

A Vitamin B12 Update 2016 (“Minimal References” Version)



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Vitamin B12 is needed in only tiny amounts, and unlike most B vitamins, it is stored well in the body. Most Americans eat foods that provide lots of it. So there shouldn't be any problem with vitamin B12, right? This is a Trick Question of course; if there were no problem I would not be here talking about it! ☺

Some references for the information provided here are included at the end. A few newer ones are sprinkled around in the text. As always, this handout is not intended to take the place of your physician or health care provider. It is simply a summary of the most recent information available in the scientific literature on this topic as of the date shown. In the interest of avoiding the unnecessary loss of trees, I did not attach those extra 20 pages or so of references/abstracts here. But there are LOTS of references available by request via email for anyone interested.

What does B12 do?

1. B12 is involved in making important chemical messengers and myelin in the brain and nervous system, so some of the major symptoms of deficiency are neurologic problems.
2. B12 is involved in the making DNA, the genetic center of every cell in the body. It is especially important during periods of growth (pregnancy, infancy and childhood), and in tissues that continually make a lot of new cells (red blood cells and the armies of cells in the immune system.)

What happens if B12 is too low?

Besides serious nerve damage and mental confusion, B12 deficiency damages the retina of the eye, and may play a role in conditions such as heart disease, stroke, alzheimer's disease, parkinson's disease, incontinence and loss of hearing.

When deficiency is severe, people can have unusually high heart rates and have trouble breathing. Vitamin B12 deficiency causes changes in testicular tissues in men, and it may be related to increased risk of breast cancer in older women.

During **pregnancy**, inadequate B12 causes birth defects such as neural tube defects and brain damage. A study also suggests that underlying vitamin B12 deficiency may be involved in the development of HELLP Syndrome, a serious complication of pregnancy.

Interestingly, many women are vitamin B12 deficient at the start of a pregnancy but it is usually not recognized because it is not looked for. When it IS recognized the woman is often simply prescribed “a prenatal vitamin” with RDA levels of vitamin B12. In that circumstance, at the end of the pregnancy her blood level will often be in the normal range ... but the baby will still be deficient.

This is because mothers do not share vitamin B12 with a fetus if their own levels are inadequate. That means that providing a CORRECTIVE dose (not a standard, RDA-type dose) of vitamin B12 as soon as inadequacy is recognized is the way to protect baby's ability to optimally make DNA, etc. **A better approach, of course, would be to assure that NOBODY is ever vitamin B12 deficient in the first place ... pregnant or not.**

What foods have B12?

Generally, the only natural food sources are animal products like meat, poultry, fish, milk, cheese and eggs. Other foods may have it added. Some yeasts are reported to provide some vitamin B12, and some vegans rely on this source. However, there are issues related to availability and usability of these various B12 forms, and even some sanitation issues.

[All these “alternative B12-source” issues are beyond the scope of this paper. However, for the reasons described below, I do recommend that vegetarians or others relying on these products monitor their vitamin B12 status to be sure it remains in the safe range to avoid any chance of injury due to deficiency.]

Who is at risk of low B12 status?

1. People with inadequate B12 in their diet.

- A. **Vegans** (people using no animal products) **and the infants they deliver and breast-feed** are at high risk unless they take adequate B12 supplementation.
- B. **Some people just eat a really poor diet** that happens to be very low in both meats and dairy foods.

2. Some people do not absorb B12 well in spite of an adequate diet.

A. People with stomach problems that decrease B12 absorption:

Gastrectomy (surgical stomach removal);

Gastric surgery for weight loss [Anemia after bariatric surgery: more than just iron deficiency. Nutr Clin Pract. 2009];

Low stomach acid production or "atopic gastritis" (both are common problems among the elderly);

Infection with H. Pylori, a bacteria that causes ulcers and gastritis;

Genetic factors causing low levels of "Intrinsic Factor," a B12 carrier made in the stomach. This problem is called "Pernicious Anemia."

B. Conditions that affect the part of the small intestine where it joins the large intestine (called the "terminal ileum"):

Surgical removal of that part of the intestine;

Crohn's disease (inflammatory bowel disease) or celiac disease;

Overgrowth of the intestine surface by bacteria or parasites such as giardia. This is especially common among adults older than 70 who have chronic diarrhea, loss of appetite, or nausea.

5. Some medications interfere with absorption of B12 from food.

Medications probably account for the surprisingly greater number of younger adults now being found to be deficient in B12.

- A. **Drugs that block stomach acid production, especially “proton pump inhibitors” – “PPIs” like Prilosec, Nexium, Prevacid, Protonics, etc/)** interfere with B12 absorption from food. However, they do not impair absorption of vitamin B12 in the form added to food or found in vitamin pills.
- B. The diabetes drug **Metformin (Glucophage)** also clearly seriously interferes with B12 absorption. The mechanism of the absorption problem is different from the problem with PPIs, and at present there is no clear way to improve the situation other than by-passing the problem with an “under-the-tongue” type of vitamin B12 supplement or a B12 shot .
- C. Some drugs for **parkinson’s disease** such as certain forms of **levodopa** also impair absorption of vitamin B12 in the intestine, both in food sources and in oral B12 supplement forms

This is especially true when the levodopa is administered directly into the intestine via jejunostomy tube or gastrostomy tube. This approach has been found to be quite useful for achieving and maintaining more consistent function in the latter stages of parkinson’s disease.

However, it accidentally also results in significant impairment of absorption of vitamin B12, folic acid and other nutrients. This increases risk of elevated homocysteine levels, which are known to greatly increase risk of neuropathy, cardiovascular disease and contribute to further progression of Parkinson’s Disease.

Compared with “healthy” people, vitamin B12 and folic acid deficiency (and vitamin D deficiency) are much more common in people with Parkinson’s disease even without the use of levodopa.

For this reason, vitamin B12 injections or generous sub-lingual vitamin B12 are recommended. Additionally, careful monitoring of _vitamin B12 folic acid and 25hydroxyvitamin D levels and correcting low levels of any of these nutrients is very important.

[A few specific newer references: Parkinsonism Relat Disord. 2014 Jan;20(1):27-31. Prevalence and features of peripheral neuropathy in Parkinson's disease patients under different therapeutic regimens. Mov Disord. 2013 Sep;28(10):1391-7. Neuropathy and

levodopa in Parkinson's disease: evidence from a multicenter study. J Neurol. 2013 Nov;260(11):2844-8. Levodopa, vitamins, ageing and the neuropathy of Parkinson's disease.]

6. People with autoimmune disorders such as insulin-dependent diabetes, celiac disease, multiple sclerosis, certain thyroid disorders and parkinson's disease have a higher risk of deficiency for several reasons.

- A. Sometimes it is related to nutrient malabsorption related to intestinal damage from poorly controlled **celiac disease**. However, as another autoimmune disorder, the severe vitamin B12 deficiency called pernicious anemia is also more common in this population. **In some people with celiac disease, neurologic symptoms are not uncommon ... it is important to monitor their B12 levels carefully.**
- B. **In insulin dependent diabetes or multiple sclerosis, however, neurologic symptoms of pernicious anemia are often missed because they are written off as likely due to neurologic damage from those overriding conditions.**

[An adult friend of mine **with type 1 diabetes** experienced extremely debilitating neurologic symptoms because of having **developed the autoimmune disease pernicious anemia**. She could no longer walk and the pain was severe. Her symptoms were ascribed to complications of diabetes, and I am sorry to report that it took quite a lot of pressure and several months to get the professionals involved in her care to check her vitamin B12 level.

She has improved greatly on vitamin B12 shots since then, but the painful neurologic damage will never be completely gone. Pernicious anemia has been documented in adolescents with diabetes, celiac disease, and autoimmune thyroid disorders as well as in adults, especially among those already identified as having two or more autoimmune diseases]

Interestingly, parenteral **vitamin B12 does look like it can be helpful in diabetic and parkinson related neuropathy**, whether related to underlying pernicious anemia or not.

[Parkinsonism Relat Disord. 2014 Jan;20(1):27-31. Prevalence and features of peripheral neuropathy in Parkinson's disease patients under different therapeutic regimens. Pernicious anemia in an adolescent with type 1 diabetes mellitus. Arch Pediatr Apr;16(4):357-9] Vitamin B12 may be more effective than nortriptyline in improving painful diabetic neuropathy. Int. J. Food Sci 2009 Feb 12:1-6]

7. An additional safety issue is that **people with low vitamin B12 status are at great risk of injury if nitrous oxide anesthesia is used to prevent pain during surgery.** Overt symptomatic vitamin B12 deficiency is also found among people who abuse nitrous oxide by breathing it recreationally. (A separate paper and references are available just on this issue.)

How is B12 deficiency recognized?

Most commonly it is not recognized at all. When it IS identified, it is often when a blood test called a CBC shows red blood cells that are very large ("**macrocytic anemia.**")

Unfortunately, **this is a very late-appearing symptom** and some nerve damage will have already happened by the time the problem is recognized. **It takes up to three years for symptoms of deficiency to develop**, so people often fail to associate the symptoms with a change in diet or health (such as having had stomach surgery, starting to use a certain medication, or deciding to follow a vegan diet.)

Some researchers estimate that as many as **30% of elderly people have unrecognized B12 deficiency**, often due to changes in the stomach and intestine caused by aging. This can contribute to symptoms such as confusion and other mental changes; correcting B12 inadequacy often results in great improvement.

Doctors can check **B12 levels in the blood**, and there are other markers called **homocysteine** and **methylmalonic acid (MMA)**. This testing is not commonly done unless symptoms or risk factors suggest that there is a problem. However, it is impractical, expensive and unnecessary to do these tests regularly on everyone.

What should be done?

Quite a lot can be done to decrease the likelihood of B12 deficiency ever developing. Why risk possible inadequacy? **Assuring adequacy** is by far more cost-effective, health-protective and safe than waiting to act until symptoms of inadequacy become apparent.

1. **An inexpensive generic standard multivitamin with minerals is a very good investment for most people.**

These provide the adult RDA of 2 mcg of well-absorbed B12. Products designed for older adults ("**Silver**"-**type multivitamins**) often have 25 mcg. Some have quite a lot more, as do some "B-100 complex" supplements. **Some researches now recommend >50 mcg/day. B12 is a very safe vitamin and overdose is extremely unlikely.** For some of the conditions (such as **low stomach acid**), simply taking a generous amount of vitamin B12 in a supplement form can solve the problem.

- 2. For other conditions (such as surgical removal of the stomach or part of the intestine or autoimmune-related pernicious anemia), prescription B12 shots are often needed to assure that there is enough in the body.**

New techniques include nasal inhalers, sub-lingual (under the tongue) versions, or extremely high oral doses of B12.

As always, it is extremely important to monitor the effectiveness of any of these methods and to not assume that the problem has been corrected. That is especially true when one is relying on an individual to remember to actually use the supplement.

Summary:

- 1. Vitamin B12 deficiency is not uncommon (although it is often unrecognized) and it is very dangerous.** In the extreme, it is fatal. Before that, it is associated with increased cardiovascular risk birth defects, severe nerve damage and pain, and it contributes to worsening of many health problems a person may have.
- 2. At present, attention to the big problem of vitamin B12 inadequacy is not in our radar and people are**

assumed to be fine unless they have obvious symptoms. However, symptoms are often seen only after significant (and sometimes irreparable damage is done.) **Improving awareness of the threat, and standardly screening for problems ... not just with labs ... are essential first steps.**

- 3. Certain diet patterns and many health conditions increase the risk of unrecognized B12 deficiency.** People with any of the risk factors described earlier should be sure to ask their doctors about this issue. **[Sharing this paper with the doctor may be very helpful,** as much of this is new and they will want to know more about these issues before ordering any tests or supplements, etc.]
- 4. The problem of unrecognized vitamin B12 deficiency is just one of the many reasons why it is (still) regarded as “prudent” for all adults to take a daily multivitamin.** (Journal of the American Medical Association, June 2002.)
- 5. Vitamin B12 in oral supplement forms are very tiny, very cheap, very safe (even in very high doses) and very beneficial for many people.**
- 6. In a number of circumstances described above, some special forms of vitamin B12 are required to**

assure adequacy. These include vitamin B12 as an injection, a nasal spray or a sub-lingual supplement.

- 7. Additionally, a standard (RDA-level) supplement or intake from food is almost always quite insufficient for optimally or even reliably correcting deficiency.**
- 8. The presence of vitamin B12 deficiency presents a great risk if nitrous oxide is used for pain management in surgery or for recreational purposes.**

Nitrous oxide myelopathy in a pediatric patient. Pediatr Emerg Care. 2014 Apr;30(4):266-7. Nitrous oxide induced myeloneuropathy: a case report. Emerg Radiol. 2014 Feb;21(1):85-8 Vitamin B12 deficiency due to nitrous oxide use: Unrecognized cause of combined spinal cord degeneration. Rev Med Interne. 2014 May;35(5):328-32.

- 9. Always ASSURE vitamin B12 adequacy
It is not safe to simply ASSUME it.**

[More references and abstracts are available in a longer version of this paper. Please just ask to have a copy of that version emailed to you if you would like one.]

On the next page: Some cartoons showing some of the digestion and absorption issues described earlier in this paper.

Vitamin B12 Absorption

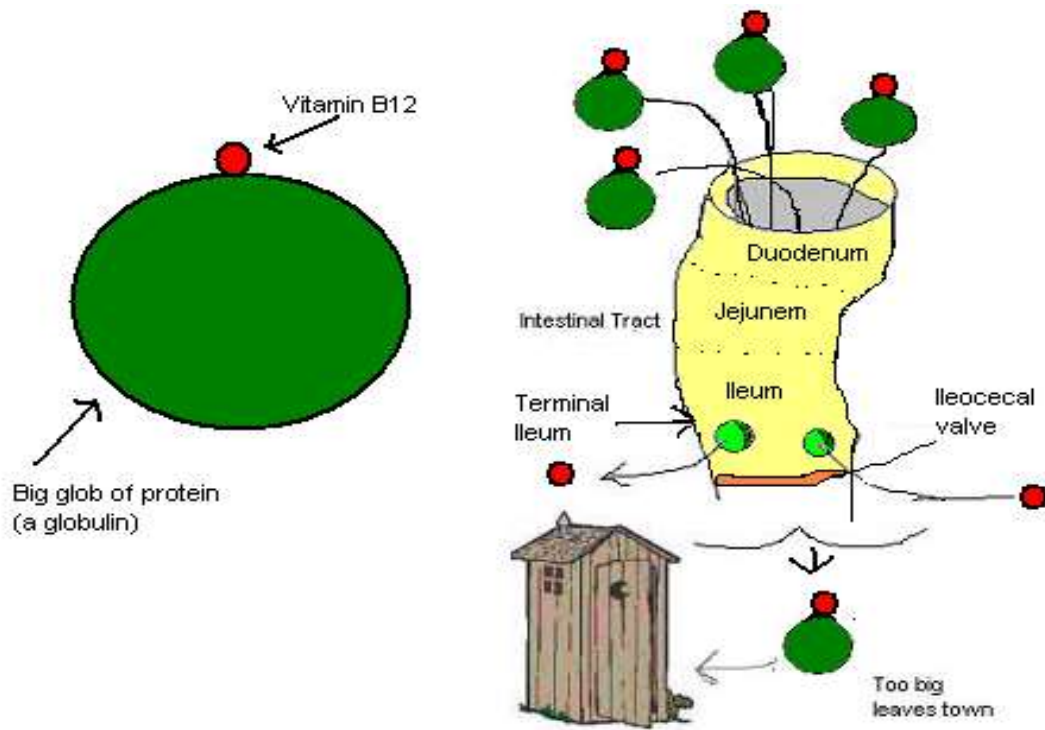
("Not scientifically correct.")



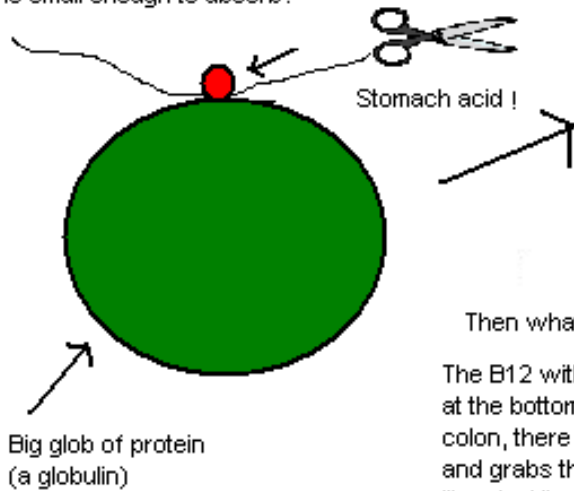
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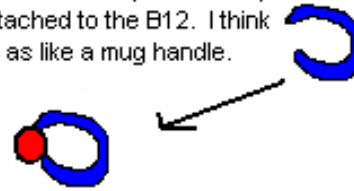


How do you cleave the glob off the B12 so it is small enough to absorb?



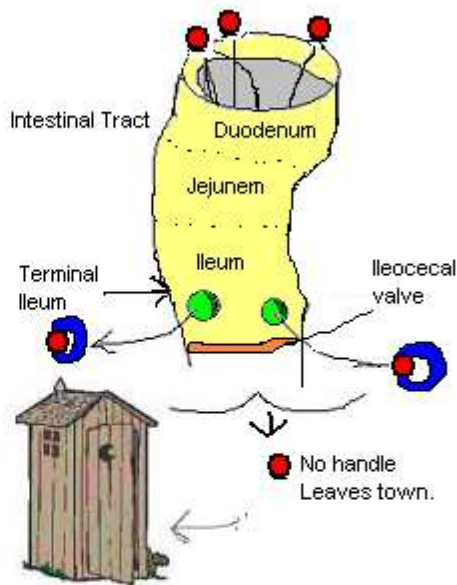
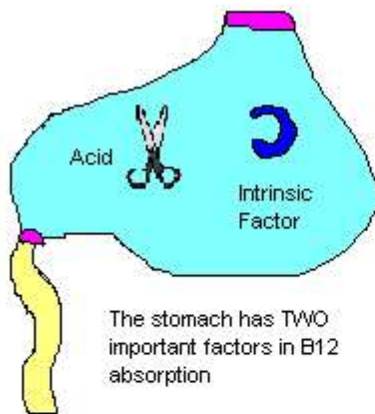
Then what happens?

Then (also in the stomach) "Intrinsic Factor (stuff inside)" is attached to the B12. I think of IF as like a mug handle.



Then what?

The B12 with its handle enters the intestines and way at the bottom of the small intestine where it meets the colon, there is one spot where ha hand reaches out and grabs the handle to pull B12 in. This place (the "terminal ileum") is the only spot in the intestines where B12 can be absorbed.



In the terminal ileum a hand reaches out and grabs the B12 by the handle (intrinsic factor) and pulls it in. Without the handle the B12 is not absorbed regardless of the size of the size of the molecule.

(Well, that's not exactly what happens, but you get the idea...)

Summary of Cartoons:

Health Situations That Can Impair Vitamin B12 Absorption:

1. **Problem: Having inadequate stomach acid due to aging (achlorhydria) or using of PPI acid blocking medications** for gastroesophageal reflux means that the protein glob cannot be removed and the B12 is too big to absorb.

Solution: The form in vitamin pills is just the vitamin B12 without the protein glob, so the problem is eliminated.

2. **Problem: Failure to make or use intrinsic factor in the stomach** (as in the genetic condition pernicious anemia or in people with stomach removal, stomach damage or gastric bypass surgery.)

Solution: The “handle” is not available to efficiently absorb B12 regardless of the molecular size. This requires an alternate route of administration, such as B12 shots or supplement forms that are inhaled or sublingual.

3. **Problem: The diabetes medication Metformin (Glucophage) impairs vitamin B12 absorption in the intestine.**

Solution: A generous intake can help, but vitamin B12 levels should be monitored for anyone on this medication, especially with long term use. Looking at “Mean Cell Volume” on a blood test will not detect a problem soon enough. At least a vitamin B12 serum level should be monitored.

4. **Problem: Injury to terminal ileum can impair absorption** as well as bacterial overgrowth, inflammatory bowel disease, poorly controlled celiac disease, surgical removal, etc.

5. **Solution:** This may require an alternate route of administration, such as B12 shots or supplement forms that are inhaled or sublingual.