Ischemic Bowel Disease

The majority of the GI tract is supplied by the celiac, superior mesenteric, and inferior mesenteric arteries. As they approach the intestinal wall the superior and inferior mesenteric arteries ramify into the mesenteric arcades. Interconnections between arcades, as well as collateral supplies from the proximal celiac and distal pudendal and iliac circulations, make it possible for the small intestine and colon to tolerate slowly progressive loss of blood supply from one artery.

In contrast to chronic, progressive hypoperfusion, acute compromise of any major vessel can lead to infarction of several meters of intestine. Damage can range from mucosal infarction, extending no deeper than the muscularis mucosae; to mural infarction of mucosa and submucosa; to transmural infarction involving all three wall layers. While mucosal or mural infarctions can follow acute or chronic hypoperfusion, transmural infarction is typically caused by acute vascular obstruction. Important causes of acute arterial obstruction include severe atherosclerosis (which is often prominent at the origin of mesenteric vessels), aortic aneurysm, hypercoagulable states, oral contraceptive use, and embolization of cardiac vegetations or aortic atheromas. Intestinal hypoperfusion can be associated with cardiac failure, shock, dehydration, or use of vasoconstrictive drugs. Systemic vasculitides, such as polyarteritis nodosa, Henoch-Schönlein purpura, or granulomatosis with polyangiitis (Wegener granulomatosis), may also damage intestinal arteries. Mesenteric venous thrombosis, which can also lead to ischemic disease, is uncommon but can result from inherited or acquired hypercoagulable states, invasive neoplasms, cirrhosis, trauma, or abdominal masses that compress the portal drainage.

Pathogenesis. Intestinal responses to ischemia occur in two phases. The initial *hypoxic injury* occurs at the onset of vascular compromise. While some damage occurs during this phase, the epithelial cells lining the intestine are relatively resistant to transient hypoxia. The second phase, *reperfusion injury*, is initiated by restoration of the blood supply and it is at this time that the greatest damage occurs. In severe cases this may trigger multiorgan failure. While the underlying mechanisms of reperfusion injury are incompletely understood, they include leakage of gut lumen bacterial products, e.g. lipopolysaccharide, into the systemic circulation, free radical production, neutrophil infiltration, and release of additional inflammatory mediators (Chapter 2).

The severity of vascular compromise, the time frame during which it develops, and the vessels affected are the major variables in ischemic bowel disease. Two aspects of intestinal vascular anatomy also contribute to the distribution of ischemic damage and are worthy of note:

- Intestinal segments at the end of their respective arterial supplies are particularly susceptible to ischemia. These *watershed zones* include the splenic flexure, where the superior and inferior mesenteric arterial circulations terminate, and, to a lesser extent, the sigmoid colon and rectum where inferior mesenteric, pudendal, and iliac arterial circulations end. Generalized hypotension or hypoxemia can therefore cause localized injury, and ischemic disease should be considered in the differential diagnosis of focal colitis of the splenic flexure or rectosigmoid colon.
- Intestinal capillaries run alongside the glands, from crypt to surface, before making a hairpin turn to empty into the post-capillary venules. This arrangement makes the surface epithelium particularly vulnerable to ischemic injury, relative to the crypts. Organization of the blood supply in this patterns has advantages, as it protects the epithelial stem cells, which are located within the crypts and are necessary for recovery from epithelial injury. This pattern of surface epithelial atrophy, or even necrosis and sloughing, with normal or hyperproliferative crypts is a morphologic signature of ischemic intestinal disease.

MORPHOLOGY

Although the colon is the most common site of gastrointestinal ischemia, mucosal and mural infarction may involve any level of the gut from stomach to anus. The lesions can be continuous but are most often segmental and patchy (Fig. 17-24*A*). The mucosa is hemorrhagic and may be ulcerated (Fig. 17-24*B*). The bowel wall is also thickened by edema that may involve the mucosa or extend into the submucosa and muscularis propria.

Substantial portions of the bowel are generally involved in **transmural infarction** due to acute arterial obstruction. The demarcation between normal and ischemic bowel is sharply defined and the infarcted bowel is initially intensely congested and dusky to purple-red. Later, blood-tinged mucus or frank blood accumulates in the lumen and the wall becomes edematous, thickened, and rubbery. There is coagulative necrosis of the muscularis propria within 1 to 4 days, and perforation may occur. Serositis, with purulent exudates and fibrin deposition, may be prominent.

In mesenteric venous thrombosis, arterial blood continues to flow for a time, resulting in a less abrupt transition from affected to normal bowel. However, propagation of the thrombus may lead to secondary involvement of the splanchnic bed. The ultimate result is similar to that produced by acute arterial obstruction because impaired venous drainage eventually prevents oxygenated arterial blood from entering the capillaries.

Microscopic examination of ischemic intestine demonstrates the characteristic atrophy or sloughing of surface epithelium (Fig. 17-24*C*). In contrast, crypts may be hyperproliferative. Inflammatory infiltrates are initially absent in acute ischemia, but neutrophils are recruited within hours of reperfusion. Chronic ischemia is accompanied by fibrous scarring of the lamina propria (Fig. 17-24*D*) and, uncommonly, stricture formation. In both acute and chronic ischemia, bacterial superinfection and enterotoxin release may induce **pseudomembrane formation** that resembles *Clostridium difficile*–associated pseudomembranous colitis (discussed later).

Clinical Features. Ischemic disease of the colon is most common in patients older than 70 years of age, and occurs slightly more often in women. While frequently associated with coexisting cardiac or vascular disease ischemia can also be precipitated by therapeutic vasoconstrictors, some illicit drugs, for example, cocaine, endothelial damage and small vessel occlusion after cytomegalovirus or *Escherichia*