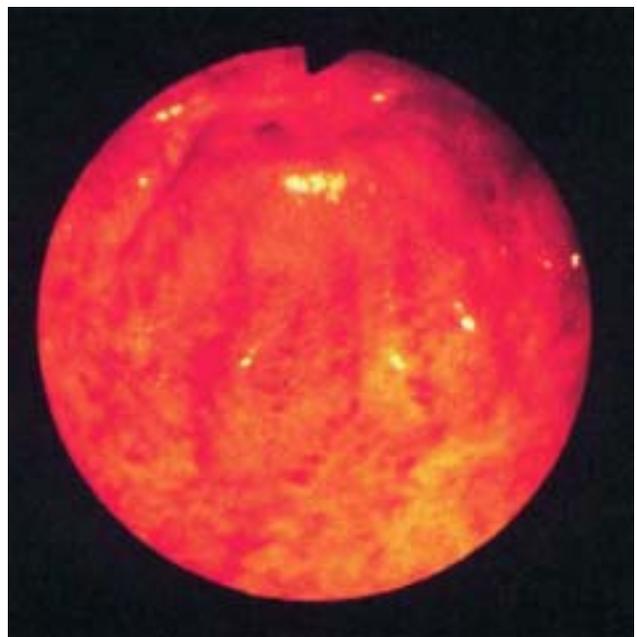
#### DISRUPTION OF THE GASTRIC MUCOSA AND ULCER DEVELOPMENT

- The stomach is protected by tight cellular junctions, a protective mucus layer, and prostaglandins that serve as chemical messengers to protect the stomach lining by improving blood flow, increasing bicarbonate secretion, and enhancing mucus production.
- Two of the major causes of gastric irritation and ulcer formation are aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs) and infection with *Helicobacter pylori*.
- Aspirin and NSAIDs exert their destructive effects by damaging epithelial cells, impairing mucus production, and inhibiting prostaglandin synthesis.
- *H. pylori* is an infectious agent that thrives in the acid environment of the stomach and disrupts the mucosal barrier that protects the stomach from the harmful effects of its digestive enzymes.

The gastric epithelial cells are connected by tight junctions that prevent acid penetration, and they are covered with an impermeable hydrophobic lipid layer that prevents diffusion of ionized water-soluble molecules. Aspirin, which is nonionized and lipid soluble in acid solutions, rapidly diffuses across this lipid layer, increasing mucosal permeability and damaging epithelial cells.<sup>14</sup> Gastric irritation and occult bleeding caused by gastric irritation occur in a significant number of persons who take aspirin on a regular basis (Fig. 27-1). Alcohol, which also is lipid soluble, disrupts the mucosal barrier; when aspirin and alcohol are taken in combination, as they often are, there is increased risk of gastric irritation. Bile acids also attack the lipid components of the mucosal barrier and afford the potential for gastric irritation when there is reflux of duodenal contents into the stomach.

Normally, the secretion of hydrochloric acid by the parietal cells of the stomach is accompanied by secretion of bicarbonate ions ( $\text{HCO}_3^-$ ). For every hydrogen ion ( $\text{H}^+$ ) that is secreted, a  $\text{HCO}_3^-$  is produced, and as long as  $\text{HCO}_3^-$  production is equal to  $\text{H}^+$  secretion, mucosal injury does not occur. Changes in gastric blood flow, as in shock, tend to decrease  $\text{HCO}_3^-$  production. This is particularly true in situations in which decreased blood flow is accompanied by acidosis. Aspirin and the nonsteroidal anti-inflammatory drugs (NSAIDs) also impair  $\text{HCO}_3^-$  secretion.

Prostaglandins, chemical messengers derived from cell membrane lipids, play an important role in protecting the gastrointestinal mucosa from injury. The prostaglandins probably exert their effect through improved blood flow, increased bicarbonate ion secretion, and enhanced mucus production. The fact that drugs such as aspirin and the NSAIDs inhibit prostaglandin synthesis may contribute to their ability to produce gastric irritation.<sup>14</sup> Smoking and older age have been asso-



■ **FIGURE 27-1** ■ Erosive gastritis. This endoscopic view of the stomach in a patient who was ingesting aspirin reveals acute hemorrhagic lesions. (From Rubin E., Farber J.L. [1999]. *Pathology* [3rd ed., p. 683]. Philadelphia: Lippincott Williams & Wilkins)

ciated with reduced gastric and duodenal prostaglandin concentrations; these observations may explain the predisposition to ulcer disease in smokers and older persons.<sup>15</sup>

## Gastritis

Gastritis refers to inflammation of the gastric mucosa. There are many causes of gastritis, most of which can be grouped under the headings of acute or chronic gastritis.

### Acute Gastritis

*Acute gastritis* refers to a transient inflammation of the gastric mucosa. It is most commonly associated with local irritants such as bacterial endotoxins, caffeine, alcohol, and aspirin. Depending on the severity of the disorder, the mucosal response may vary from moderate edema and hyperemia to hemorrhagic erosion of the gastric mucosa.

The complaints of persons with acute gastritis vary. Persons with aspirin-related gastritis can be totally unaware of the condition or may report only heartburn or sour stomach. Gastritis associated with excessive alcohol consumption is a different situation; it often causes transient gastric distress, which may lead to vomiting and, in more severe situations, to bleeding and hematemesis. Gastritis caused by the toxins of infectious organisms, such as the staphylococcal enterotoxins, usually has an abrupt and violent onset, with gastric distress and vomiting ensuing approximately 5 hours after the ingestion of a contaminated food source. Acute gastritis usually is a self-limiting disorder; complete regeneration and healing usually occur within several days.

### Chronic Gastritis

Chronic gastritis is a separate entity from acute gastritis. It is characterized by the absence of grossly visible erosions and the presence of chronic inflammatory changes leading eventually to atrophy of the glandular epithelium of the stomach. The changes may become dysplastic and possibly transform into carcinoma. Factors such as chronic alcohol abuse, cigarette smoking, and chronic use of NSAIDs may contribute to the development of the disease.

There are four major types of chronic gastritis: (1) autoimmune gastritis, (2) multifocal atrophic gastritis, (3) *Helicobacter pylori* gastritis, and (4) chemical gastropathy.<sup>16</sup> Autoimmune gastritis is the least common form of chronic gastritis. Most persons with the disorder have circulating antibodies to parietal cells and intrinsic factor, so this form of chronic gastritis is considered to be of autoimmune origin. Autoimmune destruction of the parietal cells leads to hypochlorhydria or achlorhydria, a high intragastric pH, and hypergastrinemia. Pernicious anemia is a megaloblastic anemia that is caused by malabsorption of vitamin B<sub>12</sub> caused by a deficiency of intrinsic factor (see Chapter 13). This type of chronic gastritis frequently is associated with other autoimmune disorders, such as Hashimoto's thyroiditis and Addison's disease.

*Multifocal atrophic gastritis* is a disorder of unknown etiology. It is more common than autoimmune gastritis and is seen more frequently in whites than in other races. It is particularly common in Asia, Scandinavia, and parts of Europe and Latin America. As with autoimmune gastritis, it is associated with reduced gastric acid secretion, but achlorhydria and pernicious anemia are less common.

Chronic autoimmune gastritis and multifocal atrophic gastritis cause few symptoms related directly to gastric changes. Persons with autoimmune chronic gastritis may have signs of pernicious anemia. More important is the development of peptic ulcer and increased risk of peptic ulcer and gastric carcinoma. Approximately 2% to 4% of persons with atrophic gastritis eventually experience gastric carcinoma.<sup>11</sup>

*H. pylori gastritis* is the most common type of chronic non-erosive gastritis in the United States. *H. pylori* are small, curved, gram-negative rods that can colonize the mucus-secreting epithelial cells of the stomach<sup>16,17</sup> (Fig. 27-2). *H. pylori* have multiple flagella, which allow them to move through the mucous layer of the stomach, and they secrete urease, which enables them to produce sufficient ammonia to buffer the acidity of their immediate environment. Because the organism adheres only to the mucus-secreting cells of the stomach, it does not usually colonize other parts of the gastrointestinal tract. *H. pylori* produce an enzyme that degrades mucin and has the capacity to interfere with the local protection of the gastric mucosa against acid. It also may produce toxins that directly damage the mucosa and produce ulceration in other ways. Chronic infection with *H. pylori* can lead to gastric atrophy and intestinal metaplasia. *H. pylori* also can cause peptic ulcer (to be discussed) and has been linked to the development of gastric adenocarcinoma.

*Chemical gastropathy* is a chronic gastric injury resulting from reflux of alkaline duodenal contents, pancreatic secretions, and bile into the stomach. It is most commonly seen in persons who have had gastroduodenostomy or gastrojejunostomy surgery. A milder form may occur in persons with gastric ulcer,



■ **FIGURE 27-2** ■ Infective gastritis. *H. pylori* appears on silver staining as small, curved rods on the surface of the gastric mucosa. (From Rubin E., Farber J.L. [1999]. *Pathology* [3rd ed., p. 687]. Philadelphia: Lippincott Williams & Wilkins)

gallbladder disease, or various motility disorders of the distal stomach.

## Ulcer Disease

### Peptic Ulcer

Peptic ulcer is a term used to describe a group of ulcerative disorders that occur in areas of the upper gastrointestinal tract (*e.g.*, stomach and duodenum) that are exposed to acid-pepsin secretions. Peptic ulcer disease, with its remissions and exacerbations, represents a chronic health problem. Approximately 10% of the population has or will experience peptic ulcer.<sup>6</sup> Duodenal ulcers occur five times more commonly than do gastric ulcers. Ulcers in the duodenum occur at any age and frequently are seen in early adulthood. Gastric ulcers tend to affect the older age group, with a peak incidence between 55 and 70 years of age. Both types of ulcers affect men three to four times more frequently than women.

A peptic ulcer can affect one or all layers of the stomach or duodenum (Fig. 27-3). The ulcer may penetrate only the mucosal surface, or it may extend into the smooth muscle layers. Occasionally, an ulcer penetrates the outer wall of the stomach or duodenum. Spontaneous remissions and exacerbations are common. Healing of the muscularis layer involves replacement with scar tissue; although the mucosal layers that cover the scarred muscle layer regenerate, the regeneration often is less than perfect, which contributes to repeated episodes of ulceration.



■ **FIGURE 27-3** ■ Gastric ulcer. The stomach has been opened to reveal a sharply demarcated, deep peptic ulcer on the lesser curvature. (From Rubin E., Farber J.L. [1999]. *Pathology* [3rd ed., p. 693]. Philadelphia: Lippincott Williams & Wilkins)

Since the early 1980s, there has been a radical shift in thinking regarding the cause of peptic ulcer. No longer is peptic ulcer thought to result from a genetic predisposition, stress, or dietary indiscretions. Most cases of peptic ulcer are caused by *H. pylori* infection.<sup>18</sup> The second most common cause of peptic ulcer is NSAID and aspirin use.<sup>18</sup> It has been reported that virtually all persons with duodenal ulcer and 70% of persons with gastric ulcer have *H. pylori* infection.<sup>11</sup> Aspirin and NSAIDs account for 10% to 20% of gastric ulcers and 2% to 5% of duodenal ulcers. Aspirin appears to be the most ulcerogenic of the NSAIDs. Ulcer development in NSAID users is dose dependent, but some risk occurs even with aspirin doses of 325 mg/day.<sup>6</sup> The pathogenesis of NSAID-induced ulcers is thought to involve mucosal injury and inhibition of prostaglandin synthesis. In contrast to peptic ulcer from other causes, NSAID-induced gastric injury often is without symptoms, and life-threatening complications can occur without warning.

The clinical manifestations of uncomplicated peptic ulcer focus on discomfort and pain. The pain, which is described as burning, gnawing, or cramplike, usually is rhythmic and frequently occurs when the stomach is empty—between meals and at 1 or 2 o'clock in the morning. The pain usually is located over a small area near the midline in the epigastrium near the xiphoid and may radiate below the costal margins, into the back, or rarely, to the right shoulder. The pain is usually relieved by food or antacids.

The complications of peptic ulcer include hemorrhage, obstruction, and perforation. Hemorrhage is caused by bleeding from granulation tissue or from erosion of an ulcer into an artery or vein. It occurs in as many as 10% to 20% of persons with peptic ulcer.<sup>6</sup> Bleeding may be sudden, severe, and without warning, or it may be insidious, producing only occult blood in the stool. As many as 20% of persons with bleeding ulcers have no antecedent symptoms of pain; this is particularly true in persons receiving NSAIDs. Acute hemorrhage is evidenced by the sudden onset of weakness, dizziness, thirst, cold, moist skin, the desire to defecate, and the passage of loose, tarry, or even red stools and emesis of coffee-ground vomitus. Signs of circulatory shock develop, depending on the amount of blood lost.

Obstruction is caused by edema, spasm, or contraction of scar tissue and interference with the free passage of gastric contents through the pylorus or adjacent areas. There is a feeling of epigastric fullness and heaviness after meals. With severe obstruction, there is vomiting of undigested food.

Perforation occurs when an ulcer erodes through all the layers of the stomach or duodenum wall. Perforation develops in approximately 5% of persons with peptic ulcers, usually from ulcers on the anterior wall of the stomach or duodenum.<sup>6</sup> With perforation, gastrointestinal contents enter the peritoneum and cause peritonitis, or penetrate adjacent structures such as the pancreas. Radiation of the pain into the back, severe night distress, and inadequate pain relief with the eating of foods or taking of antacids in persons with a long history of peptic ulcer may signify perforation.

**Diagnosis and Treatment.** Diagnostic procedures for peptic ulcer include history taking with an emphasis on aspirin and NSAID use, laboratory tests, radiologic imaging, and endoscopic examination. Laboratory findings of hypochromic anemia and occult blood in the stools indicate bleeding. X-ray

studies with a contrast medium such as barium are used to detect the presence of an ulcer crater and to exclude gastric carcinoma. Endoscopy (*i.e.*, gastroscopy and duodenoscopy) can be used to visualize the ulcer area and obtain biopsy specimens to test for *H. pylori* and exclude malignant disease.

The treatment of peptic ulcer has changed dramatically during the past several years and now aims to eradicate the cause and effect a permanent cure for the disease. Pharmacologic treatment focuses on eradicating *H. pylori* with appropriate antibiotics when present, relieving ulcer symptoms, and healing the ulcer crater. Acid-neutralizing, acid-inhibiting drugs (histamine<sub>2</sub>-receptor antagonists and proton pump blockers), and mucosal protective agents are used to relieve symptoms and promote healing of the ulcer crater. Aspirin and NSAID use should be avoided when possible.

The current surgical management of peptic ulcer disease is largely limited to treatment of complications. When surgery is needed, it usually is performed using minimally invasive methods. With bleeding ulcers, hemostasis often can be achieved by endoscopic methods, and endoscopic balloon dilation often is effective in relieving outflow obstruction.

### Zollinger-Ellison Syndrome

The Zollinger-Ellison syndrome is a rare condition caused by a gastrin-secreting tumor (gastrinoma). In persons with this disorder, gastric acid secretion reaches such levels that ulceration becomes inevitable.<sup>19</sup> The tumors may be single or multiple; although most tumors are located in the pancreas, a few develop in the submucosa of the stomach or duodenum. More than two thirds of gastrinomas are malignant, and one third have already metastasized at the time of diagnosis.<sup>11</sup> The increased gastric secretions cause symptoms related to peptic ulcer. Diarrhea may result from hypersecretion or from the inactivation of intestinal lipase and impaired fat digestion that occurs with a decrease in intestinal pH.

### Stress Ulcers

A stress ulcer, sometimes called *Curling's ulcer*, refers to gastrointestinal ulcerations that develop in relation to major physiologic stress. Persons at high risk for the development of stress ulcers include those with large surface-area burns, trauma, sepsis, acute respiratory distress syndrome, severe liver failure, and major surgical procedures. These lesions occur most often in the fundus of the stomach and proximal duodenum and are thought to result from ischemia, tissue acidosis, and bile salts entering the stomach in critically ill persons with decreased gastrointestinal tract motility.<sup>20</sup> Another form of stress ulcer, called *Cushing ulcer*, consists of gastric, duodenal, and esophageal ulcers arising in persons with intracranial injury, operations, or tumors. They are thought to be caused by hypersecretion of gastric acid resulting from stimulation of vagal nuclei by increased intracranial pressure. These ulcers are associated with a high incidence of perforation.<sup>11</sup>

Stress ulcers develop in approximately 5% to 10% of persons admitted to hospital intensive care units.<sup>11</sup> They usually are manifested by painless upper gastrointestinal tract bleeding. Monitoring and maintaining the gastric pH at 3.5 or higher helps to prevent the development of stress ulcers. H<sub>2</sub>-receptor antagonists, proton pump inhibitors, and mucosal protective agents are used in the prevention and treatment of stress ulcers.

## Cancer of the Stomach

Stomach cancer is the seventh most frequent cause of cancer mortality in the United States. In 2003, it is estimated that approximately 22,400 Americans will receive a diagnosis of stomach cancer and 12,100 will die of the disease.<sup>21</sup> The disease is much more common in other countries and regions, principally Japan, central Europe, the Scandinavian countries, South and Central America, republics of the former Soviet Union, China, and Korea. It is the major cause of cancer death worldwide.

Among the factors that increase the risk of gastric cancer are a genetic predisposition, carcinogenic factors in the diet (*e.g.*, *N*-nitroso compounds and benzopyrene found in smoked and preserved foods), autoimmune gastritis, and gastric adenomas or polyps. The incidence of stomach cancer in the United States has decreased fourfold since 1930, presumably because of improved storage of food with decreased consumption of salted, smoked, and preserved foods.<sup>11,21</sup> Infection with *H. pylori* appears to serve as a cofactor in some types of gastric carcinomas.<sup>11</sup>

Between 50% and 60% of gastric cancers occur in the pyloric region or adjacent to the antrum. Compared with a benign ulcer, which has smooth margins and is concentrically shaped, gastric cancers tend to be larger, are irregularly shaped, and have irregular margins.

Unfortunately, stomach cancers often are asymptomatic until late in their course. Symptoms, when they do occur, usually are vague and include indigestion, anorexia, weight loss, vague epigastric pain, vomiting, and an abdominal mass.

Diagnosis of gastric cancer is accomplished by means of a variety of techniques, including barium x-ray studies, endoscopic studies with biopsy, and cytologic studies (*e.g.*, Papanicolaou smear) of gastric secretions. Cytologic studies can prove particularly useful as routine screening tests for persons with atrophic gastritis or gastric polyps. Computed tomography (CT) and endoscopic ultrasonography often are used to delineate the spread of a diagnosed stomach cancer.

Surgery in the form of radical subtotal gastrectomy usually is the treatment of choice.<sup>21</sup> Irradiation and chemotherapy have not proved particularly useful as primary treatment modalities in stomach cancer. These methods usually are used for palliative purposes or to control metastatic spread of the disease.

**In summary**, disorders of the stomach include gastritis, peptic ulcer, and cancer of the stomach. Gastritis refers to inflammation of the gastric mucosa. Acute gastritis refers to a transient inflammation of the gastric mucosa; it is associated most commonly with local irritants such as bacterial endotoxins, caffeine, alcohol, and aspirin. Chronic gastritis is characterized by the absence of grossly visible erosions and the presence of chronic inflammatory changes leading eventually to atrophy of the glandular epithelium of the stomach. Chronic gastritis increases the risk of stomach cancer.

Peptic ulcer is a term used to describe a group of ulcerative disorders that occur in areas of the upper gastrointestinal tract that are exposed to acid-pepsin secretions, most commonly the duodenum and stomach. There are two main causes of peptic ulcer: *H. pylori* infection and aspirin or NSAID use. The treatment of peptic ulcer focuses on eradication of

*H. pylori*, avoidance of gastric irritation from NSAIDs, and conventional pharmacologic treatment directed at symptom relief and ulcer healing.

The Zollinger-Ellison syndrome is a rare condition caused by a gastrin-secreting tumor, in which gastric acid secretion reaches such levels that ulceration becomes inevitable. Stress ulcers occur in relation to major physiologic stresses such as burns and trauma and are thought to result from ischemia, tissue acidosis, and bile salts entering the stomach in critically ill persons with decreased gastrointestinal tract motility. Another form of stress ulcer, resulting from hypersecretion of gastric acid caused by stimulation of vagal nuclei by increased intracranial pressure, may develop in persons with intracranial injury, operations, or tumors.

Although the incidence of cancer of the stomach has declined during the past 50 years, it remains the seventh leading cause of death in the United States. Because there are few early symptoms with this form of cancer, the disease often is far advanced at the time of diagnosis.

## DISORDERS OF THE SMALL AND LARGE INTESTINES

There are many similarities in conditions that disrupt the integrity and function of the small and large intestine. The walls of the small and large intestines consist of five layers (see Chapter 26, Fig. 26-3): an outer serosal layer; a muscularis layer, which is divided into a layer of circular and a layer of longitudinal muscle fibers; a submucosal layer; and an inner mucosal layer, which lines the lumen of the intestine. Among the conditions that cause altered intestinal function are irritable bowel disease, inflammatory bowel disease, diverticulitis, appendicitis, alterations in bowel motility (*i.e.*, diarrhea, constipation, and bowel obstruction), malabsorption syndrome, and cancer of the colon and rectum.

### Irritable Bowel Syndrome

The term *irritable bowel syndrome* is used to describe a functional gastrointestinal disorder characterized by a variable combination of chronic and recurrent intestinal symptoms not explained by structural or biochemical abnormalities. There is evidence to suggest that 10% to 20% of people in Western countries have the disorder, although most do not seek medical attention.<sup>22,23</sup>

The condition is characterized by persistent or recurrent symptoms of abdominal pain, altered bowel function, and varying complaints of flatulence, bloatedness, nausea and anorexia, and anxiety or depression. A hallmark of irritable bowel syndrome is abdominal pain that is relieved by defecation and associated with a change in consistency or frequency of stools.

Irritable bowel syndrome is believed to result from dysregulation of intestinal motor and sensory functions modulated by the CNS.<sup>23</sup> Persons with irritable bowel syndrome tend to experience increased motility and abnormal intestinal contractions in response to psychological and physiologic stress. The role that psychological factors play in the disease is uncertain.

Although changes in intestinal activity are normal responses to stress, these responses appear to be exaggerated in persons with irritable bowel syndrome. Women tend to be affected more often than men. Menarche often is associated with onset of the disorder. Women frequently notice an exacerbation of symptoms during the premenstrual period, suggesting a hormonal component.

Diagnosis of irritable bowel syndrome is based on continuous or recurrent symptoms of at least 3 months' duration consisting of abdominal pain or discomfort relieved by defecation, a change in the frequency or consistency of stool, and the presence of three or more varying patterns of altered defecation that are present at least 25% of the time.<sup>24</sup> These patterns of defecation include altered stool frequency, altered stool form (*i.e.*, hard or loose, watery stool), altered stool passage (*i.e.*, straining, urgency, or feeling of incomplete evacuation), passage of mucus, and bloating or feeling of abdominal discomfort. A history of lactose intolerance should be considered because intolerance to lactose and other sugars may be a precipitating factor in some persons.

The treatment of irritable bowel syndrome focuses on methods of stress management, particularly those related to symptom production. Reassurance is important. Usually, no special diet is indicated, although adequate fiber intake usually is recommended. Avoidance of offending dietary substances such as fatty and gas-producing foods, alcohol, and caffeine-containing beverages may be beneficial. Various pharmacologic agents, including antispasmodic and anticholinergic drugs, have been used with varying success in treatment of the disorder.

### Inflammatory Bowel Disease

The term *inflammatory bowel disease* is used to designate two related inflammatory intestinal disorders: Crohn's disease and ulcerative colitis.<sup>25,26</sup> The prevalence of these diseases ranges from 300,000 to 500,000. Although the two diseases differ sufficiently to be distinguishable, they have many features in common. Both diseases produce inflammation of the bowel, both lack confirming evidence of a proven causative agent, both have a pattern of familial occurrence, and both can be accompanied by systemic manifestations.<sup>16</sup> The distinguishing characteristics of Crohn's disease and ulcerative colitis are summarized in Table 27-1.

The etiology of Crohn's disease and ulcerative colitis is largely unknown, but several theories have been proposed regarding their causation. The diseases appear to have a familial occurrence, suggesting a hereditary predisposition.<sup>11</sup> It is thought that genetic factors predispose to an autoimmune reaction, possibly triggered by a relatively innocuous environmental agent such as a dietary antigen or microbial agent. It also is thought that the diseases may have an infectious origin, such as Chlamydia, atypical bacteria, and mycobacteria.<sup>11</sup> Another theory is one of defective immunoregulation, in which the mucosal branch of the immune system is stimulated and then fails to down-regulate. Although psychogenic factors may contribute to the severity and onset of both conditions, it seems unlikely that they are the primary cause.

The clinical manifestations of both Crohn's disease and ulcerative colitis are ultimately the result of activation of inflammatory cells with elaboration of inflammatory mediators that

**TABLE 27-1** Differentiating Characteristics of Crohn's Disease and Ulcerative Colitis

Characteristic	Crohn's Disease	Ulcerative Colitis
Types of inflammation	Granulomatous	Ulcerative and exudative
Level of involvement	Primarily submucosal	Primarily mucosal
Extent of involvement	Skip lesions	Continuous
Areas of involvement	Primarily ileum, secondarily colon	Primarily rectum and left colon
Diarrhea	Common	Common
Rectal bleeding	Rare	Common
Fistulas	Common	Rare
Strictures	Common	Rare
Perianal abscesses	Common	Rare
Development of cancer	Uncommon	Relatively common

cause nonspecific tissue damage. Both diseases are characterized by remissions and exacerbations of diarrhea, fecal urgency, and weight loss. Acute complications such as intestinal obstruction may develop during periods of fulminant disease.

A number of systemic manifestations have been identified in persons with Crohn's disease and ulcerative colitis. These include axial arthritis affecting the spine and sacroiliac joints and oligoarticular arthritis affecting the large joints of the arms and legs; inflammatory conditions of the eye, usually uveitis; skin lesions, especially erythema nodosum; stomatitis; and autoimmune anemia, hypercoagulability of blood, and sclerosing cholangitis. Occasionally, these systemic manifestations may herald the recurrence of intestinal disease. In children, growth retardation may occur, particularly if the symptoms are prolonged and nutrient intake has been poor.

### Crohn's Disease

Crohn's disease is a recurrent, granulomatous type of inflammatory response that can affect any area of the gastrointestinal tract from the mouth to the anus. In nearly 40% of persons with disease, the lesions are restricted to the small intestine; in 30%, only the large bowel is affected; and in the remaining 30%, the large bowel and small bowel are affected.<sup>11</sup> It is a slowly progressive, relentless, and often disabling disease. Despite the substantial increase in the prevalence of Crohn's disease in the early 1980s, the distribution of affected sites has not changed substantially. The disease usually strikes adolescents and young adults and is most common among persons of European origin, with considerably higher frequency among Ashkenazi Jews.<sup>16</sup>

A characteristic feature of Crohn's disease is the sharply demarcated, granulomatous lesions that are surrounded by normal-appearing mucosal tissue. When the lesions are multiple, they often are referred to as *skip lesions* because they are interspersed between what appear to be normal segments of the bowel. All the layers of the bowel are involved, with the submucosal layer affected to the greatest extent. The surface of the inflamed bowel usually has a characteristic "cobblestone" appearance resulting from the fissures and crevices that develop and that are surrounded by areas of submucosal edema (Fig. 27-4). There usually is a relative sparing of the smooth muscle layers of the bowel, with marked inflammatory and fibrotic changes of the submucosal layer. The bowel wall, after

a time, often becomes thickened and inflexible; its appearance has been likened to a lead pipe or rubber hose. The adjacent mesentery may become inflamed, and the regional lymph nodes and channels may become enlarged.

The clinical course of Crohn's disease is variable; often, there are periods of exacerbations and remissions, with symptoms being related to the location of the lesions. The principal symptoms include intermittent diarrhea, colicky pain (usually in the lower right quadrant), weight loss, fluid and electrolyte disorders, malaise, and low-grade fever. Because Crohn's disease affects the submucosal layer to a greater extent than the mucosal layer, there is less bloody diarrhea than with ulcerative colitis. Ulceration of the perianal skin is common, largely because of the severity of the diarrhea. The absorptive surface of the intestine may be disrupted; nutritional deficiencies may occur, related to the specific segment of the intestine that is involved. When Crohn's disease occurs in childhood, one of its major manifestations may be retardation of growth and physical development.<sup>16</sup>

Complications of Crohn's disease include fistula formation, perforation, abdominal abscess formation, and intestinal obstruction (Fig. 27-4). Fistulas are tubelike passages that form connections between different sites in the gastrointestinal tract.



**FIGURE 27-4** Crohn's disease. The mucosal surface of the colon displays a "cobblestone" appearance owing to the presence of linear ulcerations and edema and inflammation of the intervening tissue. (From Rubin E., Farber J.L. [1999]. *Pathology* [3rd ed., p. 728]. Philadelphia: Lippincott Williams & Wilkins)

They also may develop between other sites, including the bladder, vagina, urethra, and skin. Fistulas between segments of the gastrointestinal tract may lead to malabsorption, syndromes of bacterial overgrowth, and diarrhea. They also can become infected and cause abscess formation.

**Diagnosis and Treatment.** The diagnosis of Crohn's disease requires a thorough history and physical examination. Sigmoidoscopy is used for direct visualization of the affected areas and to obtain biopsies. Measures are taken to exclude infectious agents as the cause of the disorder. This usually is accomplished by the use of stool cultures and examination of fresh stool specimens for ova and parasites. In persons suspected of having Crohn's disease, radiologic contrast studies provide a means for determining the extent of involvement of the small bowel and establishing the presence and nature of fistulas. CT scans may be used to detect an inflammatory mass or abscess.

Treatment methods focus on terminating the inflammatory response and promoting healing, maintaining adequate nutrition, and preventing and treating complications. Nutritional deficiencies are common in Crohn's disease because of diarrhea, steatorrhea (fatty stools), and other malabsorption problems. A nutritious diet that is high in calories, vitamins, and proteins is recommended. Elemental diets, which are nutritionally balanced but residue free and bulk free, may be given during the acute phase of the illness. These diets are largely absorbed in the jejunum and allow the inflamed bowel to rest. Total parenteral nutrition (*i.e.*, parenteral hyperalimentation), which is administered intravenously, may be needed when food cannot be absorbed from the intestine.

Several medications have been successful in suppressing the inflammatory reaction, including the corticosteroids, sulfasalazine, and metronidazole. Sulfasalazine is a topically active agent that has a variety of anti-inflammatory effects. Metronidazole is an antibiotic used to treat bacterial overgrowth in the small intestine. Immunosuppressive drugs such as azathioprine and its active derivative, 6-mercaptopurine, also may be used. Infliximab, a monoclonal antibody that targets tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), a mediator of the inflammatory response, may be used for treatment of moderate to severe Crohn's disease that does not respond to standard therapies.<sup>27</sup> Surgical resection of damaged bowel, drainage of abscesses, or repair of fistula tracts may be necessary.

### Ulcerative Colitis

Ulcerative colitis is a nonspecific inflammatory condition of the colon. The disease begins most often between 20 and 25 years of age, but the condition may affect both younger and older persons.<sup>11</sup> Unlike Crohn's disease, which can affect various sites in the gastrointestinal tract, ulcerative colitis is confined to the rectum and colon. The disease usually begins in the rectum and spreads proximally, affecting primarily the mucosal layer, although it can extend into the submucosal layer. The length of proximal extension varies. It may involve the rectum alone, the rectum and sigmoid colon, or the entire colon. The inflammatory process tends to be confluent and continuous, instead of skipping areas, as it does in Crohn's disease.

Characteristic of the disease are the lesions that form in the crypts of Lieberkühn in the base of the mucosal layer (see

Chapter 26, Fig. 26-10). The inflammatory process leads to the formation of pinpoint mucosal hemorrhages, which in time suppurate and develop into crypt abscesses. These inflammatory lesions may become necrotic and ulcerate. Although the ulcerations usually are superficial, they often extend, causing large denuded areas (Fig. 27-5). As a result of the inflammatory process, the mucosal layer often develops tongue-like projections that resemble polyps and thus are called *pseudopolyps*. The bowel wall thickens in response to repeated episodes of colitis.

Diarrhea, which is the characteristic manifestation of ulcerative colitis, varies according to the severity of the disease. There may be as many as 30 to 40 bowel movements a day. Because ulcerative colitis affects the mucosal layer of the bowel, the stools typically contain blood and mucus. Nocturnal diarrhea usually occurs when daytime symptoms are severe. There may be mild abdominal cramping and fecal incontinence. Anorexia, weakness, and fatigability are common.

Ulcerative colitis usually follows a course of remissions and exacerbations. The severity of the disease varies from mild to fulminating. Accordingly, the disease has been divided into three types: mild chronic, chronic intermittent, and acute fulminating. The most common form of the disease is the mild chronic, in which bleeding and diarrhea are mild and systemic signs are minimal or absent. This form of the disease usually can be managed conservatively. The chronic intermittent form continues after the initial attack. Compared with the milder form, more of the colon surface usually is involved with the chronic intermittent form, and there are more systemic signs and complications. In approximately 15% of affected persons, the disease assumes a more fulminant course, involves the entire colon, and manifests with severe, bloody diarrhea, fever, and acute abdominal pain. These persons are at risk for development of toxic megacolon, which is characterized by dilatation of the colon and signs of systemic toxicity. It results from extension of the inflammatory response, with involvement of neural and vascular components of the bowel. Contributing factors include the use of laxatives, narcotics, and



■ **FIGURE 27-5** ■ Ulcerative colitis. Prominent erythema and ulceration of the colon begin in the ascending colon and are most severe in the rectosigmoid area. (From Rubin E., Farber J.L. [1999]. *Pathology* [3rd ed., p. 731]. Philadelphia: Lippincott Williams & Wilkins)

anticholinergic drugs and the presence of hypokalemia. Cancer of the colon is one of the feared complications of ulcerative colitis.

**Diagnosis and Treatment.** Diagnosis of ulcerative colitis is based on history and physical examination. The diagnosis usually is confirmed by proctosigmoidoscopy.

Treatment depends on the extent of the disease and severity of symptoms. It includes measures to control the acute manifestations of the disease and prevent recurrence. Some people with mild to moderate symptoms are able to control their symptoms simply by avoiding caffeine, lactose (milk), highly spiced foods, and gas-forming foods. Fiber supplements may be used to decrease diarrhea and rectal symptoms.

The medications used in treatment of ulcerative colitis are similar to those used in the treatment of Crohn's disease. The corticosteroids are used selectively to lessen the acute inflammatory response. Many of these medications can be administered rectally by suppository or enema. Immunosuppressant drugs, such as cyclosporine, may be used to treat persons with severe colitis.

Surgical treatment (*i.e.*, removal of the rectum and entire colon) with the creation of an ileostomy or ileoanal anastomosis may be required for those persons with ulcerative colitis who do not experience a response to conservative methods of treatment.

## Infectious Colitis

Two forms of pathogens have emerged as important causes of infectious colitis: *Clostridium difficile* and *Escherichia coli* serotype O157:H7.

### *Clostridium Difficile* Colitis

*C. difficile*, which is part of normal flora in 2% to 10% of humans, is a gram-positive spore-forming bacillus that has been implicated as the offending organism in colitis associated with antibiotic therapy.<sup>28</sup> The spores are resistant to the acid environment of the stomach and convert to vegetative forms in the colon. Treatment with broad-spectrum antibiotics predisposes to disruption of the normal bacterial flora of the colon, leading to colonization by *C. difficile*. Almost any antibiotic may cause *C. difficile* colitis, but broad-spectrum antibiotics with activity against the gram-negative bacteria of the normal intestinal flora are the most common agents.<sup>28</sup> After antibiotic therapy has made the bowel susceptible to infection, colonization by *C. difficile* occurs by the oral-fecal route. *C. difficile* infection usually is acquired in the hospital, where the organism is commonly encountered.

*C. difficile*, which is not invasive, produces its effects through the release of toxins that cause mucosal damage and inflammation. The infection commonly manifests with diarrhea that is mild to moderate and sometimes is accompanied by lower abdominal cramping. Symptoms usually begin during or shortly after antibiotic therapy has been initiated, although they can be delayed for weeks. In most cases, systemic manifestations are absent, and the symptoms subside after the antibiotic has been discontinued. In the more severe cases, mucosal damage results in the development of a pseudomembranous colitis. It is a life-threatening form of the disease characterized by an adherent inflammatory membrane overlying

the areas of mucosal injury. Persons with the disease are acutely ill, with lethargy, fever, tachycardia, abdominal pain and distention, and dehydration. The smooth muscle tone of the colon may be lost, resulting in toxic dilatation of the colon. Prompt therapy is needed to prevent perforation of the bowel.

Diagnostic findings include a history of antibiotic use and laboratory tests that confirm the presence of *C. difficile* toxins in the stool. Treatment includes the immediate discontinuation of antibiotic therapy. Specific treatment aimed at eradicating *C. difficile* is used when symptoms are severe or persistent.<sup>28,29</sup>

### *Escherichia Coli* O157:H7 Infection

*E. coli* O157:H7 is a strain of *E. coli* found in feces and contaminated milk of healthy dairy and beef cattle, but it also has been found in pork, poultry, and lamb. Infection usually is by food-borne transmission, often by ingesting undercooked hamburger. The organism also can be transferred to nonmeat products such as fruits and vegetables. Person-to-person transmission may occur, particularly in nursing homes, day care settings, and hospitals. The very young and the very old are particularly at risk for the infection and its complications.

The infection may cause no symptoms or cause a variety of manifestations, including acute, nonbloody diarrhea, hemorrhagic colitis, hemolytic-uremic syndrome, and thrombotic thrombocytopenic purpura. The infection often presents with abdominal cramping and watery diarrhea and subsequently may progress to bloody diarrhea. The diarrhea commonly lasts 3 to 7 days or longer, with 10 to 12 diarrheal episodes per day. Fever occurs in up to one third of the cases.

An important aspect of the disease is the production of toxins and the ability to produce toxemia. The two complications of the infection, hemolytic-uremic syndrome and thrombotic thrombocytopenic purpura, reflect the effects of toxins. Hemolytic-uremic syndrome is characterized by hemolytic anemia, thrombocytopenia, and renal failure. It occurs predominantly in infants and young children and is the most common cause of acute renal failure in children.<sup>30</sup> It has a mortality rate of 5% to 10%, and one third of the survivors are left with permanent disability. Thrombotic thrombocytopenic purpura is manifested by thrombocytopenia, renal failure, fever, and neurologic manifestations. It often is regarded as the severe end of the disease that leads to hemolytic-uremic syndrome plus neurologic problems.

No specific therapy is available for *E. coli* O157:H7 infection. Treatment is largely symptomatic and directed toward treating the effects of complications. Antibiotics have not proved useful and may even be harmful, extending the duration of bloody diarrhea.

Because of the seriousness of the infection and its complications, education of the public about techniques for decreasing primary transmission of the infection from animal sources is important. Undercooked meats and unpasteurized milk are sources of transmission. The FDA recommends a minimal internal temperature of 155°F for cooked hamburger. Food handlers and consumers should be aware of the proper methods for handling uncooked meat to prevent cross-contamination of other foods. Particular attention should be paid to hygiene in day care centers and nursing homes, where

the spread of infection to the very young and very old may result in severe complications.<sup>30</sup>

## Diverticular Disease

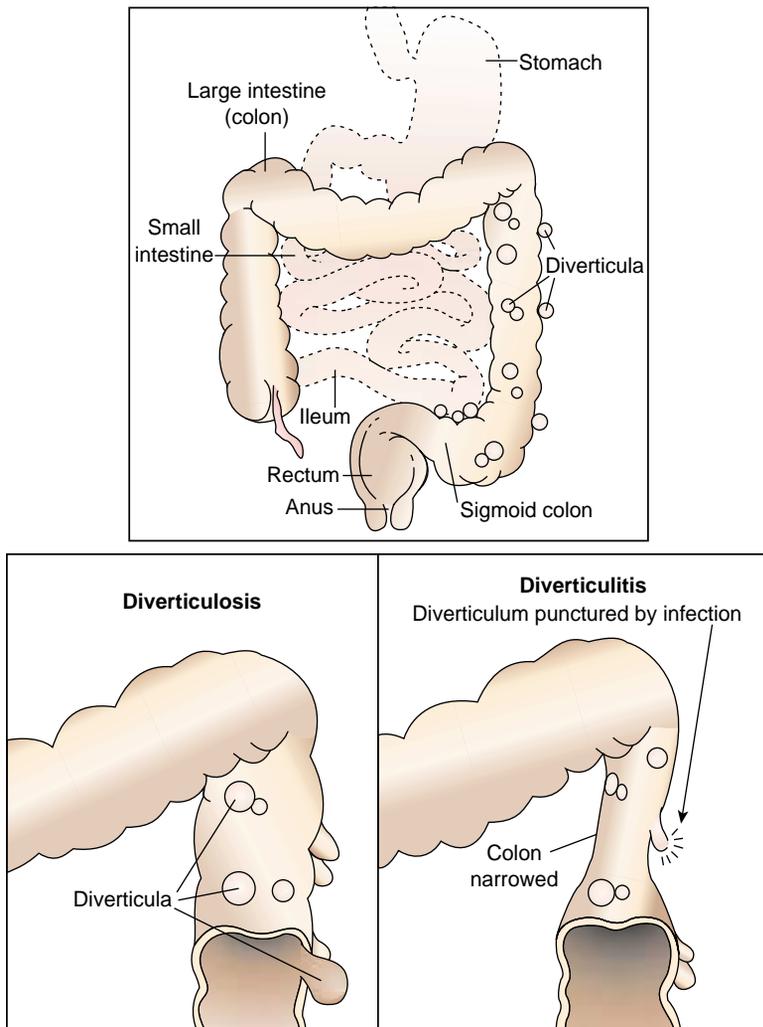
*Diverticulosis* is a condition in which the mucosal layer of the colon herniates through the muscularis layer.<sup>31</sup> Often, there are multiple diverticula, and most occur in the sigmoid colon (Fig. 27-6). Diverticular disease is common in Western society, affecting approximately 5% to 10% of the population older than 45 years and almost 80% of those older than 85 years.<sup>31</sup> Although the disorder is prevalent in the developed countries of the world, it is almost nonexistent in many African nations and underdeveloped countries. This suggests that dietary factors (e.g., lack of fiber content), a decrease in physical activity, and poor bowel habits (e.g., neglecting the urge to defecate), along with the effects of aging, contribute to the development of the disease.

Diverticula, in which the mucosal and submucosal layers herniate through the muscle layers of the colon, are located primarily in the sigmoid colon but can affect any area of the colon. They vary in number from a few to several hundred. The diverticula, which measure up to 1 cm in greatest dimension, are attached to the intestinal lumen by necks of varying size.

Hardened feces may be present in the diverticula without causing symptoms.

Most persons with diverticular disease remain asymptomatic. The disease often is found when x-ray studies are done for other purposes. When symptoms do occur, they often are attributed to irritable bowel syndrome or other causes. Ill-defined lower abdominal discomfort, a change in bowel habits (e.g., diarrhea, constipation), bloating, and flatulence are common.

*Diverticulitis* is a complication of diverticulosis in which there is inflammation and gross or microscopic perforation of the diverticulum. One of the most common complaints of diverticulitis is pain in the lower left quadrant, accompanied by nausea and vomiting, tenderness in the lower left quadrant, a slight fever, and an elevated white blood cell count. These symptoms usually last for several days, unless complications occur, and usually are caused by localized inflammation of the diverticula with perforation and development of a small, localized abscess. Complications include perforation with peritonitis, hemorrhage, and bowel obstruction. Fistulas can form, usually involving the bladder (i.e., vesicosigmoid fistula) but sometimes involving the skin, perianal area, or small bowel. Pneumaturia (i.e., air in the urine) is a sign of vesicosigmoid fistula.



■ **FIGURE 27-6** ■ (Top) Location of diverticula in the sigmoid colon. (Bottom left) Diverticulosis. (Bottom right) Diverticulitis. (National Digestive Diseases Information Clearinghouse. [1989]. *Clearinghouse fact sheet: Diverticulosis and diverticulitis*. NIH publication 90-1163. Washington, DC: US Department of Health and Human Services)

The diagnosis of diverticular disease is based on history and presenting clinical manifestations. The disease may be confirmed by barium enema x-ray studies (except when acute diverticulitis is suspected), CT scans, and ultrasonographic studies. The treatment goals for diverticular disease focus on prevention of symptoms and complications. This includes increasing the bulk in the diet and bowel retraining so that the person has at least one bowel movement each day. Acute diverticulitis is treated by withholding solid food and administering a broad-spectrum antibiotic. Surgical treatment is reserved for complications.

## Appendicitis

Acute appendicitis is extremely common. It is seen most frequently in the 5- to 30-year-old age group, but it can occur at any age. The appendix becomes inflamed, swollen, and gangrenous, and it eventually perforates if not treated. Although the cause of appendicitis is unknown, it is thought to be related to intraluminal obstruction with a fecalith (*i.e.*, hard piece of stool) or to twisting.

Appendicitis usually has an abrupt onset, with pain referred to the epigastric or periumbilical area. This pain is caused by stretching of the appendix during the early inflammatory process. At approximately the same time that the pain appears, there are one or two episodes of nausea. Initially, the pain is vague, but over a period of 2 to 12 hours, it gradually increases and may become colicky. When the inflammatory process has extended to involve the serosal layer of the appendix and the peritoneum, the pain becomes localized to the lower right quadrant. There usually is an elevation in temperature and a white blood cell count greater than 10,000/mm<sup>3</sup>, with 75% or more polymorphonuclear cells. Palpation of the abdomen usually reveals a deep tenderness in the lower right quadrant, which is confined to a small area approximately the size of the fingertip. It usually is located at approximately the site of the inflamed appendix. Rebound tenderness, which is pain that occurs when pressure is applied to the area and then released, and spasm of the overlying abdominal muscles are common.

Treatment consists of surgical removal of the appendix. Complications include peritonitis, localized periappendiceal abscess formation, and septicemia.

## Alterations in Intestinal Motility

The movement of contents through the gastrointestinal tract is controlled by neurons located in the submucosal and myenteric plexuses of the gut (see Chapter 26). The axons from the cell bodies in the myenteric plexus innervate the circular and longitudinal smooth muscle layers of the gut. These neurons receive impulses from local receptors located in the mucosal and muscle layers of the gut and extrinsic input from the parasympathetic and sympathetic nervous systems. As a general rule, the parasympathetic nervous system tends to increase the motility of the bowel, whereas sympathetic stimulation tends to slow its activity.

The colon has sphincters at both ends: the ileocecal sphincter, which separates it from the small intestine, and the anal sphincter, which prevents the movement of feces to the outside of the body. The colon acts as a reservoir for fecal material. Normally, approximately 400 mL of water, 55 mEq of sodium, 30 mEq of chloride, and 15 mEq of bicarbonate are absorbed

## KEY CONCEPTS

### DISORDERS OF GASTROINTESTINAL MOTILITY

- The enteric nervous system that is incorporated into the wall of the gut controls the basic movement of the gastrointestinal tract, with input from the autonomic nervous system.
- Local irritation and the composition and constituents of gastrointestinal contents influence motility through the submucosal afferent neurons of the enteric nervous system. Gastrointestinal wall distention, chemical irritants, osmotic gradients, and bacterial toxins exert many of their effects on gastrointestinal motility through these afferent pathways.
- Autonomic influences generated by factors such as medications, trauma, and emotional experiences interact with the enteric nervous system to alter gastrointestinal motility.

each day in the colon. At the same time, approximately 5 mEq of potassium is secreted into the lumen of the colon. The amount of water and electrolytes that remains in the stool reflects the absorption or secretion that occurs in the colon. The average adult ingesting a typical American diet evacuates approximately 200 to 300 g of stool each day.

## Diarrhea

The usual definition of *diarrhea* is excessively frequent passage of stools. Diarrhea can be acute or chronic. Diarrhea is considered to be chronic when the symptoms persist for 3 weeks in children or adults and 4 weeks in infants. Acute diarrhea affects 500 million children throughout the world and is the leading cause of death of children younger than 4 years of age.<sup>32</sup> Although diarrheal disease in the United States is less prevalent than it is in other countries, it places a burden on the health care system. Approximately 220,000 children are hospitalized each year for gastroenteritis.<sup>33</sup>

The complaint of diarrhea is a general one and can be related to a number of pathologic and nonpathologic factors. It can be caused by infectious organisms, food intolerance, drugs, or intestinal disease. Acute diarrheas that last less than 4 days are predominantly caused by infectious agents and follow a self-limited course.<sup>34</sup> Chronic diarrheas are those that persist for longer than 3 to 4 weeks. They often are caused by conditions such as inflammatory bowel disease, irritable bowel syndrome, malabsorption syndrome, endocrine disorders (hyperthyroidism, diabetic autonomic neuropathy), or radiation colitis.

Diarrhea commonly is divided into two types, large volume and small volume, based on the characteristics of the diarrheal stool. Large-volume diarrhea results from an increase in the water content of the stool, and small-volume diarrhea results from an increase in the propulsive activity of the bowel. Some of the common causes of small- and large-volume diarrhea are summarized in Chart 27-1. Often, diarrhea is a combination of these two types.

### CHART 27-1 Causes of Large- and Small-Volume Diarrhea

#### Large-Volume Diarrhea

Osmotic diarrhea  
 Saline cathartics  
 Lactase deficiency  
 Secretory diarrhea  
 Acute infectious diarrhea  
 Failure to absorb bile salts  
 Fat malabsorption  
 Chronic laxative abuse  
 Carcinoid syndrome  
 Zollinger-Ellison syndrome  
 Fecal impaction

#### Small-Volume Diarrhea

Inflammatory bowel disease  
 Crohn's disease  
 Ulcerative colitis  
 Infectious disease  
 Shigellosis  
 Salmonellosis  
 Irritable colon

**Large-Volume Diarrhea.** Large-volume diarrhea can be classified as secretory or osmotic, according to the cause of the increased water content in the feces. Water is pulled into the colon along an osmotic gradient (*i.e.*, osmotic diarrhea) or is secreted into the bowel by the mucosal cells (*i.e.*, secretory diarrhea). The large-volume form of diarrhea usually is a painless, watery type without blood or pus in the stools.

In osmotic diarrhea, water is pulled into the bowel by the hyperosmotic nature of its contents. It occurs when osmotically active particles are not absorbed. In persons with lactase deficiency, the lactose in milk cannot be broken down and absorbed. Magnesium salts, which are contained in milk of magnesia and many antacids, are poorly absorbed and cause diarrhea when taken in sufficient quantities. Another cause of osmotic diarrhea is decreased transit time, which interferes with absorption. Osmotic diarrhea usually disappears with fasting.

Secretory diarrhea occurs when the secretory processes of the bowel are increased. Most acute infectious diarrheas are of this type. Enteric organisms cause diarrhea by several ways. Some are noninvasive but secrete toxins that stimulate fluid secretion (*e.g.*, pathogenic *E. coli* or *Vibrio cholerae*). Others (*e.g.*, *Staphylococcus aureus*, *Bacillus cereus*, *Clostridium perfringens*) invade and destroy intestinal epithelial cells, thereby altering fluid transport so that secretory activity continues while absorption activity is halted.<sup>35</sup> Diarrhea with vomiting and fever suggests food poisoning, often caused by staphylococcal enterotoxin. Secretory diarrhea also occurs when excess bile acids remain in the intestinal contents as they enter the colon. This often happens with disease processes of the ileum because bile salts are absorbed there. It also may occur with bacterial overgrowth in the small bowel, which interferes with bile absorption.

**Small-Volume Diarrhea.** Small-volume diarrhea commonly is associated with acute or chronic inflammation or intrinsic disease of the colon, such as ulcerative colitis or Crohn's disease. Small-volume diarrhea usually is evidenced by frequency and urgency and colicky abdominal pain. It commonly is accompanied by tenesmus (*i.e.*, painful straining at stool), fecal soiling of clothing, and awakening during the night with the urge to defecate.

**Diagnosis and Treatment.** The diagnosis of diarrhea is based on complaints of frequent stools and a history of accompanying factors such as concurrent illnesses, medication use, and exposure to potential intestinal pathogens. Disorders such as inflammatory bowel disease should be considered. If the onset of diarrhea is related to travel outside the United States, the possibility of traveler's diarrhea must be considered.

Although most acute forms of diarrhea are self-limited and require no treatment, diarrhea can be particularly serious in infants and small children, persons with other illnesses, the elderly, and even previously healthy persons if it continues for any length of time. Thus, the replacement of fluids and electrolytes is considered to be a primary therapeutic goal in the treatment of diarrhea. Oral electrolyte replacement solutions can be given in situations of uncomplicated diarrhea that can be treated at home. Evidence suggests that feeding should be continued during diarrheal illness, particularly in children.<sup>33,36</sup> It is recommended that children who require rehydration therapy because of diarrhea be fed an age-appropriate diet. Starch and simple proteins are thought to provide cotransport molecules with little osmotic activity, increasing fluid and electrolyte uptake by intestinal cells. When oral rehydration is not feasible or adequate, intravenous fluid replacement may be needed.

Drugs used in the treatment of diarrhea include diphenoxylate and loperamide, which are opium-like drugs. These drugs decrease gastrointestinal motility and stimulate water and electrolyte absorption. Adsorbents, such as kaolin and pectin, adsorb irritants and toxins from the bowel. These ingredients are included in many over-the-counter antidiarrheal preparations. Bismuth subsalicylate can be used to reduce the frequency of unformed stools and increase stool consistency, particularly in cases of traveler's diarrhea. The drug is thought to inhibit intestinal secretion caused by enterotoxigenic *E. coli* and cholera toxins. Diarrheal medications should not be used in persons with bloody diarrhea, high fever, or signs of toxicity for fear of worsening the disease. Antibiotics are reserved for persons with identified enteric pathogens.

### Constipation

Constipation can be defined as the infrequent passage of stools. The difficulty with this definition arises from the many individual variations of function that are normal. What is considered normal for one person (*e.g.*, two or three bowel movements per week) may be considered evidence of constipation by another. The problem increases with age; there is a sharp rise in health care visits for constipation after 65 years of age.

Constipation can occur as a primary problem or as a problem associated with another disease condition. Some common causes of constipation are failure to respond to the urge to defecate, inadequate fiber in the diet, inadequate fluid intake, weakness of the abdominal muscles, inactivity and bed rest, pregnancy, and hemorrhoids. Diseases associated with chronic

constipation include neurologic diseases such as spinal cord injury, Parkinson's disease, and multiple sclerosis; endocrine disorders such as hypothyroidism; and obstructive lesions in the gastrointestinal tract. Drugs such as narcotics, anticholinergic agents, calcium channel blockers, diuretics, calcium (antacids and supplements), iron supplements, and aluminum antacids tend to cause constipation. Elderly people with long-standing constipation may experience dilation of the rectum, colon, or both. This condition allows large amounts of stool to accumulate with little or no sensation. Constipation, in the context of a change in bowel habits, may be a sign of colorectal cancer.

Diagnosis of constipation usually is based on a history of infrequent stools, straining with defecation, the passing of hard and lumpy stools, or the sense of incomplete evacuation with defecation.<sup>37</sup> Constipation as a sign of another disease condition should be excluded. The treatment of constipation usually is directed toward relieving the cause. Adequate fluid intake and bulk in the diet should be encouraged. Moderate exercise is essential, and persons on bed rest benefit from passive and active exercises. Laxatives and enemas should be used judiciously. They should not be used on a regular basis to treat simple constipation because they interfere with the defecation reflex and enemas may damage the rectal mucosa.

### Intestinal Obstruction

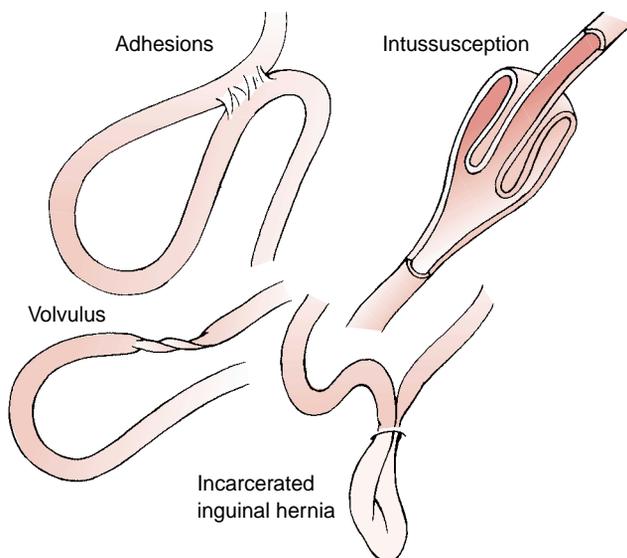
Intestinal obstruction designates an impairment of movement of intestinal contents in the usual oral to anal direction. The causes can be categorized as mechanical or paralytic obstruction. Strangulation with necrosis of the bowel may occur and lead to perforation, peritonitis, and sepsis. This is a serious complication and may increase the mortality rate associated with intestinal obstruction to approximately 25% if surgery is delayed.<sup>6</sup>

Mechanical obstruction can result from a number of conditions, intrinsic or extrinsic, that encroach on the patency of the bowel lumen (Fig. 27-7). Major inciting causes include external hernia (*i.e.*, inguinal, femoral, or umbilical) and postoperative adhesions. Less common causes are strictures, tumor, for-

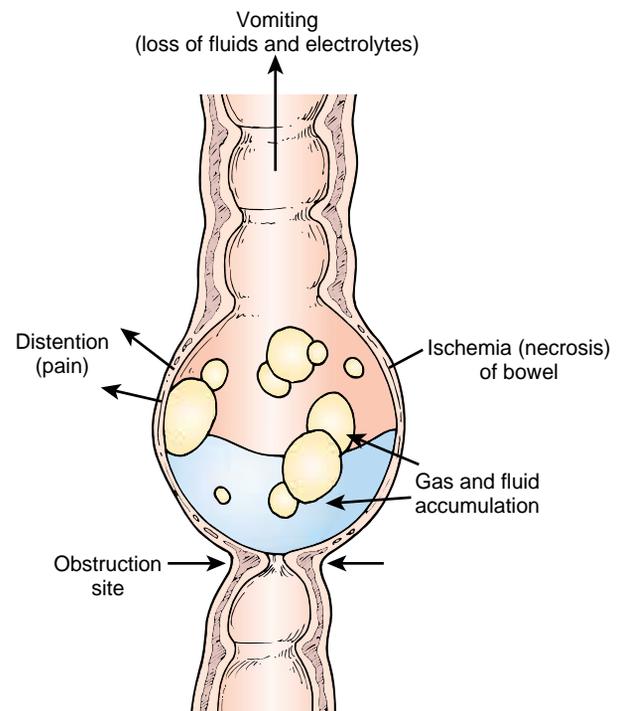
eign bodies, intussusception, and volvulus. Intussusception involves the telescoping of bowel into the adjacent segment. It is the most common cause of intestinal obstruction in children younger than 2 years.<sup>38</sup> The most common form is intussusception of the terminal ileum into the right colon, but other areas of the bowel may be involved. In most cases, the cause of the disorder is unknown. The condition can also occur in adults when an intraluminal mass or tumor acts as a traction force and pulls the segment along as it telescopes into the distal segment. Volvulus refers to a complete twisting of the bowel on an axis formed by its mesentery (see Fig. 27-7). Mechanical bowel obstruction may be a simple obstruction, in which there is no alteration in blood flow, or a strangulated obstruction, in which there is impairment of blood flow and necrosis of bowel tissue.

Paralytic, or adynamic, obstruction results from neurogenic or muscular impairment of peristalsis. Paralytic ileus is seen most commonly after abdominal surgery. It also accompanies inflammatory conditions of the abdomen, intestinal ischemia, pelvic fractures, and back injuries. It occurs early in the course of peritonitis and can result from chemical irritation caused by bile, bacterial toxins, electrolyte imbalances as in hypokalemia, and vascular insufficiency.

The major effects of both types of intestinal obstruction are abdominal distention and loss of fluids and electrolytes (Fig. 27-8). Gases and fluids accumulate in the area; if untreated, the distention resulting from bowel obstruction tends to perpetuate itself by causing atony of the bowel and further distention. Distention is further aggravated by the accumulation of gases. Approximately 70% of these gases are derived from swallowed air. As the process continues, the distention moves proximally (*i.e.*, toward the mouth), involving additional segments of bowel. Either form of obstruction eventually



■ FIGURE 27-7 ■ Causes of mechanical bowel obstruction.



■ FIGURE 27-8 ■ Pathophysiology of intestinal obstruction.

may lead to strangulation (*i.e.*, interruption of blood flow), gangrenous changes, and ultimately, perforation of the bowel. The increased pressure in the intestine tends to compromise mucosal blood flow, leading to necrosis and movement of blood into the luminal fluids. This promotes rapid growth of bacteria in the obstructed bowel. Anaerobes grow rapidly in this favorable environment and produce a lethal endotoxin.

The manifestations of intestinal obstruction depend on the degree of obstruction and its duration. With acute obstruction, the onset usually is sudden and dramatic. With chronic conditions, the onset often is more gradual. The cardinal symptoms of intestinal obstruction are pain, absolute constipation, abdominal distention, and vomiting. With mechanical obstruction, the pain is severe and colicky, in contrast with the continuous pain and silent abdomen of paralytic ileus. There also is borborygmus (*i.e.*, rumbling sounds made by propulsion of gas in the intestine); audible, high-pitched peristalsis; and peristaltic rushes. Visible peristalsis may appear along the course of the distended intestine. Extreme restlessness and conscious awareness of intestinal movements are experienced along with weakness, perspiration, and anxiety. Should strangulation occur, the symptoms change. The character of the pain shifts from the intermittent colicky pain caused by the hyperperistaltic movements of the intestine to a severe and steady type of pain. Vomiting and fluid and electrolyte disorders occur with both types of obstruction.

Diagnosis of intestinal obstruction usually is based on history and physical findings. Abdominal x-ray studies reveal a gas-filled bowel.

Treatment depends on the cause and type of obstruction. Most cases of adynamic obstruction respond to decompression of the bowel through nasogastric suction and correction of fluid and electrolyte imbalances. Strangulation and complete bowel obstruction require surgical intervention.

## Peritonitis

Peritonitis is an inflammatory response of the serous membrane that lines the abdominal cavity and covers the visceral organs. It can be caused by bacterial invasion or chemical irritation. Most commonly, enteric bacteria enter the peritoneum because of a defect in the wall of one of the abdominal organs. The most common causes of peritonitis are perforated peptic ulcer, ruptured appendix, perforated diverticulum, gangrenous bowel, pelvic inflammatory disease, and gangrenous gallbladder. Other causes are abdominal trauma and wounds. Generalized peritonitis, although no longer the overwhelming problem it once was, is still a leading cause of death after abdominal surgery.

The peritoneum has several characteristics that increase its vulnerability to or protect it from the effects of peritonitis. One weakness of the peritoneal cavity is that it is a large, unbroken space that favors the dissemination of contaminants. For the same reason, it has a large surface that permits rapid absorption of bacterial toxins into the blood. The peritoneum is particularly well adapted for producing an inflammatory response as a means of controlling infection. For example, it tends to exude a thick, sticky, and fibrinous substance that adheres to other structures, such as the mesentery and omentum, and that seals off the perforated viscus and aids in localizing the process. Localization is enhanced by sympathetic stimulation that lim-

its intestinal motility. Although the diminished or absent peristalsis that occurs tends to give rise to associated problems, it does inhibit the movement of contaminants throughout the peritoneal cavity.

One of the most important manifestations of peritonitis is the translocation of extracellular fluid into the peritoneal cavity (through weeping or serous fluid from the inflamed peritoneum) and into the bowel as a result of bowel obstruction. Nausea and vomiting cause further losses of fluid. The fluid loss may encourage development of hypovolemia and shock. The onset of peritonitis may be acute, as with a ruptured appendix, or it may have a more gradual onset, as occurs in pelvic inflammatory disease. Pain and tenderness are common symptoms. The pain usually is more intense over the inflamed area. The person with peritonitis usually lies still because any movement aggravates the pain. Breathing often is shallow to prevent movement of the abdominal muscles. The abdomen usually is rigid and sometimes described as boardlike because of reflex muscle guarding. Vomiting is common. Fever, an elevated white blood cell count, tachycardia, and hypotension are common. Hiccups may develop because of irritation of the phrenic nerve. Paralytic ileus occurs shortly after the onset of widespread peritonitis and is accompanied by abdominal distention. Peritonitis that progresses and is untreated leads to toxemia and shock.

Treatment measures for peritonitis are directed toward preventing the extension of the inflammatory response, correcting the fluid and electrolyte imbalances that develop, and minimizing the effects of paralytic ileus and abdominal distention. Surgical intervention may be needed to remove an acutely inflamed appendix or close the opening in a perforated peptic ulcer. Oral fluids are forbidden. Nasogastric suction, which entails the insertion of a tube placed through the nose into the stomach or intestine, is used to decompress the bowel and relieve the abdominal distention. Fluid and electrolyte replacement is essential. These fluids are prescribed on the basis of frequent blood chemistry determinations. Antibiotics are given to combat infection. Narcotics often are needed for pain relief.

## Alterations in Intestinal Absorption

Malabsorption is the failure to transport dietary constituents, such as fats, carbohydrates, proteins, vitamins, and minerals, from the lumen of the intestine to the extracellular fluid compartment for transport to the various parts of the body. It can selectively affect a single component, such as vitamin B<sub>12</sub> or lactose, or its effects can extend to all the substances absorbed in a specific segment of the intestine. When one segment of the intestine is affected, another may compensate. For example, the ileum may compensate for malabsorption in the proximal small intestine by absorbing substantial amounts of fats, carbohydrates, and amino acids. Similarly, the colon, which normally absorbs water, sodium, chloride, and bicarbonate, can compensate for small intestine malabsorption by absorbing additional end-products of bacterial carbohydrate metabolism.

The conditions that impair one or more steps involved in digestion and absorption of nutrients can be divided into three broad categories: intraluminal maldigestion, mucosal malabsorption, and lymphatic obstruction. Intraluminal maldigestion involves a defect in processing of nutrients in the intestinal lumen. The most common causes are pancreatic insuf-

iciency, hepatobiliary disease, and intraluminal bacterial growth. Mucosal malabsorption is caused by mucosal lesions that impair uptake and transport of available intraluminal nutrients across the mucosal surface of the intestine. They include disorders such as celiac disease, and Crohn's disease. Lymphatic obstruction interferes with the transport of the products of fat digestion to the systemic circulation after they have been absorbed by the intestinal mucosa. The process can be interrupted by congenital defects, neoplasms, trauma, and selected infectious diseases.

### Malabsorption Syndrome

The term *syndrome* implies a common constellation of symptoms arising from multiple causes. Persons with conditions that diffusely affect the small intestine and reduce its absorptive functions share certain common features referred to as *malabsorption syndrome*. Among the causes of malabsorption syndrome are celiac sprue, Crohn's disease, and resection of large segments of the small bowel.

Celiac sprue is a relatively rare chronic disease in which there is a characteristic mucosal lesion of the small intestine and impaired nutrient absorption, which improves when gluten is removed from the diet.<sup>6,11</sup> There is convincing evidence that the disorder is caused by an immunologic response to the gliadin fraction of gluten. The condition results in loss of absorptive villi from the small intestine. When the resulting lesions are extensive, they may impair absorption of virtually all nutrients. In approximately one third of the cases, symptoms begin in childhood. The effects of celiac sprue usually are reversed after removal of all wheat, rye, barley, and oat gluten from the diet. Corn and rice products are not toxic and can be used as substitutes.

Persons with intestinal malabsorption usually have symptoms directly referable to the gastrointestinal tract that include diarrhea, steatorrhea (fatty stools), flatulence, bloating, abdominal pain, and cramps. Weakness, muscle wasting, weight loss, and abdominal distention often are present. Weight loss often occurs despite normal or excessive caloric intake. In a person consuming a diet containing 80 to 100 g of fat each day, excretion of 7 to 9 g of fat indicates steatorrhea.

Along with loss of fat in the stools, there is failure to absorb the fat-soluble vitamins. This can lead to easy bruising and bleeding (*i.e.*, vitamin K deficiency), bone pain, a predisposition to the development of fractures and tetany (*i.e.*, vitamin D and calcium deficiency), macrocytic anemia, and glossitis (*i.e.*, folic acid deficiency). Neuropathy, atrophy of the skin, and peripheral edema may be present. Table 27-2 describes the signs and symptoms of impaired absorption of dietary constituents.

### Neoplasms

Epithelial cell tumors of the intestines are a major cause of morbidity and mortality worldwide. Although the small intestine accounts for approximately 75% of the length of the gastrointestinal tract, its tumors account for only 3% to 6% of gastrointestinal tumors.<sup>11</sup>

### Adenomatous Polyps

By far the most common types of neoplasms of the intestine are adenomatous polyps. A gastrointestinal polyp can be described as a mass that protrudes into the lumen of gut.<sup>11,16</sup>

Polyps can be subdivided according to their attachment to the bowel wall (sessile [raised mucosal nodules] or pedunculated [attached by a stalk]); their histopathologic appearance (hyperplastic or adenomatous); and their neoplastic potential (benign or malignant).<sup>16</sup>

Adenomatous polyps (adenomas) are benign neoplasms that arise from the mucosal epithelium of the intestine (Fig. 27-9). They are composed of neoplastic cells that have proliferated in excess of those needed to replace the cells that normally are shed from the mucosal surface. The pathogenesis of adenoma formation involves neoplastic alteration in the replication of the crypt epithelial cells in the crypts of Lieberkühn. There may be diminished apoptosis (see Chapter 2), persistence of cell replication, and failure of cell maturation and differentiation of the cells that migrate to the surface of the crypts.<sup>16</sup> Normally, DNA synthesis ceases as the cells reach the upper two thirds of the crypts, after which they mature, migrate to the surface, and become senescent. They then become apoptotic and are shed from the surface.<sup>16</sup> Adenomas arise from a disruption in this sequence, such that the epithelial cells retain their proliferative ability throughout the entire length of the crypt. Alterations in cell differentiation can lead to dysplasia and progression to the development of invasive carcinoma.

Most cases of colorectal cancer begin as benign adenomatous colonic polyps (Fig. 27-10). The frequency of polyps increases with age, and the prevalence of adenomatous polyps, which is approximately 20% to 30% before 40 years of age, rises to 40% to 50% after age 60 years.<sup>11</sup> Men and women are equally affected. The peak incidence of adenomatous polyps precedes by some years the peak for colorectal cancer. Programs that provide careful follow-up for persons with adenomatous polyps and removal of all suspect lesions have substantially reduced the incidence of colorectal cancer.<sup>11</sup>

### Colorectal Cancer

Colorectal cancer is the second leading cause of cancer death in the United States. In 2003, there will be an estimated 105,500 new cases of colorectal cancer and 57,100 deaths associated with the disease.<sup>21</sup> The death rate for colorectal cancer has been steadily declining since the early 1980s. This may be attributable to a decreased number of cases, because more of the cases are found earlier, and because treatments have improved.

The cause of cancer of the colon and rectum is largely unknown. Its incidence increases with age, as evidenced by the fact that approximately 80% of persons who have this form of cancer are older than 50 years.<sup>11</sup> The incidence of colorectal cancer is increased among persons with a family history of cancer, persons with Crohn's disease or ulcerative colitis, and those with familial adenomatous polyposis of the colon. Diet also is thought to play a role. Attention has focused on dietary fat intake, refined sugar intake, fiber intake, and the adequacy of such protective micronutrients as vitamins A, C, and E in the diet. Reports indicate that aspirin may protect against colorectal cancer.<sup>40,41</sup> Although the mechanism of aspirin's action is unknown, it may be related to its effect on the synthesis of prostaglandins, one or more of which may be involved in signal systems that influence cell proliferation or tumor growth.

Usually, cancer of the colon and rectum is present for a long time before it produces symptoms. Bleeding is a highly significant early symptom, and it usually is the one that causes persons to seek medical care. Other symptoms include a change in

**TABLE 27-2** Sites of and Requirements for Absorption of Dietary Constituents and Manifestations of Malabsorption

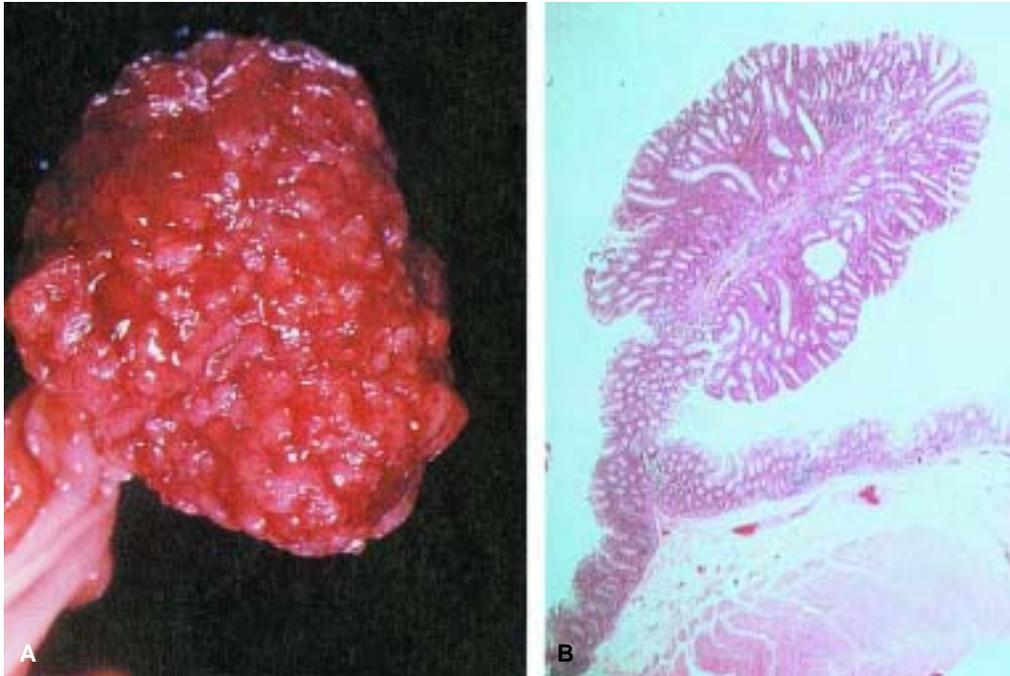
Dietary Constituent	Site of Absorption	Requirements	Manifestations
Water and electrolytes	Mainly small bowel	Osmotic gradient	Diarrhea Dehydration Cramps
Fat	Upper jejunum	Pancreatic lipase Bile salts Functioning lymphatic channels	Weight loss Steatorrhea Fat-soluble vitamin deficiency
Carbohydrates			
Starch	Small intestine	Amylase Maltase Isomaltase $\alpha$ -dextrins	Diarrhea Flatulence Abdominal discomfort
Sucrose	Small intestine	Sucrase	
Lactose	Small intestine	Lactase	
Maltose	Small intestine	Maltase	
Fructose	Small intestine		
Protein	Small intestine	Pancreatic enzymes ( <i>e.g.</i> , trypsin, chymotrypsin, elastin)	Loss of muscle mass Weakness Edema
Vitamins			
A	Upper jejunum	Bile salts	Night blindness Dry eyes Corneal irritation
Folic acid	Duodenum and jejunum	Absorptive; may be impaired by some drugs ( <i>i.e.</i> , anticonvulsants)	Cheilosis Glossitis Megaloblastic anemia
B <sub>12</sub>	Ileum	Intrinsic factor	Glossitis Neuropathy Megaloblastic anemia
D	Upper jejunum	Bile salts	Bone pain Fractures Tetany
E	Upper jejunum	Bile salts	Uncertain
K	Upper jejunum	Bile salts	Easy bruising and bleeding
Calcium	Duodenum	Vitamin D and parathyroid hormone	Bone pain Fractures Tetany
Iron	Duodenum and jejunum	Normal pH (hydrochloric acid secretion)	Iron-deficiency anemia Glossitis

bowel habits, diarrhea or constipation, and sometimes a sense of urgency or incomplete emptying of the bowel. Pain usually is a late symptom.

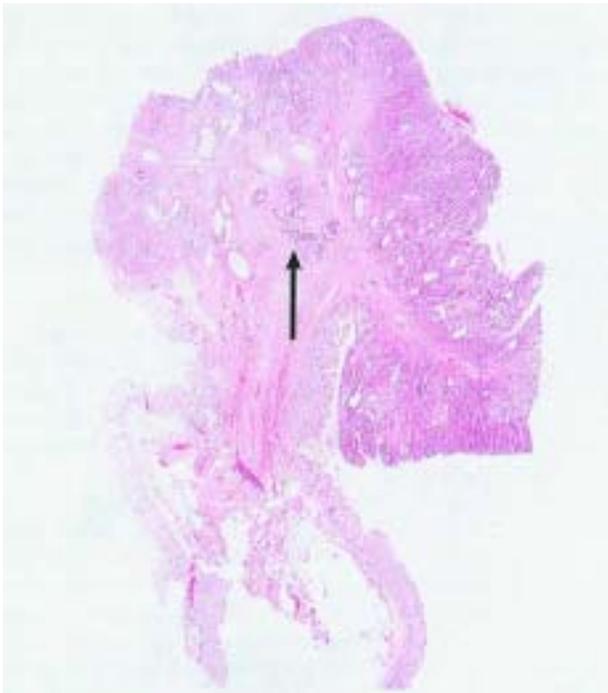
The prognosis for persons with colorectal cancer depends largely on the extent of bowel involvement and on the presence of metastasis at the time of diagnosis. Colorectal cancer commonly is divided into four categories according to the Dukes classification or its variants.<sup>15,20</sup> A stage A tumor is limited to invasion of the mucosal and submucosal layers of the colon and is associated with a 5-year survival rate of almost 100%.<sup>11</sup> A stage B tumor involves the entire wall of the colon, but without lymph node involvement, and is associated with a 5-year survival rate of 43% to 67%.<sup>11</sup> With a stage C tumor, there is invasion of the serosal layer and involvement of the regional lymph nodes. The 5-year survival rate is approximately 23%.<sup>11</sup> Stage D

colorectal cancers involve far-advanced metastasis and have a much poorer prognosis.

**Screening, Diagnosis, and Treatment.** Among the methods used for the detection of colorectal cancers are stool occult blood tests and digital rectal examination, usually done during routine physical examinations; x-ray studies using barium (*e.g.*, barium enema); and flexible sigmoidoscopy and colonoscopy. Digital rectal examinations are most helpful in detecting neoplasms of the rectum. Rectal examination should be considered a routine part of a good physical examination. The American Cancer Society recommends that all asymptomatic men and women older than 40 years should have a digital rectal examination performed annually as a part of their physical examination, and that those older than 50 years should have



■ **FIGURE 27-9** ■ Tubular adenoma of the colon. (A) A pedunculated tubular adenoma. (B) A low-power photomicrograph of a tubular adenoma shows closely packed epithelial tubules. The fibrous stalk is vascular and covered with normal colonic epithelium. (From Rubin E., Farber J.L. [1999]. *Pathology* [3rd ed., p. 737]. Philadelphia: Lippincott Williams & Wilkins)



■ **FIGURE 27-10** ■ Adenocarcinoma arising from a pedunculated adenomatous polyp. A low-grade micrograph shows irregular neoplastic glands (arrow) invading the stalk. (From Rubin E., Farber J.L. [1999]. *Pathology* [3rd ed., p. 738]. Philadelphia: Lippincott Williams & Wilkins)

an annual stool test for occult blood and a flexible sigmoidoscopy examination every 5 years and colonoscopy every 10 years or double contrast barium enema every 5 years, as recommended by their physician.<sup>39</sup>

Carcinoembryonic antigen (CEA) can be used as a marker for colorectal cancer. However, blood levels are of little screening or diagnostic value because they become elevated only after the tumor has reached considerable size. Moreover, CEA is produced by other types of cancers and noncancerous conditions, such as alcoholic cirrhosis, pancreatitis, and ulcerative colitis. This marker is of greatest value for monitoring tumor recurrence in persons after resection of the primary tumor.<sup>11,39</sup>

The only recognized treatment for cancer of the colon and rectum is surgical removal. Preoperative radiation therapy may be used and has in some cases demonstrated increased 5-year survival rates. Postoperative adjuvant chemotherapy may be used. Radiation therapy and chemotherapy are used as palliative treatment methods.

**In summary,** disorders of the small and large intestines include irritable bowel syndrome, inflammatory bowel disease, diverticular disease, disorders of motility (*i.e.*, diarrhea, constipation, infectious colitis, and intestinal obstruction), peritonitis alterations in intestinal absorption, and colorectal cancer.

Irritable bowel syndrome is a functional disorder characterized by a variable combination of chronic and recurrent intestinal symptoms not explained by structural or biochemical

abnormalities. The term *inflammatory bowel disease* is used to designate two inflammatory conditions: Crohn's disease, which affects the small and large bowel, and ulcerative colitis, which affects the colon and rectum. Both are chronic diseases characterized by remissions and exacerbations of diarrhea, weight loss, fluid and electrolyte disorders, and systemic signs of inflammation.

Infectious forms of colitis include those caused by *C. difficile*, which is associated with antibiotic therapy, and *E. coli* O157:H7, which is found in undercooked hamburger and unpasteurized milk. Diverticular disease includes diverticulosis, which is a condition in which the mucosal layer of the colon herniates through the muscularis layer, and diverticulitis, in which there is inflammation and gross or microscopic perforation of the diverticulum.

Diarrhea and constipation represent disorders of intestinal motility. Diarrhea, characterized by excessively frequent passage of stools, can be divided into large-volume diarrhea, characterized by an increased water content in the feces, and small-volume diarrhea, associated with intrinsic bowel disease and frequent passage of small stools. Constipation can be defined as the infrequent passage of stools; it commonly is caused by failure to respond to the urge to defecate, inadequate fiber or fluid intake, weakness of the abdominal muscles, inactivity and bed rest, pregnancy, hemorrhoids, and gastrointestinal disease. Intestinal obstruction designates an impairment of movement of intestinal contents in a cephalocaudal direction as the result of mechanical or paralytic mechanisms. Peritonitis is an inflammatory response of the serous membrane that lines the abdominal cavity and covers the visceral organs. It can be caused by bacterial invasion or chemical irritation resulting from perforation of the viscera or abdominal organs.

Malabsorption results from the impaired absorption of nutrients and other dietary constituents from the intestine. It can involve a single dietary constituent, such as vitamin B<sub>12</sub>, or extend to involve all of the substances absorbed in a particular part of the small intestine. Malabsorption can result from disease of the small bowel and disorders that impair digestion and in some cases obstruct the lymph flow by which fats are transported to the general circulation.

Colorectal cancer, the second most common fatal cancer, is seen most commonly in persons older than 50 years. Most, if not all, cancers of the colon and rectum arise in pre-existing adenomatous polyps. Programs that provide careful follow-up for persons with adenomatous polyps and removal of all suspect lesions have substantially reduced the incidence of colorectal cancer.

## REVIEW QUESTIONS

- Relate the pathophysiology of gastroesophageal reflux to measures used in diagnosis and treatment of the disorder in adults and children.
- State the reason for the poor prognosis associated with esophageal cancer.
- Describe the factors that contribute to the gastric mucosal barrier.

- Characterize the proposed role of *Helicobacter pylori* in the development of chronic gastritis and peptic ulcer and cite methods for diagnosing the infection.
- Describe the predisposing factors in the development of peptic ulcer and cite the three complications of peptic ulcer.
- State the diagnostic criteria for irritable bowel syndrome.
- Compare the characteristics of Crohn's disease and ulcerative colitis.
- Compare the causes and manifestations of small-volume diarrhea and large-volume diarrhea.
- Differentiate between mechanical and paralytic intestinal obstruction in terms of cause and manifestations.
- List conditions that cause malabsorption by impaired intraluminal malabsorption, mucosal malabsorption, and lymphatic obstruction.
- List the risk factors associated with colorectal cancer and cite the screening methods for detection.

## connection

Visit the Connection site at [connection.lww.com/go/porth](http://connection.lww.com/go/porth) for links to chapter-related resources on the Internet.

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