syndrome damage the intestinal mucosa, impair pancreatic enzyme activation, and accelerate transit due to excess gastric acid. Biliary obstruction from stricture or neoplasm impairs fat digestion. Impaired pancreatic enzyme release in chronic pancreatitis or pancreatic cancer decreases intraluminal digestion and can lead to malnutrition.

Altered Secretion Selected GI diseases result from dysregulation of gut secretion. Gastric acid hypersecretion occurs in Zollinger-Ellison syndrome, G cell hyperplasia, retained antrum syndrome, and some individuals with duodenal ulcers. Conversely, patients with atrophic gastritis or pernicious anemia release little or no gastric acid. Inflammatory and infectious small-intestinal and colonic diseases produce fluid loss through impaired absorption or enhanced secretion. Common intestinal and colonic hypersecretory conditions cause diarrhea and include acute bacterial or viral infection, chronic *Giardia* or cryptosporidia infections, small-intestinal bacterial overgrowth, bile salt diarrhea, microscopic colitis, diabetic diarrhea, and abuse of certain laxatives. Less common causes include large colonic villus adenomas and endocrine neoplasias with tumor overproduction of secretagogue transmitters like vasoactive intestinal polypeptide.

Altered Gut Transit Impaired gut transit may be secondary to mechanical obstruction. Esophageal occlusion often results from acid-induced stricture or neoplasm. Gastric outlet obstruction develops from peptic ulcer disease or gastric cancer. Small-intestinal obstruction most commonly results from adhesions but may also occur with Crohn's disease, radiation- or drug-induced strictures, and less likely malignancy. The most common cause of colonic obstruction is colon cancer, although inflammatory strictures develop in patients with inflammatory bowel disease, after certain infections such as diverticulitis, or with some drugs.

Retardation of propulsion also develops from disordered motor function. Achalasia is characterized by impaired esophageal body peristalsis and incomplete lower esophageal sphincter relaxation. Gastroparesis is the symptomatic delay in gastric emptying of meals due to impaired gastric motility. Intestinal pseudoobstruction causes marked delays in small-bowel transit due to enteric nerve or intestinal smooth-muscle injury. Slow-transit constipation is produced by diffusely impaired colonic propulsion. Constipation also is produced by outlet abnormalities such as rectal prolapse, intussusception, or dyssynergia—a failure of anal or puborectalis relaxation upon attempted defecation.

Disorders of rapid propulsion are less common than those with delayed transit. Rapid gastric emptying occurs in postvagotomy dumping syndrome, with gastric hypersecretion, and in some cases of functional dyspepsia and cyclic vomiting syndrome. Exaggerated intestinal or colonic motor patterns may be responsible for diarrhea in irritable bowel syndrome. Accelerated transit with hyperdefecation is noted in hyperthyroidism.

Immune Dysregulation Many inflammatory GI conditions are consequences of altered gut immune function. The mucosal inflammation of celiac disease results from dietary ingestion of gluten-containing grains. Some patients with food allergy also exhibit altered immune populations. Eosinophilic esophagitis and eosinophilic gastroenteritis are inflammatory disorders with prominent mucosal eosinophils. Ulcerative colitis and Crohn's disease are disorders of uncertain etiology that produce mucosal injury primarily in the lower gut. The microscopic colitides, lymphocytic and collagenous colitis, exhibit colonic subepithelial infiltrates without visible mucosal damage. Bacterial, viral, and protozoal organisms may produce ileitis or colitis in selected patient populations.

Impaired Gut Blood Flow Different GI regions are at variable risk for ischemic damage from impaired blood flow. Rare cases of gastroparesis result from blockage of the celiac and superior mesenteric arteries. More commonly encountered are intestinal and colonic ischemia that are consequences of arterial embolus, arterial thrombosis, venous thrombosis, or hypoperfusion from dehydration, sepsis, hemorrhage, or reduced cardiac output. These may produce mucosal injury, hemorrhage, or even perforation. Chronic ischemia may result in intestinal stricture. Some cases of radiation enterocolitis exhibit reduced mucosal blood flow.

Neoplastic Degeneration All GI regions are susceptible to malignant degeneration to varying degrees. In the United States, colorectal cancer is most common and usually presents after age 50 years. Worldwide, gastric cancer is prevalent especially in certain Asian regions. Esophageal cancer develops with chronic acid reflux or after an extensive alcohol or tobacco use history. Small-intestinal neoplasms are rare and occur with underlying inflammatory disease. Anal cancers arise after prior anal infection or inflammation. Pancreatic and biliary cancers elicit severe pain, weight loss, and jaundice and have poor prognoses. Hepatocellular carcinoma usually arises in the setting of chronic viral hepatitis or cirrhosis secondary to other causes. Most GI cancers exhibit carcinomatous histology; however, lymphomas and other cell types also are observed.

Disorders Without Obvious Organic Abnormalities The most common GI disorders show no abnormalities on biochemical or structural testing and include irritable bowel syndrome, functional dyspepsia, functional chest pain, and functional heartburn. These disorders exhibit altered gut motor function; however, the pathogenic relevance of these abnormalities is uncertain. Exaggerated visceral sensory responses to noxious stimulation may cause discomfort in these disorders. Symptoms in other patients result from altered processing of visceral pain sensations in the central nervous system. Functional bowel patients with severe symptoms may exhibit significant emotional disturbances on psychometric testing. Subtle immunologic defects may contribute to functional symptoms as well.

Genetic Influences Although many GI diseases result from environmental factors, others exhibit hereditary components. Family members of inflammatory bowel disease patients show a genetic predisposition to disease development themselves. Colonic and esophageal malignancies arise in certain inherited disorders. Rare genetic dysmotility syndromes are described. Familial clustering is even observed in the functional bowel disorders, although this may be secondary learned familial illness behavior rather than a true hereditary factor.

SYMPTOMS OF GASTROINTESTINAL DISEASE

The most common GI symptoms are abdominal pain, heartburn, nausea and vomiting, altered bowel habits, GI bleeding, and jaundice (Table 344-1). Others are dysphagia, anorexia, weight loss, fatigue, and extraintestinal symptoms.

Abdominal Pain Abdominal pain results from GI disease and extraintestinal conditions involving the genitourinary tract, abdominal wall, thorax, or spine. Visceral pain generally is midline in location and vague in character, whereas parietal pain is localized and precisely described. Common inflammatory diseases with pain include peptic ulcer, appendicitis, diverticulitis, inflammatory bowel disease, and infectious enterocolitis. Other intraabdominal causes of pain include gallstone disease and pancreatitis. Noninflammatory visceral sources include mesenteric ischemia and neoplasia. The most common causes of abdominal pain are irritable bowel syndrome and functional dyspepsia.

Heartburn Heartburn, a burning substernal sensation, is reported intermittently by at least 40% of the population. Classically, heartburn is felt to result from excess gastroesophageal reflux of acid. However, some cases exhibit normal esophageal acid exposure and may result from reflux of nonacidic material or heightened sensitivity of esophageal mucosal nerves.

Nausea and Vomiting Nausea and vomiting are caused by GI diseases, medications, toxins, acute and chronic infection, endocrine disorders, labyrinthine conditions, and central nervous system disease. The best-characterized GI etiologies relate to mechanical obstruction of the upper gut; however, disorders of propulsion including gastroparesis and intestinal pseudoobstruction also elicit prominent symptoms. Nausea and vomiting also are commonly reported by patients with