chemotherapy. Agents that inhibit DNA synthesis or the mitotic apparatus, including those used in cancer chemotherapy, may cause generalized mucosal damage due to insufficient epithelial renewal.

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Histologically, gastropathy and mild acute gastritis may be difficult to recognize, since the lamina propria shows only moderate edema and slight vascular congestion. The surface epithelium is intact, but foveolar cell hyperplasia, with characteristic corkscrew profiles and epithelial proliferation are typically present. Neutrophils are not abundant, but a few may be found among the epithelial cells or within mucosal glands in gastritis. There are few lymphocytes and plasma cells.

The presence of neutrophils above the basement membrane in direct contact with epithelial cells is abnormal in all parts of the GI tract and signifies active inflammation, or, in this case, gastritis (rather than gastropathy). The term active inflammation is preferred over acute inflammation, since active inflammation may be present in both acute and chronic disease states. With more severe mucosal damage, erosions and hemorrhage develop. Erosion denotes loss of the epithelium, resulting in a superficial mucosal defect. It is accompanied by a pronounced mucosal neutrophilic infiltrate and a fibrin-containing purulent exudate in the lumen. Hemorrhage may occur and cause dark punctae in hyperemic mucosa. Concurrent erosion and hemorrhage is termed **acute erosive hemorrhagic gastritis.** Large areas of the gastric surface may be denuded, although the involvement is typically superficial. When erosions extend deeply, they may progress to ulcers, as described later.

Clinical Features. The presentation of gastropathy and acute gastritis varies according to etiology, and the two cannot be distinguished on clinical grounds. Patients with NSAID-induced gastropathy may be asymptomatic or have persistent epigastric pain that responds to antacids or proton pump inhibitors. In contrast, pain associated with bile reflux is typically refractory to such therapies and may be accompanied by occasional bilious vomiting.

Stress-Related Mucosal Disease

Stress-related mucosal disease occurs in patients with severe trauma, extensive burns, intracranial disease, major surgery, serious medical disease, and other forms of severe physiologic stress. More than 75% of critically ill patients develop endoscopically visible gastric lesions during the first 3 days of their illness. In some cases, the associated ulcers are given specific names based on location and clinical associations. For example:

- *Stress ulcers* are most common in individuals with shock, sepsis, or severe trauma.
- Ulcers occurring in the proximal duodenum and associated with severe burns or trauma are called *Curling ulcers.*
- Gastric, duodenal, and esophageal ulcers arising in persons with intracranial disease are termed *Cushing ulcers* and carry a high incidence of perforation.

Pathogenesis. The pathogenesis of stress-related gastric mucosal injury is most often related to local ischemia. This may be due to systemic hypotension or reduced blood flow caused by stress-induced splanchnic vasoconstriction. Upregulation of inducible NO synthase and increased release of the vasoconstrictor endothelin-1 also contribute to ischemic gastric mucosal injury, while increased COX-2 expression appears to be protective.

Lesions associated with intracranial injury are thought to be caused by direct stimulation of vagal nuclei, which causes hypersecretion of gastric acid. Systemic acidosis, a frequent finding in these settings, may also contribute to mucosal injury by lowering the intracellular pH of mucosal cells.

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Stress-related gastric mucosal injury ranges from shallow erosions caused by superficial epithelial damage to deeper lesions that penetrate the depth of the mucosa. Acute ulcers are rounded and less than 1 cm in diameter. The ulcer base is frequently stained brown to black by acid digestion of extravasated blood and may be associated with transmural inflammation and local serositis. Unlike peptic ulcers, which arise in the setting of chronic injury, acute stress ulcers are found anywhere in the stomach and are most often multiple. Microscopically, acute stress ulcers are sharply demarcated, with essentially normal adjacent mucosa. There may be a suffusion of blood into the mucosa and submucosa and an associated inflammatory reaction. Conspicuously absent are the scarring and blood vessel thickenings that characterize chronic peptic ulcers. Healing with complete re-epithelialization occurs within days to several weeks after removal of the injurious factors.

Clinical Features. **Most critically ill patients admitted to hospital intensive care units have histologic evidence of gastric mucosal damage.** Bleeding from superficial gastric erosions or ulcers that may require transfusion develops in 1% to 4% of these patients. Other complications, including perforation, can also occur. Prophylactic proton pump inhibitors may blunt the impact of stress ulceration, but the most important determinant of clinical outcome is the ability to correct the underlying condition. The gastric mucosa can recover completely if the patient does not succumb to the primary disease.

Other, non-stress-related causes of gastric bleeding include the *Dieulafoy lesion* and *gastric antral vascular ectasia* (GAVE).

- Dieulafoy lesion is caused by a submucosal artery that does not branch properly within the wall of the stomach. This results in a mucosal artery with a diameter of up to 3 mm, or 10 times the size of mucosal capillaries. Dieulafoy lesions are most commonly found along the lesser curvature, near the gastroesophageal junction. Erosion of the overlying epithelium can cause gastric bleeding that, while usually self-limited, can be copious. Bleeding is often associated with NSAID use and may be recurrent.
- GAVE is responsible for 4% of non-variceal upper gastrointestinal bleeding. It can be recognized endoscopically as longitudinal stripes of edematous erythematous mucosa that alternate with less severely injured, paler mucosa, and is sometimes referred to as watermelon