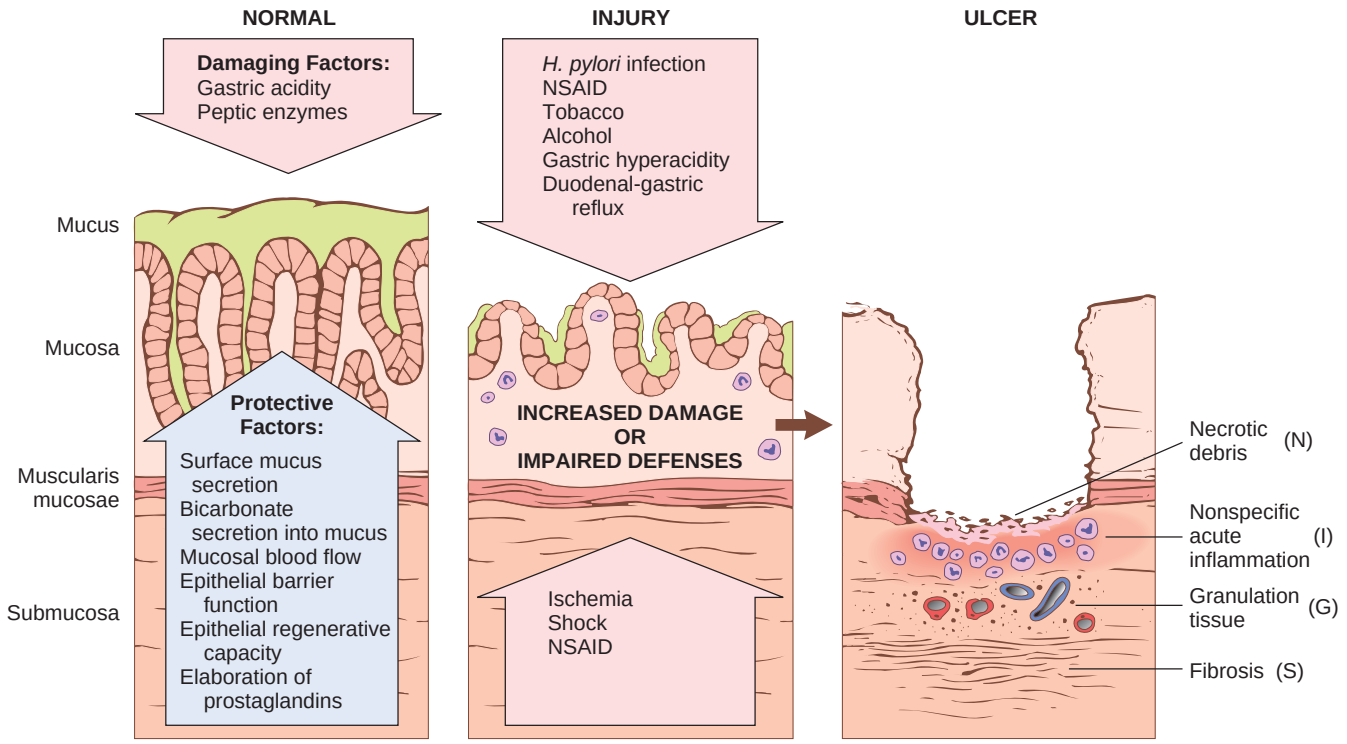

Figure 17-11 Mechanisms of gastric injury and protection. This diagram illustrates the progression from more mild forms of injury to ulceration that may occur with acute or chronic gastritis. Ulcers include layers of necrosis (N), inflammation (I), and granulation tissue (G), but a fibrotic scar (S), which takes time to develop, is only present in chronic lesions.

Both gastropathy and acute gastritis may be asymptomatic or cause variable degrees of epigastric pain, nausea, and vomiting. In more severe cases there may be mucosal erosion, ulceration, hemorrhage, hematemesis, melena, or, rarely, massive blood loss.

Pathogenesis. The gastric lumen has a pH of close to 1, more than a million times more acidic than the blood. This harsh environment contributes to digestion but also has the potential to damage the gastric mucosa. Multiple mechanisms have evolved to protect the gastric mucosa (Fig. 17-11). Mucin secreted by surface foveolar cells forms a thin layer of mucus and phospholipids that prevents large food particles from directly touching the epithelium. The mucus covering also promotes formation of an "unstirred" layer of fluid over the epithelium that protects the mucosa and has a neutral pH as a result of bicarbonate ion secretion by surface epithelial cells. Beneath the mucus, a continuous layer of gastric epithelial cells forms a physical barrier that limits back diffusion of acid and leakage of other luminal materials, including pepsin, into the lamina propria. Complete replacement of the surface foveolar cells every 3 to 7 days is essential for both the maintenance of the epithelial layer and the secretion of mucus and bicarbonate from these cells. In acid-secreting parts of the stomach, a capillary "alkaline tide" is generated as parietal cells secrete hydrochloric acid into the gastric lumen and bicarbonate into the vessels. In addition to delivering bicarbonate, the rich mucosal vasculature delivers oxygen and nutrients while washing away acid that has back-diffused into the lamina propria.

Gastropathy, acute gastritis, and chronic gastritis can occur following disruption of any of these protective mechanisms.

- Nonsteroidal antiinflammatory drugs (NSAIDs) inhibit cyclooxygenase- (COX) dependent synthesis of prostaglandins E_2 and I_2, which stimulate nearly all of the above defense mechanisms including mucus, bicarbonate, and phospholipid secretion, mucosal blood flow, and epithelial restitution while reducing acid secretion. Although COX-1 plays a larger role than COX-2, both isoenzymes contribute to mucosal protection. Thus, while the risk of NSAID-induced gastric injury is greatest with nonselective inhibitors, for example, aspirin, ibuprofen, and naproxen, selective COX-2 inhibition, for example, by celecoxib, can also result in gastropathy or gastritis.
- The gastric injury that occurs in uremic patients and those infected with urease-secreting *H. pylori* may be due to inhibition of gastric bicarbonate transporters by ammonium ions.
- Reduced mucin and bicarbonate secretion have been suggested as factors that explain the increased susceptibility of older adults to gastritis.
- Decreased oxygen delivery may account for an increased incidence of acute gastritis at high altitudes.

Ingestion of harsh chemicals, particularly acids or bases, either accidentally or as a suicide attempt, also results in severe gastric injury, predominantly as a result of direct injury to mucosal epithelial and stromal cells. Direct cellular damage also contributes to gastritis induced by excessive alcohol consumption, NSAIDs, radiation therapy, and