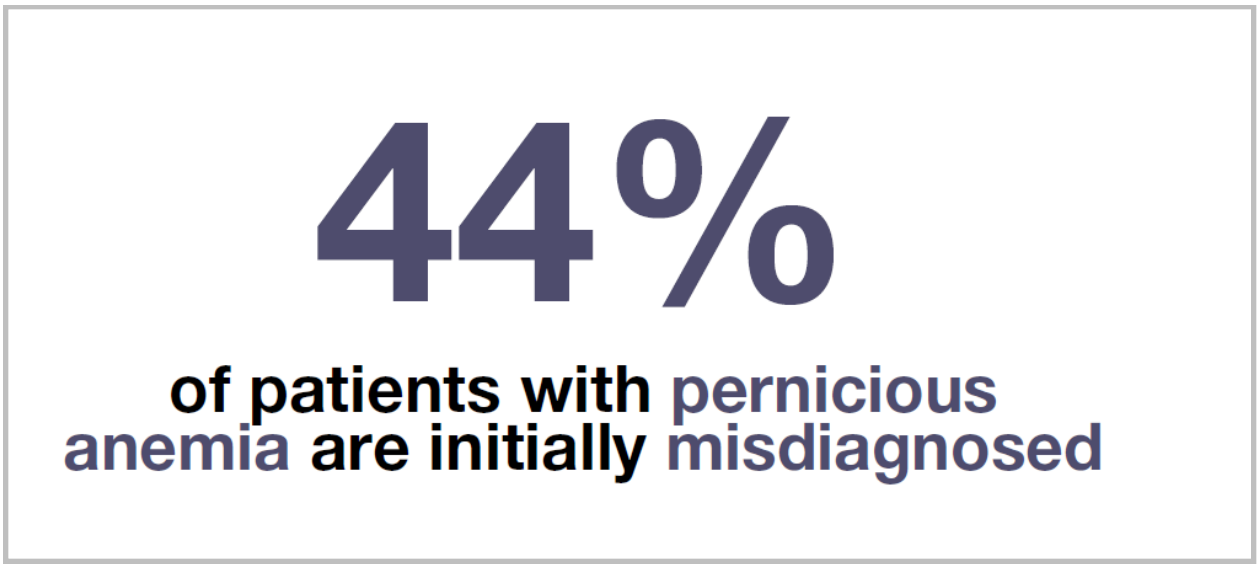
KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

B12 Deficiency - Part Four

Let's talk a little bit more about the diagnosis of pernicious anemia, since we've seen it come up a few times here, and you're likely to see it in your practice. Note that it is often missed in a clinical workup.

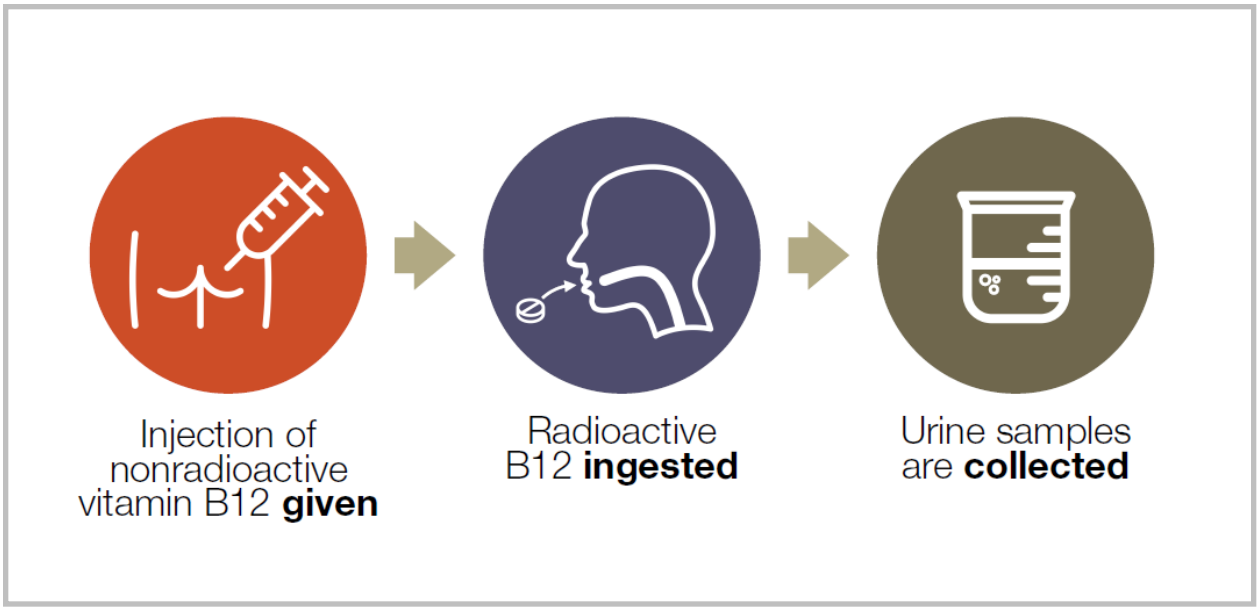


According to the Pernicious Anemia Society, 44 percent of patients with pernicious anemia are initially diagnosed as having a different problem, 22 percent had to wait two years for the correct diagnosis, 19 percent had to wait five years, and 14 percent had to wait 10 years or more. That's because B12 is not part of a typical blood panel, and certainly MMA, homocysteine, and holotranscobalamin, which are way more accurate, as you now know, are not part of a routine blood panel, and holoTC is not even available in the U.S. with the exception of a few hospitals.

If I have a patient with low B12, I will run intrinsic factor antibodies, and they approach 100 percent specificity, so if it's positive, you can be virtually sure that he has it. However, intrinsic factor antibodies only are 50 to 70 percent sensitive, so that test alone would miss 30 to 50 percent of patients with pernicious anemia.

Elevated serum gastrin levels, low pepsinogen I levels, and a low ratio of pepsinogen I to pepsinogen II are highly sensitive for diagnosing pernicious anemia, ranging from 90 to 92 percent sensitivity, but those tests lack specificity. If one of those is positive and intrinsic factor antibodies are negative, you can't really confirm the diagnosis of pernicious anemia without further workup. Pepsinogen is also not widely available, at least in the U.S., so when B12 is low, I usually follow up with serum gastrin and intrinsic factor antibodies. Note that parietal cell antibodies are only slightly more sensitive than intrinsic factor antibodies and much less specific, so I don't recommend this as a routine test for pernicious anemia.

If the results are still equivocal after initial follow-up testing, you could order a Schilling test. This is less sensitive on its own for detecting B12 deficiency, but it can be helpful for clarifying a pernicious anemia diagnosis when other blood work is equivocal. If you're able to absorb B12 normally, you'll absorb it through your gut cells, and it will get into your bloodstream, where it circulates throughout your body and does its job. If you can't absorb it correctly, however, it won't get in through your gut mucosa, and it will just stay in your gut and be excreted in your feces.

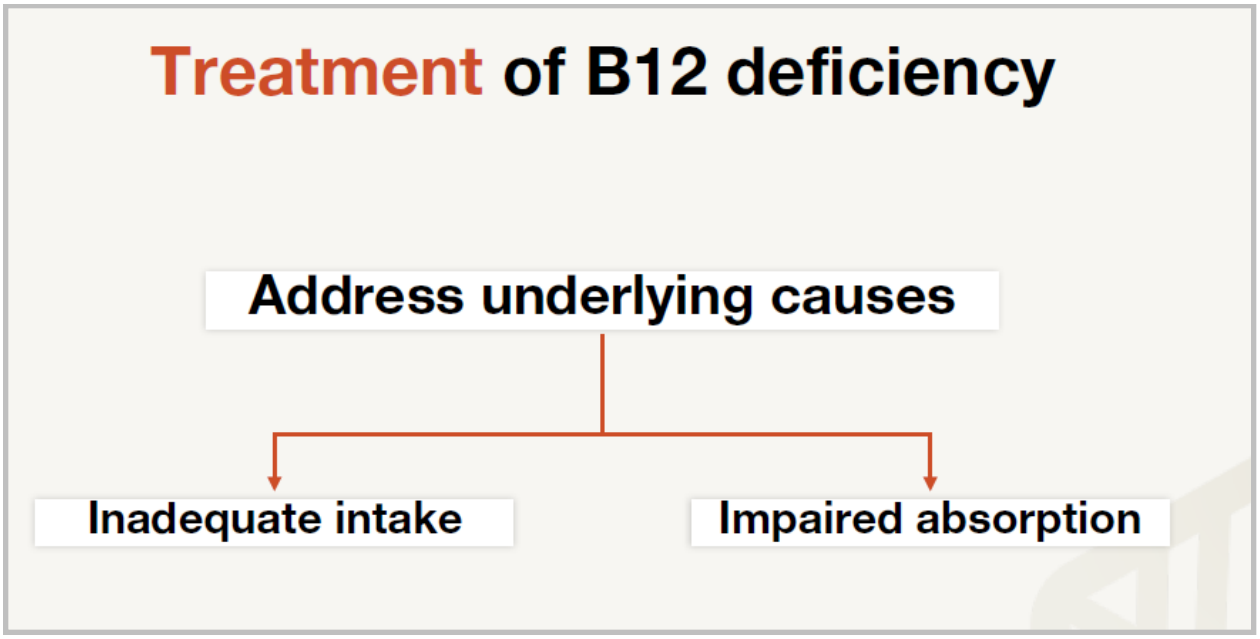


The Schilling test works like this: Step one, the patient is injected with intramuscular B12 to saturate B12 binding sites. Step two, they drink a radiolabeled B12 solution. In step three, if B12 is absorbed through the gut mucosal cells, it enters the blood, is filtered by the kidneys, and is excreted in the urine. If you don't see B12 in the urine, it suggests that the patient can't absorb B12 in the gut, and it won't enter the bloodstream and the urine.

Is testing for pernicious anemia clinically relevant?

How useful is it clinically to know if a patient has pernicious anemia? On the one hand, it's not helpful in guiding treatment because you're still going to be looking at B12 levels and treat until they are normal regardless of the cause. On the other hand, there are three reasons why I think it's really important for both clinicians and patients to know if pernicious anemia is present. First, if

they have pernicious anemia, they'll have to supplement for the rest of their lives, even after addressing other conditions that may impair B12 absorption. Second, it helps patients to take B12 deficiency more seriously and stay consistent with supplementation. Third, patients with pernicious anemia will need sublingual B12 supplements or B12 injections because they don't absorb B12 orally through food or oral supplements, so for those reasons, I think it is important to do the follow-up testing.



Let's talk about the treatment of B12 deficiency. As usual, the first order of business is addressing the underlying cause, and the two main categories here are inadequate intake and impaired absorption. Inadequate intake is most often seen with vegetarians and vegans. Impaired absorption can be GI issues such as hypochlorhydria, celiac disease, IBD, or dysbiosis, as we've seen in the case studies; pernicious anemia; alcoholism; or pancreatic insufficiency. We've talked about identifying and addressing GI issues and pernicious anemia elsewhere, so let's talk a little bit more about adequate intake.

B12 intake recommendations

Source	Amount (mcg)
Current RDA	2.4
Studies on minimizing chromosomal damage and improving DNA repair	7
Average daily intake of hunter-gatherers	17.6

The current RDA for B12 is 2.4 mcg per day, and this is for healthy adults under 50 with normal absorption of B12. For adults over 50 or adults with impaired absorption, the RDA increases to 150 to 200 mcg per day, and in those populations, less than 1 percent of oral B12 that is consumed is actually absorbed. Studies that looked at optimal B12 levels based on minimizing chromosomal damage and improving DNA repair suggest an RDA of 7 mcg per day in people without absorption issues. Loren Cordain's research suggests that the average daily intake of hunter–gatherers was 17.6 mcg per day, which is significantly higher than the U.S. RDA or the other recommended amount that I just mentioned.

If we use this higher number from hunter–gatherers as the recommended daily intake for healthy people below 50 with no absorption issues, that number for people over 50 or with absorption issues would be 1,700 mcg per day, which is almost impossible to achieve without supplementation, so this, of course, suggests that many elderly people or those with absorption issues might do better taking a B12 supplement. This is supported by research showing that patients with no overt B12 deficiency, as defined by serum cobalamin, which is not even the most sensitive marker, experience remarkable improvements after high-dose B12 supplementation. There is no known tolerable upper intake level for B12, and no toxicity threshold has been found. Therefore, I believe it's safer to advise higher intakes than lower intakes. In other words, you're better off giving a patient B12 unnecessarily than you are not giving them B12 when they may need it.

Highest dietary sources of B12

Food	Amount (mcg per 100g)
Clam	99
Lamb liver	90
Beef liver	83
Duck liver	54
Oyster	35
Pork liver	26
Caviar	20
Mackerel	19
Herring	19
Mussel	12
Crab	11
Sardine	9
Salmon	6

Here's a chart listing the B12 content of foods. Once again, we see that organ meats and shellfish top the list. They are almost always the most nutrient-dense foods. Clams here are the highest, with 99 mcg per 100-gram serving. If you recall, they are also one of the richest sources of iron. They top the list for iron, so clams are really excellent food for people to eat. Then we've got a bunch of different organ meats such as beef liver, lamb liver, duck liver, and pork liver. We have other types of seafood such as oyster, caviar, mackerel, herring, mussels, crab, sardines, and salmon. Notice what is not on this list. Muscle meats are nowhere to be found in the top sources of B12. It doesn't, of course, mean that we shouldn't eat them. It just means that organ meats and shellfish play a very crucial role in the diet. Also note, of course, that there are no plant foods on this list. Remember that plant foods don't contain true B12. They have substances called cobamides that actually block true B12 absorption.

Increase absorption	Decrease absorption
Address GI issues	Alcohol
Betaine HCL	Metformin
Cranberry juice	Acid-suppressing drugs
Calcium (from food sources)	

In addition to ensuring adequate intake, you want to do things to increase absorption and avoid things that decrease absorption. Things that could increase absorption of B12 include addressing GI issues; betaine hydrochloric acid; one study showed that cranberry juice may increase B12 absorption; and calcium is required for B12 absorption, so make sure that the patient is getting enough of that in the diet, not through supplements, for reasons that we have discussed. A patient could consider consuming some dairy products with meals if he tolerates it.

You want to avoid things that decrease B12 absorption, so that would include minimizing alcohol intake. If the patient is taking metformin, which has been shown to reduce B12 absorption, he can increase his calcium intake. One study showed that increasing calcium intake reversed metformin-induced B12 deficiency. Then, of course, get your patients off PPIs and other acid-suppressing drugs if possible.