diarrhea, peripheral neuropathy, spinal cord lesions, and cerebral dysfunction. Neuropathic changes include demyelination, axonal degeneration, and neuronal death. The most frequent manifestations of peripheral neuropathy are paresthesias and numbness. The spinal lesions result from demyelination of the dorsal and lateral spinal tracts, giving rise to a clinical picture that is often referred to as *subacute combined degeneration of the cord.* It is associated with a mixture of loss of vibration and position sense, sensory ataxia with positive Romberg sign, limb weakness, spasticity, and extensor plantar responses. Cerebral manifestations range from mild personality changes and memory loss to psychosis. In contrast to anemia, neurologic changes are not reversed by vitamin B_{12} replacement therapy.

Uncommon Forms of Gastritis

Eosinophilic Gastritis. This form of gastritis is characterized by tissue damage associated with dense infiltrates of eosinophils in the mucosa and muscularis, usually in the antral or pyloric region. The lesion may also be present at other sites within the GI tract and is associated with peripheral eosinophilia and increased serum IgE levels. Allergic reactions are one cause of eosinophilic gastritis, with cow's milk and soy protein being the most common allergens in children. Eosinophilic gastritis can also occur in association with immune disorders such as systemic sclerosis and polymyositis, parasitic infections, and even *H. pylori* infection.

Lymphocytic Gastritis. This disease preferentially affects women and produces nonspecific abdominal symptoms. It is idiopathic, but approximately 40% of cases are associated with celiac disease, suggesting an immune-mediated pathogenesis. Lymphocytic gastritis typically affects the entire stomach and is often referred to as *varioliform gastritis* based on the distinctive endoscopic appearance (thickened folds covered by small nodules with central aphthous ulceration). Histologically there is a marked increase in the number of intraepithelial T lymphocytes.

Granulomatous Gastritis. This descriptive term is applied to any gastritis that contains well-formed granulomas or aggregates of epithelioid macrophages. It encompasses a diverse group of diseases with widely varying clinical and pathologic features. Many cases are idiopathic. In Western populations, gastric involvement by Crohn disease is the most common specific cause of granulomatous gastritis, followed by sarcoidosis and infections (including mycobacteria, fungi, CMV, and *H. pylori*). In addition to the presence of histologically evident granulomas, narrowing and rigidity of the gastric antrum may occur secondary to transmural granulomatous inflammation.

Complications of Chronic Gastritis

Peptic Ulcer Disease

Peptic ulcer disease (PUD) refers to chronic mucosal ulceration affecting the duodenum or stomach. Nearly all peptic ulcers are associated with *H. pylori* infection, NSAIDs, or cigarette smoking. The most common form of peptic ulcer disease (PUD) occurs within the gastric antrum or duodenum as a result of chronic, *H. pylori*-induced antral gastritis, which is associated with increased gastric acid secretion, and decreased duodenal bicarbonate secretion. In contrast, PUD within the gastric fundus or body is usually accompanied by lesser acid secretion as a result of mucosal atrophy (associated with some cases of *H. pylori*-induced or autoimmune chronic gastritis, as discussed earlier). While these patients still secrete more acid than normal individuals, they are incapable of secreting the much larger amounts needed to overcome the defense mechanisms that "protect" the antral and duodenal mucosa. Thus, individuals with gastric mucosal atrophy are generally protected from antral and duodenal ulcers. PUD may also be caused by acid secreted by ectopic gastric mucosa within the duodenum or an ileal Meckel diverticulum. PUD may also occur in the esophagus as a result of GERD or acid secretion by esophageal ectopic gastric mucosa (an inlet patch).

Table 17-3 Risk factors for Peptic Ulcer Disease

- *H. pylori* infection
- Cigarette use (synergizes with *H. pylori* for gastric PUD)
- Chronic obstructive pulmonary disease
- Illicit drugs, e.g. cocaine, that reduce mucosal blood flow
- NSAIDs (potentiated by corticosteroids)
- Alcoholic cirrhosis (primarily duodenal PUD)
- Psychological stress (can increase gastric acid secretion)
- Endocrine cell hyperplasia (can stimulate parietal cell growth and gastric acid secretion)
- Zollinger-Ellison Syndrome (PUD of stomach, duodenum, and jejunum)
- Viral infection (CMV, herpes simplex virus)

Epidemiology. The incidence of PUD is falling in developed countries along with reduced prevalence of *H. pylori*, infection. However, a new group of duodenal PUD patients older than 60 years of age has emerged as a result of increased NSAID use. This is particularly true when low-dose aspirin (for cardiovascular benefits) is combined with other NSAIDs. This is facilitated if concurrent *H. pylori* infection is also present. PUD has been associated with cigarette use and cardiovascular disease, likely due to reduced mucosal blood flow, oxygenation, and healing. Other risk factors for PUD are listed in Table 17-3.

Pathogenesis. **PUD results from imbalances between mucosal defense mechanisms and damaging factors that cause chronic gastritis** (discussed earlier). Thus, PUD generally develops on a background of chronic gastritis. The reasons why some people develop only chronic gastritis while others develop PUD are poorly understood. However, as with *H. pylori* gastritis, it is likely that host factors as well as variation between bacterial strains are involved.

MORPHOLOGY

Peptic ulcers occur in the context of chronic gastritis, but are most common in the proximal duodenum, where they occur within a few centimeters of the pyloric valve and involve the anterior duodenal wall. Gastric peptic ulcers are predominantly located along the lesser curvature near the interface of the body and antrum.