metastases should be surgically explored with the intent of removing local and regional disease. Unfortunately, despite careful diagnostic testing, no tumor is found in at least 10% of diagnosed instances of ZES.

ZES should be considered in patients with recurrent PUD in the absence of *H. pylori* infection or NSAID use, as well as in patients with multiple duodenal ulcers, ulcers in unusual locations (distal duodenum or jejunum), or severe or refractory diarrhea or gastroesophageal reflux disease. Although peptic ulcer occurs in more than 90% of patients with ZES, as many as 35% of individuals exhibit only diarrhea. The diagnosis of ZES is made when a fasting gastrin concentration of more than 1000 pg/mL exists in the setting of gastric acid hypersecretion. In equivocal cases (e.g., gastrin <1000 pg/mL), a positive secretin provocative test will confirm the diagnosis. The secretin test is positive (≥200 pg/mL increase over the preinjection fasting gastrin level) in about 90% of patients with ZES and moderately elevated gastrin levels. Basal acid output is elevated (>15 mmol per hour without previous gastric acid–reducing surgery and >5 mmol per hour with prior surgery) in more than 90% of patients with ZES. Because gastrinomas constitute a relatively uncommon cause of hypergastrinemia, other causes of an elevated gastrin level should be considered. The most common causes of hypergastrinemia are antrum-dominant *H. pylori* infection or achlorhydria related to either decreased intraluminal acid in the setting of atrophic gastritis or antisecretory therapy with PPIs. Hypergastrinemia may be related to other causes, including retained gastric antrum (after ulcer surgery), massive small bowel resection, chronic gastric outlet obstruction, and chronic renal failure. Therefore, the presence of acid hypersecretion, as documented by gastric acid analysis, may be necessary to establish the diagnosis.

Once hypergastrinemia has been established and obvious causes have been excluded, efforts should focus on localizing and resecting the gastrin-secreting tumor. The single best imaging test for gastrinoma is somatostatin-receptor scintigraphy (SRS), which is more sensitive than conventional imaging studies, including CT, magnetic resonance imaging (MRI), and ultrasonography, although endoscopic ultrasonography (EUS) is equally sensitive for localizing primary tumors of the pancreas. If liver metastasis is present, a CT- or ultrasound-guided liver biopsy should be performed. In patients without liver metastasis, SRS will localize a possible primary tumor in 60% of cases. If the patient is a surgical candidate and SRS is positive for a primary tumor, no additional localization studies are required. If the SRS is negative for a possible primary tumor, the use of MRI, angiography, or EUS will detect a possible primary tumor in an additional 15% of patients. Multiple pancreatic or duodenal tumors are generally detected in patients with MEN-I syndrome, and although the precise role of surgery in these patients is less certain, some physicians recommend surgery if a lesion larger than 3 cm is identified with preoperative imaging techniques to decrease the possibility of hepatic metastasis. However, successful and long-lasting remission of MEN-I syndrome occurs rarely, if at all.

All patients with ZES, whether sporadic or familial, require antisecretory therapy after the diagnosis is established and during initial evaluation as attempts are made to localize the gastrinoma. Patients with ZES should be treated initially with a PPI using twice the dose normally employed to treat common gastroduodenal ulcers. Intravenous PPIs such as pantoprazole in daily doses ranging from 80 to 240 mg can be used in patients who are unable to take medications by mouth, including those undergoing surgery. The goal of therapy is a basal acid output of less than 10 mmol per hour in the hour preceding the next dose of the drug. Chronic therapy with PPIs uniformly results in continued inhibition of acid secretion, good symptom control, complete healing of any mucosal lesions, and few adverse effects.

GASTROPARESIS

Gastroparesis is a syndrome characterized by delayed gastric emptying, resulting in impaired transit of food from the stomach to the duodenum in the absence of mechanical obstruction. Symptoms of gastric stasis include early or easy satiety, bloating, nausea and vomiting, and abdominal discomfort. Because eating exacerbates symptoms, patients frequently exhibit anorexia, weight loss, and nutritional deficiencies. A wide range of clinical disorders is associated with impaired gastric emptying (Table 36-4).

Diabetes mellitus is the most common cause of gastroparesis, and up to 60% of patients with diabetes complain of symptoms consistent with gastric stasis. Although gastroparesis is typically seen in individuals with long-standing (>10 years) type 1 diabetes who have other complications, such as peripheral and autonomic neuropathy, nephropathy, and retinopathy, GI complaints are also common within the first decade of diagnosis. Diabetic gastroparesis appears to occur as a result of permanent neuropathy of autonomic and enteric nerves, transitory variations in glycemic control, or a combination of both. Idiopathic gastroparesis is also common and comprises those instances with no clearly identifiable cause. Up to one third of these patients have virus-induced gastroparesis, with viral infiltration of the myenteric plexus in the stomach. Patients who have undergone gastric

TABLE 36-4 CAUSES OF DELAYED GASTRIC EMPTYING

MECHANICAL CAUSES
Peptic ulcer disease, scarred pylorus
Malignancy: gastric cancer, gastric lymphoma, pancreatic cancer
Gastric surgery: vagotomy, gastric resection, roux-en-Y anastomosis
Crohn disease
ENDOCRINE AND METABOLIC CAUSES
Diabetes mellitus
Hypothyroidism
Hypoadrenal states
Electrolyte abnormalities
Chronic renal failure
Medications
Anticholinergics
Opiates
Dopamine agonists
Tricyclic antidepressants
ABNORMALITIES OF GASTRIC SMOOTH MUSCLE
Scleroderma
Polymyositis, dermatomyositis
Amyloidosis
Pseudo-obstruction
Myotonic dystrophy
Neuropathy
Scleroderma
Amyloidosis
Autonomic neuropathy
CENTRAL NERVOUS SYSTEM OR PSYCHIATRIC DISORDERS
Brainstem tumors
Spinal cord injury
Anorexia nervosa
Stress
MISCELLANEOUS
Idiopathic gastroparesis
Gastroesophageal reflux disease
Nonulcer (functional) dyspepsia
Cancer cachexia or anorexia