Therefore, the demonstration of diminished absorption of a dietary nutrient provides unequivocal evidence for small-intestinal disease, although colonic dysfunction may also be present (e.g., Crohn's disease may involve both the small and large intestines). Dietary nutrient absorption may be segmental or diffuse along the small intestine and is site specific. Thus, for example, calcium, iron, and folic acid are exclusively absorbed by active-transport processes in the proximal small intestine, especially the duodenum; in contrast, the active-transport mechanisms for both cobalamin and bile acids are operative only in the ileum. Therefore, in an individual who years previously has had an intestinal resection, the details of which are not presently available, a presentation with evidence of calcium, folic acid, and/or iron malabsorption but without cobalamin deficiency makes it likely that the duodenum and proximal jejunum, but not the ileum, were resected.

Some nutrients—e.g., glucose, amino acids, and lipids—are absorbed throughout the small intestine, although their rate of absorption is greater in the proximal than in the distal segments. However, after segmental resection of the small intestine, the remaining segments undergo both morphologic and functional "adaptation" to enhance absorption. Such adaptation is secondary to the presence of luminal nutrients and hormonal stimuli and may not be complete in humans for several months after resection. Adaptation is critical for the survival of individuals who have undergone massive resection of the small intestine and/or colon.

Establishing the diagnosis of steatorrhea and identifying its specific cause are often quite difficult. The "gold standard" remains a timed, quantitative stool-fat determination. From a practical standpoint, stool collections are invariably difficult and often incomplete, as nobody wants to handle stool. A qualitative test—Sudan III staining—has long been available to document an increase in stool fat. This test is rapid and inexpensive but, as a qualitative test, does not establish the degree of fat malabsorption and is best used as a preliminary screening study. Many of the blood, breath, and isotopic tests that have been developed (1) do not directly measure fat absorption; (2) exhibit excellent sensitivity when steatorrhea is obvious and severe but poor sensitivity when steatorrhea is mild (e.g., assays for stool chymotrypsin and elastase, which can potentially distinguish pancreatic from nonpancreatic etiologies of steatorrhea); or (3) have not survived the transition from the research laboratory to commercial application.

Nevertheless, routine laboratory studies (i.e., complete blood count, prothrombin time, serum protein determination, alkaline phosphatase) may suggest dietary nutrient depletion, especially deficiencies of iron, folate, cobalamin, and vitamins D and K. Additional studies include measurement of serum carotene, cholesterol, albumin, iron, folate, and cobalamin levels. The serum carotene level can also be reduced if the patient's dietary intake of leafy vegetables is poor.

If steatorrhea and/or altered absorption of other nutrients is suspected, then history, clinical observations, and laboratory testing can help detect deficiency of a nutrient, especially of a fat-soluble vitamin (A, D, E, or K). Thus, evidence of metabolic bone disease with elevated alkaline phosphatase concentrations and/or reduced serum calcium levels suggests vitamin D malabsorption. A deficiency of vitamin K is suggested by an elevated prothrombin time in an individual without liver disease who is not taking anticoagulants. Macrocytic anemia leads to an evaluation for possible cobalamin or folic acid malabsorption. Iron-deficiency anemia in the absence of occult bleeding from the gastrointestinal tract in either a male patient or a nonmenstruating female patient requires an evaluation for iron malabsorption and the exclusion of celiac disease, as iron is absorbed exclusively in the proximal small intestine.

At times, however, a timed (72-h) quantitative stool collection, preferably while the patient is on a defined diet, must be undertaken in order to determine stool fat content and establish the diagnosis of steatorrhea. The presence of steatorrhea then requires further assessment to identify the pathophysiologic process(es) responsible for the defect in dietary lipid digestion/absorption (Table 349-4). Other studies include the Schilling test (Chap. 350e), the D-xylose test, duodenal mucosal biopsy, small-intestinal radiologic examination, and tests of pancreatic exocrine function.

THE SCHILLING TEST

This test (Chap. 350e) is performed to determine the cause of cobalamin malabsorption. An understanding of the physiology and pathophysiology of cobalamin absorption is very valuable, enhancing comprehension of aspects of gastric, pancreatic, and ileal function. Unfortunately, the Schilling test has not been available commercially in the United States for the past few years.

URINARY D-XYLOSE TEST

The urinary D-xylose test for carbohydrate absorption provides an assessment of proximal small-intestinal mucosal function. D-Xylose, a pentose, is absorbed almost exclusively in the proximal small intestine. The D-xylose test is usually performed by administering 25 g of D-xylose and collecting urine for 5 h. An abnormal test (excretion of <4.5 g) primarily reflects duodenal/jejunal mucosal disease. The D-xylose test can also be abnormal in patients with blind loop syndrome (as a consequence primarily of an abnormal intestinal mucosa) and, as a false-positive study, in patients with large collections of fluid in a third space (i.e., ascites, pleural fluid). The ease of obtaining a mucosal biopsy of the small intestine by endoscopy and the false-negative rate of the D-xylose test have led to its diminished use. When small-intestinal mucosal disease is suspected, a small-intestinal mucosal biopsy should be performed.

RADIOLOGIC EXAMINATION

Radiologic examination of the small intestine using barium contrast (small-bowel series or study) can provide important information in the evaluation of the patient with presumed or suspected malabsorption. This study is most often performed in conjunction with an examination of the esophagus, stomach, and duodenal bulb. Because insufficient barium is given to the patient to permit an adequate examination of the small-intestinal mucosa, especially in the ileum, many gastrointestinal radiologists alter the procedure by performing either a small-bowel series in which a large amount of barium is given by mouth, without concurrent examination of the esophagus and stomach, or an enteroclysis study in which a large amount of barium is introduced into the duodenum via a fluoroscopically placed tube. In addition, many of the diagnostic features initially described by radiologists to denote the presence of small-intestinal disease (e.g., flocculation, segmentation) are rarely seen with current barium suspensions. Nonetheless, in skilled hands, barium contrast examination of the small intestine can yield important information. For example, with extensive mucosal disease, intestinal dilation can be seen as a dilution of barium from increased intestinal fluid secretion (Fig. 349-3). A normal barium contrast study does *not* exclude the possibility of small-intestinal disease. However, a small-bowel series remains useful in the search for anatomic abnormalities, such as strictures and fistulas (as in Crohn's disease) or blind loop syndrome (e.g., multiple jejunal diverticula) and to define the extent of a previous surgical resection. Other imaging studies that assess the integrity of small-intestinal morphology are CT enterography and magnetic resonance enterography. Capsule endoscopy and double-balloon enteroscopy are other useful aids in the diagnostic assessment of small-intestinal pathology.

BIOPSY OF SMALL-INTESTINAL MUCOSA

A small-intestinal mucosal biopsy is essential in the evaluation of a patient with documented steatorrhea or chronic diarrhea (i.e., that lasting >3 weeks) (Chap. 55). The ready availability of endoscopic equipment to examine the stomach and duodenum has led to its almost uniform use as the preferred method of obtaining