or, with much greater sensitivity, abdominal CT scans) can be obtained next to identify pancreatic disease. If the urinary D-xylose excretion is abnormal, the breath hydrogen test may be used to diagnose bacterial overgrowth using glucose for the carbohydrate load. If no bacterial overgrowth is present, a mucosal biopsy should be performed (see Table 33-5). Imaging studies of the small bowel may be helpful on occasion.

If the cause of malabsorption remains unclear, other considerations should include parasitic infection, such *Giardia lamblia*, or ascariasis involvement of the pancreatic duct (more common in undeveloped countries). These diagnoses require a careful stool examination for ova and parasites or fecal antigen studies.

TREATMENT

The specific treatment of malabsorption depends on identification of the underlying condition. Occasionally, therapeutic trials for treatable conditions should be instituted, such as a gluten-free diet for celiac disease, pancreatic enzyme replacement for pancreatic exocrine malfunction, metronidazole for *G. lamblia* infection, or broad-spectrum antibiotics for suspected bacterial overgrowth. Parenteral nutrition may have a role in maintaining adequate nutritional status. Treatment modalities are discussed in later chapters focusing on specific diseases. Two disorders, celiac disease and bacterial overgrowth, are discussed here as illustrative of the pathophysiology.

Celiac Disease

Celiac disease (also called celiac sprue, nontropical sprue, or gluten-sensitive enteropathy) is characterized by intestinal mucosal injury resulting from gluten-related immunologic damage in persons genetically predisposed to this condition. The prevalence of the disease among relatives of patients with celiac disease is approximately 10%. There is a strong association of celiac disease with human leukocyte antigen (HLA) class II molecules, particularly HLA-DQ2 and HLA-DQ8. The disease is induced by exposure to storage proteins found in grain plants such as wheat (which contains gliadin), barley, and rye and their products. Oats are implicated, not because of gliadin, but because of contamination with wheat during packaging and transportation. The exposure initiates a cellular immune response that results in mucosal damage, particularly in the proximal intestine. Results of investigations suggest that an enzyme, tissue transglutaminase, may be the autoantigen of celiac disease.

Clinical Presentation

Celiac disease can manifest with the classic constellation of symptoms and signs of a malabsorption syndrome. Not uncommonly, however, the manifestation is atypical, with nonspecific GI symptoms such as bloating, chronic diarrhea (with or without steatorrhea), flatulence, lactose intolerance, or deficiencies of a single micronutrient (e.g., iron deficiency anemia). Extraintestinal complaints such as depression, weakness, fatigue, arthralgias, osteoporosis, or osteomalacia may predominate. A number of diseases, including dermatitis herpetiformis, type 1 diabetes mellitus, autoimmune thyroid disease, and selective immunoglobulin A (IgA) deficiency, are found in significant association with celiac disease.

Diagnosis

Celiac disease is a leading consideration in every patient with the malabsorption syndrome, and it should be included as well in the differential of atypical manifestations. Fiberoptic or capsule endoscopy may show the typical features of broad and flattened villi; with the former instrument, tissue can be sampled for histologic analysis. Intestinal biopsy is the most valuable test in establishing the diagnosis. The spectrum of pathologic changes ranges from normal villous architecture with an increase in mucosal lymphocytes and plasma cells (the infiltrative lesion) to partial blunting or total villous flattening. Although abnormal biopsy findings are not specific, they are highly suggestive, particularly because most other conditions that can mimic celiac disease (e.g., Crohn's disease, gastrinoma, lymphoma, tropical sprue, graft-versus-host disease, immune deficiency) may be distinguished clinically. A clinical response to a gluten-free diet establishes the diagnosis and precludes the need, in adults, to document healing by repeated biopsies. Serologic blood tests (antigliadin, antiendomysial, and reticulin antibodies) are helpful in screening of patients with atypical symptoms and asymptomatic relatives of patients with celiac disease.

Treatment

Strict, lifelong adherence to a gluten-free diet is the only treatment for celiac disease. Specific nutritional supplementation should be provided to correct deficiencies, particularly those of iron, vitamins, and calcium. A clinical response may be seen within a few weeks. Patients should be monitored to ensure adequate response and proper adherence to the diet. The long-term prognosis is excellent for patients who adhere to the diet, although there may be a slight increase in the incidence of malignancies, particularly lymphoma.

Bacterial Overgrowth Syndrome

The proximal small bowel normally contains fewer than 10^4 bacteria per milliliter of fluid, with no anaerobic *Bacteroides* organisms and few coliforms. Overgrowth of luminal bacteria can result in diarrhea and malabsorption by a number of mechanisms, including (1) deconjugation of bile salts, which leads to impaired micelle formation and impaired uptake of fat; (2) patchy injury to the enterocytes (small intestinal epithelial cells); (3) direct competition for the use of nutrients (e.g., uptake of vitamin B_{12} by gram-negative bacteria or the fish tapeworm *Diphyllobothrium latum*); and (4) stimulated secretion of water and electrolytes by products of bacterial metabolism, such as hydroxylated bile acids and short-chain (volatile) organic acids.

Conditions Associated with Bacterial Overgrowth

The most important factors maintaining the relative sterility of the upper gut are gastric acidity, peristalsis, and intestinal immunoglobulins (IgA). Conditions that impair these functions can result in bacterial overgrowth. Impaired peristalsis may be caused by motility disorders (e.g., scleroderma, amyloidosis, diabetes mellitus) or by anatomic changes (e.g., surgically created blind loops, obstruction, jejunal diverticulosis). Achlorhydria, pancreatic insufficiency, and hypogammaglobulinemia are also