compared with radiographic studies. However, capsule endoscopy should be avoided in patients in whom a stricture is suspected because of the risk of retention. The detection of mucosal lesions by the capsule endoscopy can often be followed by deep enteroscopy (double-balloon endoscopy, single-balloon endoscopy, or spiral enteroscopy), allowing for tissue biopsy, tattoo placement before surgery, balloon dilatation, and foreign body retrieval.

## Schilling Test

Vitamin $B_{12}$ is an essential micronutrient, and its absorption requires several steps. First, the ingested vitamin binds to salivary R-factor protein. In the stomach, gastric parietal cells secrete intrinsic factor, which mixes with the ingested meal. In the duodenum, pancreatic trypsin hydrolyzes the R protein, freeing the vitamin to bind with intrinsic factor. The vitamin $B_{12}$–intrinsic factor complex is then absorbed by specific receptors that are found only on enterocytes in the distal ileum. Malabsorption of vitamin $B_{12}$ can occur because of lack of intrinsic factor (e.g., pernicious anemia, gastric resection), pancreatic insufficiency, bacterial overgrowth, or ileal resection or mucosal disease (e.g., Crohn's disease).

The Schilling test quantifies vitamin $B_{12}$ absorption using radiolabeled vitamin $B_{12}$ as a marker. The test may be expanded to several stages to amplify its diagnostic spectrum. In stage 1, after the injection of 1000 µg of unlabeled vitamin $B_{12}$ to saturate hepatic storage, the patient ingests 0.5 µg of radiolabeled vitamin. Urine is then collected for the measurement of radioactivity; reduced radioactivity suggests $B_{12}$ malabsorption. The test is repeated (stage 2) with the addition of oral intrinsic factor to the ingested vitamin $B_{12}$. If urinary excretion of the radiolabel is corrected, pernicious anemia is diagnosed. If malabsorption is still present, the patient is given a short course of oral antibiotics (stage 3), and the test is repeated; correction of radiolabeled $B_{12}$ excretion establishes bacterial overgrowth. If the test result remains abnormal, oral pancreatic enzymes are given (stage 4), and the test is repeated; correction of the abnormality at this stage implies pancreatic deficiency. Finally, if all these interventions fail, ileal disease or absence of transcobalamin protein is determined by other diagnostic tests. This long outline serves is merely an example of an algorithm of clinical analysis; the usual routine in clinical settings is to administer parenteral vitamin $B_{12}$ while the etiology is delineated by other modalities.

## D-Xylose Test

The D-xylose test serves as an indicator of mucosal absorption in the proximal small bowel and is used to determine whether defects in the epithelium of the intestine are responsible for malabsorption. D-Xylose is a 5-carbon monosaccharide that is transported across the intestinal mucosa largely by passive diffusion. In this test, the subject ingests 25 g of D-xylose, and urine is collected for the next 5 hours. Healthy subjects excrete more than 4.5 g of D-xylose in 5 hours (or ≥20% of the ingested load). Excretion of a lower amount of D-xylose suggests abnormal absorption. However, an abnormally low (false-positive) result may occur in the presence of impaired renal excretory function, gastroparesis, massive peripheral edema, or ascites. Abnormal results can also be seen in the presence of bacterial overgrowth as a result of bacterial degradation of D-xylose in the lumen, but this "pseudomalabsorption" may be corrected after treatment with antibiotics serving as a therapeutic trial.

## Breath Tests

Breath tests rely on bacterial degradation of luminal compounds, which releases metabolic byproduct gases (e.g., hydrogen, methane, carbon dioxide) that can be measured in the exhaled breath. In the case of disaccharidase deficiency, a specific disaccharide (e.g., lactose) that is orally ingested but not properly absorbed in the small intestine is delivered to the colon, where bacterial fermentation liberates metabolites; hydrogen gas is the marker assayed in the breath. In the presence of bacterial overgrowth of the small intestine, orally ingested glucose ferments in the proximal small bowel (instead of being absorbed), resulting in increased hydrogen in the breath; here, the timing of exhaled hydrogen aids in the diagnosis. The measurement of radioactive carbon dioxide in the breath after ingestion of a nutrient labeled with carbon 14 ($^{14}C$) has been used to estimate the malabsorption of fat or bile acids and for measurement of bacterial overgrowth ($^{14}C$-xylose). The radioactive tests are cumbersome, and their usefulness in clinical practice is limited.

The overlap of symptoms and the large number of diagnostic tests available for evaluation of malabsorption necessitate the use of a systematic approach and a rational algorithm (see Fig. 33-3). The most accurate test for fat malabsorption remains the 72-hour fecal fat analysis; however, the test is difficult to carry out in clinical practice. Surrogate screening for steatorrhea is done with the qualitative stool fat examination (Sudan stain) and measurement of serum carotene. If the stool fat content is normal, the patient may still have selective impairment of absorption of a specific carbohydrate. This latter condition should be suspected if the primary symptoms are cramps, flatulence, and diarrhea. The most common example of carbohydrate malabsorption is lactose intolerance; specific tests include the oral lactose tolerance test, but measurement of breath hydrogen is more sensitive and more specific.

More generally, an osmotic gap in fecal water suggests a dietary (rather than a secretory) cause of the diarrhea related to luminal short-chain fatty acids or carbohydrates. The osmotic gap is calculated by the following formula:

$$\text{Osmotic gap} = \text{Plasma osmolality} - [2 \times (\text{fecal}[Na^+] + \text{fecal}[K^+])]$$

The osmotic gap is not calculated by directly measuring stool osmolality because it increases with time in the specimen container. In addition, luminal osmolality is equal to serum osmolality because the colon cannot establish a gradient against the serum concentration of solutes.

When fat malabsorption is demonstrated (>6 g/24 hours, or increased qualitative stool fat and decreased serum carotene), a D-xylose absorption-excretion test should be performed next. A normal D-xylose test result makes diffuse mucosal disease unlikely and suggests maldigestion, principally pancreatic enzyme or bile salt deficiency. Clues to chronic pancreatitis include a history of alcohol abuse or previous episodes of pancreatitis. Unusual causes of pancreatic malabsorption, such as cystic fibrosis, microlithiasis, or drug toxicity, require specific testing and a detailed history. Serum enzyme tests and abdominal imaging (plain films