350e The Schilling Test

Henry J. Binder

The Schilling test is performed to determine the cause of cobalamin malabsorption. Unfortunately, this test has not been available commercially in the United States for the last few years. Since an understanding of the physiology and pathophysiology of cobalamin absorption is very valuable in enhancing one's understanding of aspects of gastric, pancreatic, and ileal function, discussion of the Schilling test is provided as supplemental information to Chap. 349. Because cobalamin absorption requires multiple steps, including gastric, pancreatic, and ileal processes, the Schilling test also can be used to assess the integrity of the organs involved in those processes (Chap. 128).

Cobalamin is present primarily in meat. Except in strict vegans, *dietary* cobalamin deficiency is exceedingly uncommon. Dietary cobalamin is bound in the stomach to a glycoprotein called *R-binder protein*, which is synthesized in both the stomach and the salivary glands. This cobalamin–R binder complex is formed in the acid milieu of the stomach. Cobalamin absorption has an absolute requirement for *intrinsic factor*, another glycoprotein synthesized and released by gastric parietal cells, to promote its uptake by specific cobalamin receptors on the brush border of ileal enterocytes. Pancreatic protease enzymes split the cobalamin–R binder complex to release cobalamin in the proximal small intestine, where cobalamin then is bound by intrinsic factor.

As a consequence, cobalamin absorption may be abnormal in the following conditions:

1. *Pernicious anemia*. In this disease, immunologically mediated atrophy of gastric parietal cells leads to an absence of both gastric acid and intrinsic factor secretion.
2. *Chronic pancreatitis* can result from a deficiency of pancreatic proteases to split the cobalamin–R binder complex. Although 50% of patients with chronic pancreatitis reportedly have an abnormal Schilling test that is corrected by pancreatic enzyme replacement, cobalamin-responsive macrocytic anemia in chronic pancreatitis is extremely rare. Although this probably reflects a difference in the digestion/absorption of cobalamin in food versus that in a crystalline form, the Schilling test still can be used to assess pancreatic exocrine function.
3. *Achlorhydria* is the absence of hydrochloric acid; intrinsic factor is also secreted with acid which is responsible for splitting cobalamin away from the proteins in food to which it is bound. Up to one-third of individuals >60 years of age have marginal vitamin B_{12} absorption because of an inability to release cobalamin from food; these people have no defects in the absorption of crystalline vitamin B_{12}.
4. *Bacterial overgrowth syndromes*, which are most often secondary to stasis in the small intestine, lead to bacterial utilization of cobalamin (often referred to as *stagnant bowel syndrome*; see below).
5. *Ileal dysfunction* (as a result of either inflammation or prior intestinal resection) is due to impaired function of the mechanism of cobalamin–intrinsic factor uptake by ileal intestinal epithelial cells.

In the Schilling test, ^{58}Co-labeled cobalamin is administered orally, and urine is collected for 24 h. The test is dependent on normal renal and bladder function. Urinary excretion of cobalamin reflects cobalamin absorption, provided that intrahepatic binding sites for cobalamin are fully occupied. To ensure saturation of these binding sites so that all absorbed radiolabeled cobalamin will be excreted in urine, 1 mg of cobalamin is administered intramuscularly 1 h after ingestion of the radiolabeled cobalamin. The Schilling test may yield an abnormal result (usually defined as <10% excretion in 24 h) in pernicious anemia, chronic pancreatitis, blind loop syndrome, and ileal disease (Table 350e-1). Therefore, whenever an abnormal Schilling result is obtained, ^{58}Co-labeled cobalamin should be administered on another occasion, this time bound to intrinsic factor, with pancreatic enzymes, or after a 5-day course of antibiotic treatment (often with tetracycline). A variation of the Schilling test can detect failure to split cobalamin from food proteins. The labeled cobalamin is cooked together with a scrambled egg and administered orally. People with achlorydria excrete <10% of the labeled cobalamin in the urine. In addition to establishing the etiology for cobalamin deficiency, the Schilling test can help delineate the pathologic process responsible for steatorrhea by assessing ileal, pancreatic, and small-intestinal luminal function. Unfortunately, the Schilling test is performed infrequently because of the unavailability of human intrinsic factor.

TABLE 350e-1 DIFFERENTIAL RESULTS OF THE SCHILLING TEST IN SEVERAL DISEASES ASSOCIATED WITH COBALAMIN MALABSORPTION

	^{58}Co-Labeled Cobalamin	With Intrinsic Factor	With Pancreatic Enzymes	After 5 Days of Antibiotics
Pernicious anemia	Reduced	Normal	Reduced	Reduced
Chronic pancreatitis	Reduced	Reduced	Normal	Reduced
Bacterial overgrowth	Reduced	Reduced	Reduced	Normal
Ileal disease	Reduced	Reduced	Reduced	Reduced