sprue represent different ends of the spectrum of a single entity, but convincing evidence to support this concept is lacking.

Etiology Because tropical sprue responds to antibiotics, the consensus is that it may be caused by one or more infectious agents. Nonetheless, the etiology and pathogenesis of tropical sprue are uncertain. First, its occurrence is not evenly distributed in all tropical areas; rather, it is found in specific locations, including southern India, the Philippines, and several Caribbean islands (e.g., Puerto Rico, Haiti), but is rarely observed in Africa, Jamaica, or Southeast Asia. Second, an occasional individual does not develop symptoms of tropical sprue until long after having left an endemic area. For this reason, celiac disease (often referred to as celiac sprue) was originally called *nontropical sprue* to distinguish it from tropical sprue. Third, multiple microorganisms have been identified in jejunal aspirates, with relatively little consistency among studies. *Klebsiella pneumoniae, Enterobacter cloacae*, and *E. coli* have been implicated in some studies of tropical sprue, while other studies have favored a role for a toxin produced by one or more of these bacteria. Fourth, the incidence of tropical sprue appears to have decreased substantially during the past two or three decades, perhaps in relation to improved sanitation in many tropical countries during this time. Some have speculated that the reduced occurrence is attributable to the wider use of antibiotics in acute diarrhea, especially in travelers to tropical areas from temperate countries. Fifth, the role of folic acid deficiency in the pathogenesis of tropical sprue requires clarification. Folic acid is absorbed exclusively in the duodenum and proximal jejunum, and most patients with tropical sprue have evidence of folate malabsorption and depletion. Although folate deficiency can cause changes in small-intestinal mucosa that are corrected by folate replacement, several earlier studies reporting that tropical sprue could be cured by folic acid did not provide an explanation for the "insult" that was initially responsible for folate malabsorption.

The clinical pattern of tropical sprue varies in different areas of the world (e.g., India vs. Puerto Rico). Not infrequently, individuals in southern India initially report the occurrence of acute enteritis before the development of steatorrhea and malabsorption. In contrast, in Puerto Rico, a more insidious onset of symptoms and a more dramatic response to antibiotics are seen than in some other locations. Tropical sprue in different areas of the world may not be the same disease, and similar clinical entities may have different etiologies.

Diagnosis The diagnosis of tropical sprue is best based on an abnormal small-intestinal mucosal biopsy in an individual with chronic diarrhea and evidence of malabsorption who is either residing or has recently lived in a tropical country. The small-intestinal biopsy in tropical sprue does not reveal pathognomonic features but resembles, and can often be indistinguishable from, that seen in celiac disease (Fig. 349-4). The biopsy sample in tropical sprue has less villous architectural alteration and more mononuclear cell infiltrate in the lamina propria. In contrast to those of celiac disease, the histologic features of tropical sprue manifest with a similar degree of severity throughout the small intestine, and a gluten-free diet does not result in either clinical or histologic improvement in tropical sprue.

TREATMENT **TROPICAL SPRUE**

Broad-spectrum antibiotics and folic acid are most often curative, especially if the patient leaves the tropical area and does not return. Tetracycline should be used for up to 6 months and may be associated with improvement within 1–2 weeks. Folic acid alone induces hematologic remission as well as improvement in appetite, weight gain, and some morphologic changes in small-intestinal biopsy. Because of marked folate deficiency, folic acid is most often given together with antibiotics.

SHORT-BOWEL SYNDROME

Short-bowel syndrome is a descriptive term for the myriad clinical problems that follow resection of various lengths of small intestine or, on rare occasions, are congenital (e.g., microvillous inclusion disease). The factors that determine both the type and degree of symptoms include (1) the specific segment (jejunum vs. ileum) resected, (2) the length of the resected segment, (3) the integrity of the ileocecal valve, (4) whether any large intestine has also been removed, (5) residual disease in the remaining small and/or large intestine (e.g., Crohn's disease, mesenteric artery disease), and (6) the degree of adaptation in the remaining intestine. Short-bowel syndrome can occur in persons of any age, from neonates to the elderly.

Three different situations in adults mandate intestinal resection: (1) mesenteric vascular disease, including atherosclerosis, thrombotic phenomena, and vasculitides; (2) primary mucosal and submucosal disease (e.g., Crohn's disease); and (3) operations without preexisting small-intestinal disease (e.g., after trauma).

After resection of the small intestine, the residual intestine undergoes adaptation of both structure and function that may last for up to 6–12 months. Continued intake of dietary nutrients and calories is required to stimulate adaptation via direct contact with the intestinal mucosa, the release of one or more intestinal hormones, and pancreatic and biliary secretions. Thus, enteral nutrition with calorie administration must be maintained, especially in the early postoperative period, even if an extensive intestinal resection requiring parenteral nutrition (PN) has been performed. The subsequent ability of such patients to absorb nutrients will not be known for several months, until adaptation is complete.

Multiple factors besides the absence of intestinal mucosa (required for lipid, fluid, and electrolyte absorption) contribute to diarrhea and steatorrhea in these patients. Removal of the ileum, and especially the ileocecal valve, is often associated with more severe diarrhea than jejunal resection. Without part or all of the ileum, diarrhea can be caused by an increase in bile acids entering the colon; these acids stimulate colonic fluid and electrolyte secretion. Absence of the ileocecal valve is also associated with a decrease in intestinal transit time and bacterial overgrowth from the colon. The presence of the colon (or a major portion) is associated with substantially less diarrhea and a lower likelihood of *intestinal failure* (an inability to maintain nutrition without parenteral support) as a result of fermentation of nonabsorbed carbohydrates to SCFAs. The latter are absorbed in the colon and stimulate Na and water absorption, improving overall fluid balance. Lactose intolerance as a result of the removal of lactase-containing mucosa as well as gastric hypersecretion may also contribute to the diarrhea.

In addition to diarrhea and/or steatorrhea, a range of nonintestinal symptoms is observed in some patients. The frequency of renal calcium oxalate calculi increases significantly in patients with a small-intestinal resection and an intact colon; this greater frequency is due to an increase in oxalate absorption by the large intestine, with subsequent *enteric hyperoxaluria*. Two possible mechanisms for the increase in oxalate absorption in the colon have been suggested: (1) increased bile acids and fatty acids that augment colonic mucosal permeability, resulting in enhanced oxalate absorption; and (2) increased fatty acids that bind calcium, resulting in an enhanced amount of soluble oxalate that is then absorbed. Since oxalate is high in relatively few foods (e.g., spinach, rhubarb, tea), dietary restrictions alone do not constitute adequate treatment. Cholestyramine (an anion-binding resin) and calcium have proved useful in reducing hyperoxaluria. Similarly, an increase in cholesterol gallstones is related to a decrease in the bile-acid pool size, which results in the generation of cholesterol supersaturation in gallbladder bile. Gastric hypersecretion of acid occurs in many patients after large resections of the small intestine. The etiology is unclear but may be related to either reduced hormonal inhibition of acid secretion or increased gastrin levels due to reduced small-intestinal catabolism of circulating gastrin. The resulting gastric acid secretion may be an important factor contributing to diarrhea and steatorrhea. A reduced pH in the duodenum can inactivate pancreatic lipase and/or precipitate duodenal bile acids, thereby increasing steatorrhea, and an increase in gastric secretion can create a volume overload relative to the reduced small-intestinal absorptive capacity. Inhibition of gastric acid secretion with proton pump inhibitors can help reduce diarrhea and steatorrhea, but only for the first 6 months.