range from isolated gastric disease to diffuse eosinophilic gastroenteritis. Antral involvement predominates, with prominent edematous folds being observed on endoscopy. These prominent antral folds can lead to outlet obstruction. Patients can present with epigastric discomfort, nausea, and vomiting. Treatment with glucocorticoids has been successful.

Several systemic disorders may be associated with *granulomatous gastritis.* Gastric involvement has been observed in Crohn's disease. Involvement may range from granulomatous infiltrates noted only on gastric biopsies to frank ulceration and stricture formation. Gastric Crohn's disease usually occurs in the presence of small-intestinal disease. Several rare infectious processes can lead to granulomatous gastritis, including histoplasmosis, candidiasis, syphilis, and tuberculosis. Other unusual causes of this form of gastritis include sarcoidosis, idiopathic granulomatous gastritis, and eosinophilic granulomas involving the stomach. Establishing the specific etiologic agent in this form of gastritis can be difficult, at times requiring repeat endoscopy with biopsy and cytology. Occasionally, a surgically obtained full-thickness biopsy of the stomach may be required to exclude malignancy.

Russell body gastritis (RBG) is a mucosal lesion of unknown etiology that has a pseudotumoral endoscopic appearance. Histologically, it is defined by the presence of numerous plasma cells containing Russell bodies (RBs) that express kappa and lambda light chains. Only 10 cases have been reported, and 7 of these have been associated with *H. pylori* infection. The lesion can be confused with a neoplastic process, but it is benign in nature, and the natural history of the lesion is not known. There have been cases of resolution of the lesion when *H. pylori* was eradicated.

MÉNÉTRIER'S DISEASE

Ménétrier's disease (MD) is a very rare gastropathy characterized by large, tortuous mucosal folds. MD has an average age of onset of 40–60 years with a male predominance. The differential diagnosis of large gastric folds includes ZES, malignancy (lymphoma, infiltrating carcinoma), infectious etiologies (CMV, histoplasmosis, syphilis, tuberculosis), gastritis polyposa profunda, and infiltrative disorders such as sarcoidosis. MD is most commonly confused with large or multiple gastric polyps (prolonged PPI use) or familial polyposis syndromes. The mucosal folds in MD are often most prominent in the body and fundus, sparing the antrum. Histologically, massive foveolar hyperplasia (hyperplasia of surface and glandular mucous cells) and a marked reduction in oxyntic glands and parietal cells and chief cells are noted. This hyperplasia produces the prominent folds observed. The pits of the gastric glands elongate and may become extremely dilated and tortuous. Although the lamina propria may contain a mild chronic inflammatory infiltrate including eosinophils and plasma cells, MD is not considered a form of gastritis. The etiology of this unusual clinical picture in children is often CMV, but the etiology in adults is unknown. Overexpression of the growth factor TGF-α has been demonstrated in patients with MD. The overexpression of TGF-α in turn results in overstimulation of the epidermal growth factor receptor (EGFR) pathway and increased proliferation of mucus cells, resulting in the observed foveolar hyperplasia.

The clinical presentation in adults is usually insidious and progressive. Epigastric pain, nausea, vomiting, anorexia, peripheral edema, and weight loss are signs and symptoms in patients with MD. Occult GI bleeding may occur, but overt bleeding is unusual and, when present, is due to superficial mucosal erosions. In fact, bleeding is more often seen in one of the common mimics of MD, gastric polyposis. Twenty to 100% of patients (depending on time of presentation) develop a protein-losing gastropathy due to hypersecretion of gastric mucus accompanied by hypoalbuminemia and edema. Gastric acid secretion is usually reduced or absent because of the decreased parietal cells. Large gastric folds are readily detectable by either radiographic (barium meal) or endoscopic methods. Endoscopy with deep mucosal biopsy, preferably full thickness with a snare technique, is required to establish the diagnosis and exclude other entities that may present similarly. A nondiagnostic biopsy may lead to a surgically obtained full-thickness biopsy to exclude malignancy. Although MD is considered premalignant by some, the risk of neoplastic progression is not defined. Complete blood count, serum gastrin, serum albumin, CMV and *H. pylori* serology, and pH testing of gastric aspirate during endoscopy should be included as part of the initial evaluation of patients with large gastric folds.

TREATMENT **MÉNÉTRIER'S DISEASE**

Medical therapy with anticholinergic agents, prostaglandins, PPIs, prednisone, somatostatin analogues (octreotide) and H_2 receptor antagonists yields varying results. Ulcers should be treated with a standard approach. The discovery that MD is associated with overstimulation of the EGFR pathway has led to the successful use of the EGF inhibitory antibody, cetuximab, in these patients. Specifically, four of seven patients who completed a 1-month trial with this agent demonstrated near complete histologic remission and improvement in symptoms. Cetuximab is now considered the first-line treatment for MD, leaving total gastrectomy for severe disease with persistent and substantial protein loss despite therapy with this agent.

349 Disorders of Absorption

Henry J. Binder

Disorders of absorption constitute a broad spectrum of conditions with multiple etiologies and varied clinical manifestations. Almost all of these clinical problems are associated with *diminished* intestinal absorption of one or more dietary nutrients and are often referred to as the *malabsorption syndrome.* This term is not ideal as it represents a pathophysiologic state, does *not* provide an etiologic explanation for the underlying problem, and should not be considered an adequate final diagnosis. The only clinical conditions in which absorption is *increased* are hemochromatosis and Wilson's disease, in which absorption of iron and copper, respectively, is elevated.

Most malabsorption syndromes are associated with *steatorrhea*, an increase in stool fat excretion to >6% of dietary fat intake. Some malabsorption disorders are not associated with steatorrhea: primary lactase deficiency, a congenital absence of the small-intestinal brush border disaccharidase enzyme lactase, is associated with lactose "malabsorption," and pernicious anemia is associated with a marked decrease in intestinal absorption of cobalamin (vitamin B_{12}) due to an absence of gastric parietal-cell intrinsic factor, which is required for cobalamin absorption.

Disorders of absorption must be included in the differential diagnosis of diarrhea (Chap. 55). First, diarrhea is frequently associated with and/or is a consequence of the diminished absorption of one or more dietary nutrients. The diarrhea may be secondary either to the intestinal process that is responsible for the steatorrhea or to steatorrhea per se. Thus, celiac disease (see below) is associated with both extensive morphologic changes in the small-intestinal mucosa and reduced absorption of several dietary nutrients; in contrast, the diarrhea of steatorrhea is the result of the effect of nonabsorbed dietary fatty acids on intestinal (usually colonic) ion transport. For example, oleic acid and ricinoleic acid (a bacterially hydroxylated fatty acid that is also the active ingredient in castor oil, a widely used laxative) induce active colonic Cl ion secretion, most likely secondary to increasing intracellular Ca. In addition, diarrhea per se may result in mild steatorrhea (<11 g of fat excretion while on a 100-g fat diet). Second, most patients will indicate that they have diarrhea, not that they have fat malabsorption. Third, many intestinal disorders that have diarrhea as a prominent symptom (e.g., ulcerative colitis, traveler's diarrhea secondary to an enterotoxin produced by *Escherichia coli*) do not necessarily have diminished absorption of any dietary nutrient.