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ABSTRACT Vitamin B-12 is of singular interest in any discussion of vegetarian diets because this vitamin is not found in plant foods as are other vitamins. Many of the papers in the literature give values of vitamin B-12 in food that are false because as much as 80% of the activity by this method is due to inactive analogues of vitamin B-12. *Am J Clin Nutr* 1988;48:852-8

KEY WORDS Vitamin B-12, vitamin B-12 analogues, corrinoids, cyanocobalamin, vegans

Introduction

Vitamin B-12 is of singular interest in any discussion of vegetarian diets because this vitamin is not found in plant foods as are other vitamins. Confusion about what sources may yield vitamin B-12 to strict vegetarians has arisen because the standard US Pharmacopeia (USP) assay for vitamin B-12 does not assay only vitamin B-12 (1). In the USP method the content of vitamin B-12 of any given food is determined by making a water extract of that food and feeding the extract to a bacterium (*Lactobacillus leichmannii*). The quantity of vitamin B-12 is determined by the amount of bacterial growth. The problem is that what is active vitamin B-12 for bacteria is not necessarily active vitamin B-12 for humans (1-6). Many of the papers in the literature give values of vitamin B-12 in food that are false because as much as 80% of the activity by this method is due to inactive analogues of vitamin B-12. In this paper we review the origins of vitamin B-12 and its analogues, the effect of vitamin B-12 structure on absorption, assay methods for the vitamin, and issues relating to the requirements for the vitamin.

Origins of vitamin B-12

There is no active vitamin B-12 in anything that grows out of the ground; storage vitamin B-12 is found only in animal products where it is ubiquitous and where it is ultimately derived from bacteria (1, 2, 4). All the vitamin B-12 in plants is there fortuitously in bacteria contaminating the food. That contamination is usually on the outside of the plant but occasionally is internal. For example, in certain pulses in India in the nodules and on the root some bacteria of the rhizobium species grow and produce small amounts of vitamin B-12. They also produce analogues of vitamin B-12 (1, 4).

The more frequent source of vitamin B-12 in associa-

tion with plant food is external contamination with bacteria, often of fecal origin. In one of the less appetizing but more brilliant experiments in the field of vitamin B-12 metabolism in the 50s, Sheila Callender (7) in England delineated that human colon bacteria make large amounts of vitamin B-12. Although the bacterial vitamin B-12 is not absorbed through the colon, it is active for humans. Callender studied vegan volunteers who had vitamin B-12 deficiency disease characterized by classic megaloblastic anemia. She collected 24-h stools, made water extracts of them, and fed the extract to the patients, thereby curing their vitamin B-12 deficiency. This experiment demonstrated clearly that 1) colon bacteria of vegans make enough vitamin B-12 to cure vitamin B-12 deficiency, 2) the vitamin B-12 is not absorbed through the colon wall, and 3) if given by mouth, it is absorbed primarily in the small bowel. Vitamin B-12 is one of those few nutrients absorbed primarily from the lower half of the small bowel (3, 4, 6).

Structure of vitamin B-12 and analogues

The structure of the vitamin B-12 molecule is shown in **Figure 1**. This molecule (cobalamin) consists of four basic parts, the core of which is almost identical to the heme of hemoglobin, suggesting ontogenic development from the same precursor. This core structure (corrin) differs from heme in only two things: the attached metal in corrin is cobalt (it is iron in heme) and one of the alpha methene bridges (there are four in heme) is missing; there are only three alpha methene bridges in the corrin nucleus. The corrin nucleus is the central structure of all the corrinoids.

Corrinoids are cobalt-containing cyclic structures in

¹ From the Mt Sinai School of Medicine, New York, New York.

² Reprints not available.

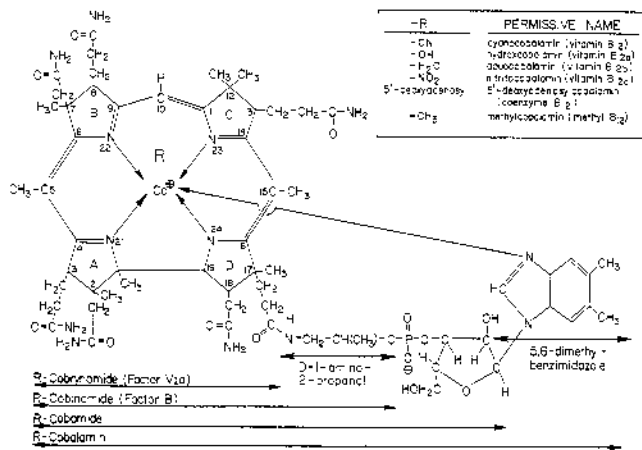


FIG 1. The structural formula of vitamin B-12. From reference 1.

the human body, in foods of animal origin (meat, poultry, eggs, fish, milk, and milk products), and in the bacteria, which make not only vitamin B-12 but also various analogues thereof (1-6). Vitamin B-12 and all its analogues are corrinoids. The human uses as vitamin B-12 only those corrin nuclei to which are added the three other basic parts of the cobalamin molecule: aminopropanol, sugar, and a nucleotide (5). To use it as a vitamin, the human cell must see it as depicted in Figure 1, ie, as a cobalamin with no alterations except in the R adduct. Cobalamins remain vitamin active for humans with a variety of R adducts, which are named *cobalamin* with whatever is attached to cobalt as a prefix. Thus, we have hydroxocobalamin (Fig 1), aquocobalamin, 5'-deoxyadenosylcobalamin, methylcobalamin, and cyanocobalamin among the naturally occurring human-active and potentially human-active forms of vitamin B-12 in various foods.

One can sequentially remove parts of the vitamin B-12 molecule, add side chains, or alter it in other ways. In such cases it ceases to be a cobalamin and thus is not a vitamin for humans. However, it may remain a corrinoid vitamin for one or more of a wide variety of simpler life forms, such as algae and bacteria, which need only the corrin nucleus for vitamin activity in contrast to humans who need the entire cobalamin structure for vitamin B-12 activity. As noted, in addition to cobalamin, bacteria synthesize a number of vitamin B-12 analogues that are noncobalamin corrinoids and therefore not vitamin active for humans.

Cyanocobalamin is stable but not vitamin active

Cyanocobalamin is the form in most pharmaceutical preparations because adding cyanide stabilizes the molecule. This was accidentally learned when vitamin B-12 was first isolated in the eluate from charcoal columns (4). The fortuitous reason that the beautiful red crystalline cobalamin structure came out of the charcoal columns intact, but not out of other columns, was because the

charcoal columns contained cyanide, which exchanged with the naturally present adduct groups attached to the cobalt. The cyanide stabilized the vitamin B-12 molecule, which otherwise is so unstable that exposure to light alone can destroy it.

Cyanocobalamin is not vitamin active for humans until the cyanide is removed within the body. This fact is dramatically illustrated in the rare infant born with a defect in the ability to enzymatically remove cyanide from various substances. Such infants are unable to use cyanocobalamin as vitamin B-12 because they cannot remove the cyanide from it (8). In fact, such infants, when they have a vitamin B-12 deficiency, are made worse by giving them cyanocobalamin because for them it acts as an anti-metabolite. This was demonstrated by Rosenblatt and his group at Yale Medical School (8) in studies of children with genetic defects in vitamin B-12 metabolism.

Differential radioassay

How does one, then, differentiate the nonvitamin analogues from the *true B-12*, which is vitamin active for humans, because it cannot be done by microbiologic assay? This is done by differential radioassay (1, 3, 6). The mixture of vitamin B-12 and vitamin B-12 analogues is assayed for the total content of corrinoids (ie, *total B-12*) by using a binder that attaches primarily to the corrin nucleus. Such a binder is ubiquitous in human and animal tissues; it is a heterogenous glycoprotein called R (for rapid mobility on electrophoresis) binder. It is also called transcobalamin I+III (TC I+III), haptocorrin, or cobalophilin (4, 6). R binder attaches only to the corrin nucleus and thereby measures the total number of corrin nuclei (true B-12 plus noncobalamin analogues). Then the vitamin B-12 active for humans (ie, cobalamin) is assayed by using a substance which attaches to both ends of the cobalamin molecule, the corrin end and the nucleotide end. The substance that accomplishes this is intrinsic factor (IF), first discovered by William Castle at Harvard and the molecule that makes it possible to absorb free vitamin B-12. This gastric parietal-cell secretion is a glycoprotein that attaches specifically to vitamin B-12 with a high affinity coefficient but does not attach to analogues of vitamin B-12 (9). When we use IF as a binder, we essentially measure only the cobalamins in the mixture.

By subtracting the value for cobalamin determined using pure IF (true B-12) from the value for total corrinoids determined by using R binder (total B-12), we determine the amount of analogues by difference, hence the term differential radioassay of analogues.

(noncobalamin) analogues = total B-12

– true B-12 (1)

Fecal contamination as a vitamin B-12 source in vegans

When we apply differential radioassay to human stool, we find that an enormous amount of vitamin B-12 in

TABLE 1
Cobalamin and analogue levels in 6-d 200 °C-dehydrated feces collections from six men

Patient	<i>L. leichmannii</i> †	Feces B-12 (µg/24 h)*			Folate (µg/24 h): <i>L. casei</i>
		Corrinoids	Radioassay Cobalamins	Analogues	
1	32.9	52.9	1.7	51.2	94.5
2	37.36	70.3	1.1	69.2	61.3
3	31.4	103.3	1.6	101.7	150.7
4	12.5	29.8	2.1	27.7	230.7
5	72.9	114.8	12.8	102.0	576.7
6	28.1	46.3	0.6	45.7	56.8
\bar{x} ± SEM (µg/24 h)	35.6 ± 20.0	69.5 ± 13.6	3.31 ± 1.08	66.25 ± 12.5	195.11 ± 80.8
\bar{x} ± SEM (µg/g)	1.83 ± 0.52	3.63 ± 0.33	0.159 ± 0.068	3.47 ± 0.32	10.53 ± 3.66

* The dehydration process destroys approximately one-third each of cobalamin and analogues as compared with fresh (refrigerated) feces. Therefore, actual content is ~150% of the values in the above table. Reprinted from reference 1.

† Not alkali boiled. Boiling in alkali destroys ~85% of stool growth activity for *L. leichmannii* (ie, ~85% is B-12 by *L. leichmannii* assay).

human stool is from analogues (Table 1). In this process 24-h stools are collected over 6 d and dehydrated down to a few ounces of powder. These results represent two-thirds of the vitamin B-12 and analogue content because approximately one-third of each is destroyed in the dehydration procedure. Correcting for this loss, we find that normal, 24-h human stool output contains ~100 µg of total B-12 (vitamin B-12 plus analogues) of which only ~5 µg is cobalamin (vitamin B-12-active for humans) and 95% are various analogues (1).

From Callender's work we know that a water extract of stool will correct human vitamin B-12 deficiency. Therefore, although about 19 out of 20 B-12 molecules in the stool are not active vitamin B-12, these analogues do not block the absorption of that one vitamin B-12 molecule when gastric intrinsic factor secretion is normal. However, some analogues do compete with vitamin B-12 for absorption and may block residual vitamin B-12 absorption when it is already impaired (3, 10).

The fact that stool vitamin B-12 can be important in human vitamin B-12 economy was delineated by James Halsted (11) working with Iranian vegans who did not get vitamin B-12 deficiency. It was difficult to understand why these people, who were strict vegetarians (vegans) for religious reasons, did not get vitamin B-12 deficiency. Halsted went to Iran and found that they grew their vegetables in *night soil* (human manure). The vegetables were eaten without being carefully washed and the amount of retained vitamin B-12 from the manure-rich soil was adequate to prevent vitamin B-12 deficiency. Thus, strict vegetarians who do not practice thorough hand washing or vegetable cleaning may be untroubled by vitamin B-12 deficiency.

Limitations of the standard Schilling test

As we get older we gradually develop, on a genetically determined basis, gastric atrophy. About 1 person in 100 has vitamin B-12 deficiency through gastric atrophy by

age 60. We have calculated that everybody in the United States will develop vitamin B-12 deficiency by age 127; it will be difficult to prove us wrong!

The sequence of events in developing vitamin B-12 deficiency is indicated in Figure 2 (12). Long before gastric IF is lost we lose our gastric acid and gastric digestive enzyme secretion and the ability to absorb vitamin B-12 from foods. This is because vitamin B-12 is peptide bound in milk and all other foods. To be absorbed, the vitamin must first be cleaved from its peptide bonds. This cleavage is brought about by gastric acid and digestive enzymes.

Negative vitamin B-12 balance characterized by the inability to absorb vitamin B-12 from food can be diagnosed by a food Schilling test (ie, vitamin B-12 in an omelet is not absorbed). Doscherholmen (3, 13) showed that the inability to absorb vitamin B-12 from food can occur in a 1-3 y period during which crystalline vitamin B-12 is still normally absorbed (ie, the standard Schilling test gives normal results). This occurs because there is still substantial IF secretion but the gastric acid and enzyme secretion has been lost. It only takes ~20% of normal IF secretion for normal absorption of 0.5-1.5 µg vitamin B-12 (3, 6).

B-12 produced by intestinal bacteria

What is the role of intestinal bacteria above the colon in vitamin B-12 absorption? We have seen that the 5 µg of vitamin B-12 made by colon bacteria per 24 h is of little, if any, value to individuals unless they ingest some of their own feces because vitamin B-12 is not absorbed across the colon mucosa. If one takes gastric aspirates from humans and looks for quantities of viable bacteria, one finds that as the gastric pH becomes closer to neutral the quantities of bacteria gradually increase (1). In the normal, healthy, acid-secreting stomach, there are very few bacteria. As we grow older and our gastric acid secretion decreases, gradually more bacteria grow in our

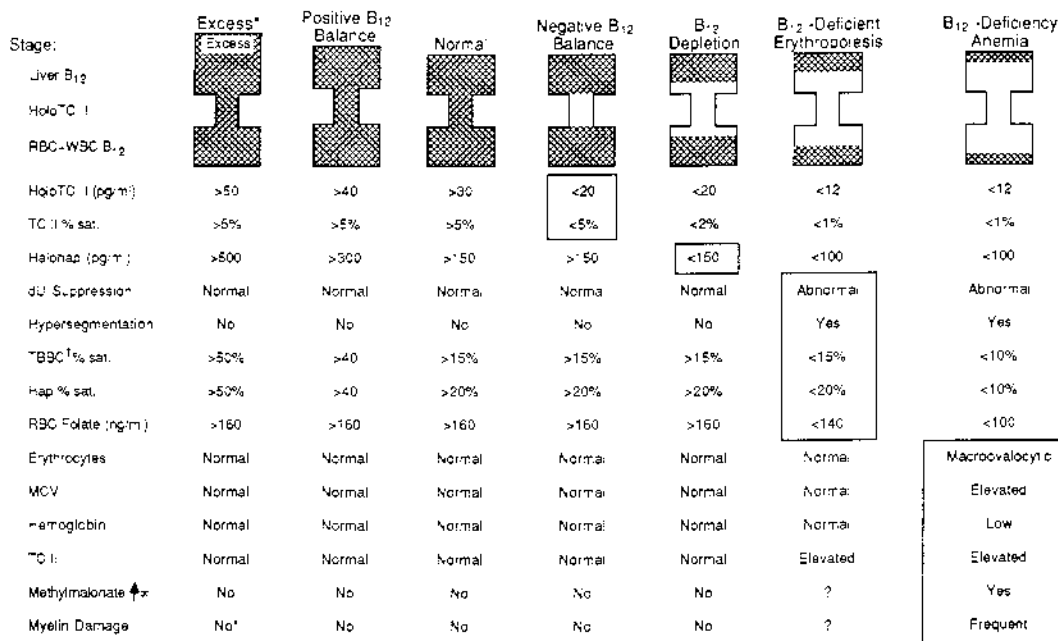


FIG 2. Sequential stages of vitamin B-12 status. *Cyanocobalamin excesses (injected or intranasal) produce transient rise in B-12 analogues on B-12 delivery protein (TC II); the significances of rises is unknown. †TBCC, total B-12 binding capacity. ‡In serum and urine. From reference 12.

stomachs and upper small bowel (Fig 3) (1). This is a very interesting phenomenon and we need to explore whether these bacteria release any unbound vitamin B-12.

The average American omnivore or vegetarian who is not a vegan get vitamin B-12 from food in which the vitamin B-12 is peptide bound. There is adequate vitamin B-12 in milk or milk products for the needs of any person with normal gastric, pancreatic, and intestinal secretions and functions. However, as noted, a negative vitamin B-12 balance may result when those secretions are decreased. Thus the potential contribution of gastric and small intestine bacteria to overall vitamin B-12 nutriture is of interest.

There is normal distribution of viable bacteria in the small intestine and the quantity of bacteria increases progressively (Fig 4) (1) down the small intestine to the ce-

cum where we have the highest colony count before the colon. Of particular importance may be bacteroides, which are present in the upper half of the small intestine and which make both vitamin B-12 and analogues. Albert, Mathan, and Baker (15) found that *Lactobacilli*, the streptococci, the bacteroides, and other enteral bacteria in the small intestine made primarily vitamin B-12. However, their studies used microbiologic assays with organisms that grow on some noncobalamin corrinoids. It is thus uncertain how much of those bacterial products were cobalamin rather than noncobalamin corrinoids.

Enterohepatic circulation of vitamin B-12

The enterohepatic circulation of vitamin B-12 is of crucial importance in human vitamin B-12 economy particularly for vegetarians (4, 6). The reason is that anywhere from 1 to 10 µg of vitamin B-12 is secreted in the

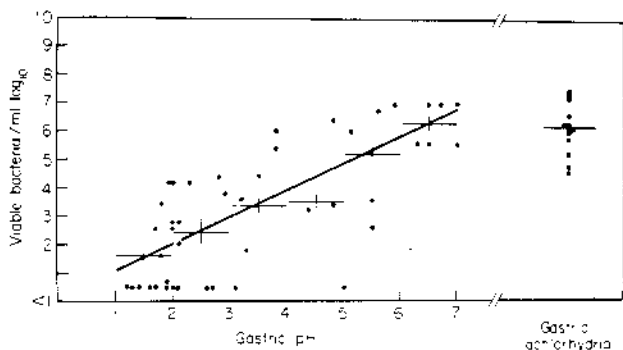


FIG 3. Increasing stomach bacteria with decreasing gastric pH. From reference 14.

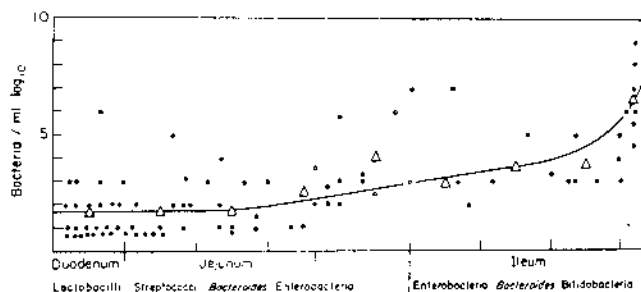


FIG 4. Flora of the small intestine. From reference 14.

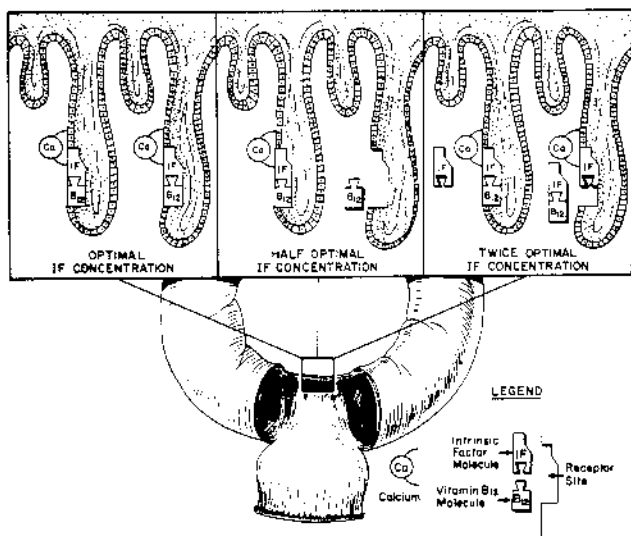


FIG 5. The ileal vitamin B-12-intrinsic factor (IF) receptors.

bile each day. Nobody needs $> 1 \mu\text{g}$ vitamin B-12/d. We normally reabsorb much of the vitamin B-12 in bile secretions. In addition, enterohepatic circulation has the effect of removing unwanted analogues from the body, returning vitamin B-12 relatively free of analogues (3, 16, 17).

The vegetarian often may be getting more vitamin B-12 by reabsorption from bile than from external foods. This would be true for those who eat very little animal protein. The reabsorption of bile vitamin B-12 explains why it takes ~ 20 y to run out of vitamin B-12 and get vitamin B-12 deficiency disease after one stops consuming dietary B-12 but only 3 y to run out and get vitamin B-12 deficiency disease if one stops absorbing the vitamin (3, 4, 6).

The mechanism of vitamin B-12 absorption

In the average omnivorous American diet there are 5–15 μg of vitamin B-12 (2). The food vitamin B-12 has to be removed from its peptide bonds in the food by proteases and acids in the stomach. When removed from food, it does not immediately attach to IF but rather to the ubiquitous R binder, which has a higher affinity for corrinoids (including cobalamin) than does IF. Because we all regularly swallow our own saliva, and saliva is loaded with R binder, the vitamin B-12 split from peptides in our food attaches to R binder and not to IF. Similarly, the vitamin B-12 secreted in bile (along with analogues) is attached to R binder. Vitamin B-12 cannot be absorbed or reabsorbed as long as it is attached to R binder.

The pancreas secretes proteases which, at the slightly alkaline pH of the upper intestine, selectively digest the R binder, releasing its vitamin B-12, which then for the first time is taken up by the dilute-alkali-resistant IF not in the acidic stomach but in the mildly alkaline upper small bowel. The vitamin B-12-IF complex then passes

down into the ileum, where it attaches to specific receptors for the vitamin B-12-IF complex (Fig 5) and is then absorbed (9).

Pancreatic secretion not only digests the R binder and releases the food vitamin B-12 but also digests the R binder that comes out in the bile with vitamin B-12 attached to it, thereby allowing that vitamin B-12 also to migrate to IF and then be absorbed across the ileum (16). Thus, a healthy pancreas is of crucial importance in the absorption of vitamin B-12 (17).

The ileal receptor is not just for IF but, as we showed 25 y ago, is a key-and-lock receptor for the complex of vitamin B-12 and IF. That is a very important distinction because the receptor is for the complex and there can be some absorption of vitamin B-12 (an incomplete key) in the absence of IF and there is evidence that does in fact occur. This direct vitamin B-12 absorption can be blocked by analogues and is an area of active research right now (3). Shaw delineated that the main site of absorption of analogues is in the ileum just as is the main site of absorption of vitamin B-12 itself (18).

There are two separate mechanisms for vitamin B-12 absorption: the IF-dependent physiologic mechanism and the mass-action pharmacologic mechanism whereby 1% of any quantity of free vitamin B-12 is absorbed by diffusion across the ileum (Table 2) (1, 4, 6).

Needed dietary intake of vitamin B-12

How much vitamin B-12 do we need? No more than 1 μg daily (2). Figure 6 is the laboratory data of an individual, aged 54 y, with relatively early pernicious anemia (PA), the form of vitamin B-12 deficiency disease that is due to inadequate or absent secretion of gastric IF. This individual, when given just 1 μg cyanocobalamin/d by injection, had a beautiful hematologic response with a

TABLE 2

Absorption of 2 vs 30 μg oral cyanocobalamin without vs with intrinsic factor*

Subject	Vitamin B-12 in 48-h urine [†]			
	After 2 μg oral cyanocobalamin		After 30 μg oral cyanocobalamin	
	B-12	B-12 + IF	B-12	B-12 + IF
1	0.02	0.36	0.24	0.18
2	0.01	0.17	0.44	0.45
3	0.01	0.35	0.48	0.60
4	0.02	0.14	0.16	0.24
5	0.01	0.11	0.12	0.27
Average	0.02	0.23	0.29	0.35

* When 2 or 30 μg of B-12 is fed to patients with pernicious anemia, there is $\sim 1\%$ urinary excretion in a Schilling test (suggesting $\sim 3\%$ diffusion absorption?) Reprinted from reference 1.

[†] Flushed into urine in 48 h by injection of 1 mg nonradioactive cyanocobalamin at 0 time and again at 24 h after the oral dose of B-12. IF, hog intrinsic factor concentrate.

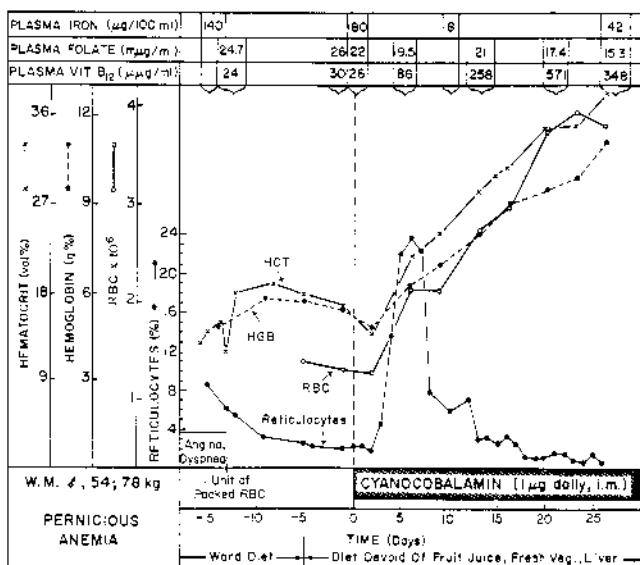


FIG 6. Excellent hematologic response of patient with vitamin B-12 deficiency (pernicious anemia) to 1 μg /vitamin B-12/d. (To convert $\mu\text{g Fe}/100\text{ mL}$ to $\mu\text{mol}/\text{L}$, multiply by 0.1791. To convert ng folate/ mL to nmol/L , multiply by 2.266. To convert pg vit B-12 to pmol/L , multiply by 0.7378.)

sharp increase in very young red cells and reticulocytes and a rise to normal in red cell count, hemoglobin, and hematocrit. Characteristically, as happens when one treats vitamin B-12 deficiency, the serum Fe plummets, in this case from 180 to 8 over the first 10 d, as the plasma

$\mu\text{g}/\text{d}$ because 1- μg would normal people with no stores omnivorous human, if each decade, has a progressive B-12 throughout life, is eating much more vitamin B-12 in continuous positive balance than is inherent

amount we need? Less than Harvard with then research that one can treat vitamin B-12 as 0.1 $\mu\text{g}/\text{d}$ (2). At this point, the response to 0.1 μg to produce a re-

ment (MDR) for vitamin B-12 probably in the range of 0.1 μg derived from food is probably not adequate. There are no objective published data that vitamin B-12 have any effect on longer life. The current Recommended Dietary Allowances (RDA) and Dietary Intakes (RDI)

for vitamin B-12 are lower than previous recommendations (2).

Sources of vitamin B-12

Fermented products, such as soy products like tempeh, do not contain substantial amounts of B-12 (1). The amounts given on the labels cannot be trusted because they were obtained by the US Pharmacopeia (USP) assay method, which sellers of products containing vitamin B-12 are required to use.

The label-stated content of vitamin B-12 is in fact the content of all corrinoids in which *L. leichmannii* grows and not just cobalamin. It should say corrinoids rather than vitamin B-12. The Food and Drug Administration (FDA) was petitioned several years ago to require vitamin B-12 assay for true vitamin B-12 and analogues and perhaps the assay will eventually be changed.

We studied several types of tempeh, including Original Soy Tempeh, a *Rhizobus oligosporus* culture with a label claim of 160% of the US RDA for vitamin B-12 per 4 oz. Using the differential radioassay we found there was practically no vitamin B-12 in it (1).

We also studied most of the spirulinas sold in health food stores as sources of vitamin B-12; there is practically no vitamin B-12 in them. The so-called vitamin B-12 is almost exclusively analogues of vitamin B-12 and we have extracted the two largest peaks of analogues and they actually block vitamin B-12 metabolism. We suspect that people taking spirulina as a source of vitamin B-12 are actually blocking their own B-12 metabolism.

The analogues in the product block human mammalian cell metabolism in culture and we suspect they will also do this in the living human. Remember that the label claim of vitamin B-12 is actually a claim of corrinoid content, not vitamin B-12 content.

The vegan diet, if it is a diet exclusively of products that grow out of the ground, which are then well washed, contains no vitamin B-12 except trace amounts in some rhizobium-bacteria-containing root nodules. Careful studies from England (19) on several hundred vegans showed that they all eventually get vitamin B-12 deficiency disease with anemia and pancytopenia, low white counts, low red counts, low platelet counts, and slowed DNA synthesis (19). Vegans all eventually have slowed DNA synthesis, which is corrected by vitamin B-12. My advice to the vegan parents of a vegan child is that you have to provide a supply of vitamin B-12. Yeast grown on vitamin B-12-enriched medium is only the answer when some of the vitamin B-12-enriching medium is mixed in with the yeast that is eaten because the yeast itself does not contain active vitamin B-12; it contains a lot of analogues but not active vitamin B-12. Differential radioassay show that all the vitamin B-12 is accounted for by vitamin B-12-enriched medium rather than by the yeast itself. Vegans must get a source for vitamin B-12. It can be 1 $\mu\text{g}/\text{d}$ of vitamin B-12 in a tablet or in something else but it has to be cobalamin.

Fe is drawn into the formation of the new red cells.

Nobody needs more than 1 μg of vitamin B-12 (2). The average omnivorous human actually treat and return to normal level of vitamin B-12 (2). The average omnivorous human does sequential studies easily showing a progressively rising liver level of vitamin B-12 indicating the average omnivorous human has more vitamin B-12 than needed and is in positive balance and progressively storing it. There is nothing about continuous positive balance that is inherently desirable (12).

What is the minimal daily requirement for vitamin B-12? 1 μg . In studies carried out at Harvard by fellow Louis Sullivan, we showed that the minimal B-12 deficiency with as little as 0.1 $\mu\text{g}/\text{d}$ level stores are not rapidly replenished. The response is submaximal but it only takes a few days for response.


The minimum daily requirement for vitamin B-12 to sustain normality is 0.1 μg . ~0.1 μg , 0.2-0.25 $\mu\text{g}/\text{d}$ absorbable is adequate for anybody (2). The published data that larger amounts of vitamin B-12 added value for greater health and longevity. The Canadian Recommended Dietary Allowance (RDA) and the recent Recommended

Bindra et al (20) note that vegetarians who boil their milk before drinking may destroy much of the milk vitamin B-12 and place themselves at risk; they also suggested that the high dietary fiber levels of Punjabi diets may increase fecal excretion of vitamin B-12 (20).

Vitamin B-12 as snake oil

Just before this conference, *Time* magazine inquired about the latest California health food fad: sniffing vitamin B-12 gel up the nose. Like most health food fads, it was created by entrepreneurs with heavy advertising budgets and light consciences. The heavily promoted fad moved east to just about every health food store across the United States. Given a deceptive name suggesting energy, it is falsely represented as giving an energy boost, which, of course, is biochemically impossible because vitamin B-12 neither supplies nor releases energy except in the vitamin B-12-deficient individual. Vitamin B-12 is involved in intermediary metabolism as a catalyst much like a traffic cop at an intersection.

Like many other pharmaceutical agents, vitamins are absorbed better through the nasal mucosa than through the alimentary mucosa. However, the increased percentage absorption of vitamin B-12 through the nasal route is of no value whatsoever to the person with a normal serum vitamin B-12 level. All that vitamin B-12-normal people get from wasting their money on vitamin B-12 nasal gels is expensive urine. In addition, the gel may be allergenic for some. Nasal gel vitamin B-12 gets no more vitamin B-12 into the bloodstream than a 10-fold greater oral dose and may not be as reliable as injected vitamin B-12 (21). The FDA has been petitioned to stop the sale of the gel as a food supplement.

What is the RDA for vitamin B-12? The suppressed (3) 1980-85 RDA appears in the April 1987 issue of the *American Journal of Clinical Nutrition* (2) as the RDI (for which read "1985 RDA") for vitamin B-12. RDI is the international term used by the World Health Organization (WHO) and many other countries. RDA is a term used primarily in the United States. We (the 1980-85 RDA Committee) reduced the RDA for vitamin B-12 to 2 µg for adults (which is still more than anybody needs) because there was no scientific basis for higher amounts (2). As delineated above, nobody needs that much, there is no evidence that it has any value whatsoever for humans and, as we discover more and more about excesses of any nutrient, we discover harms we did not know existed (12, 21, 22). It will probably turn out eventually that too much vitamin B-12, like too much of anything, is harmful (12). 

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