Methylcobalamin and the New Story of Vitamin B12
by Ed Sharpe

The 50th anniversary of the discovery of vitamin B12 came and went and nobody noticed. There were no conferences to mark the occasion, no fanfares, no speeches, not a mention in the press, not even in the nutritional media. "Vitamin B12 isn't sexy," was the way a friend, a sports nutrition consultant, put it. "just for old people, to keep them from getting anemic." Oh, yeah? Welcome to the new story of vitamin B12.

There's a buzz over B12 these days for two reasons, one scientific and the other economic. First, the science: Over the last decade or so, researchers have strongly implicated the toxic amino acid homocysteine in a variety of disease states. Homocysteine tends to accumulate in the body whenever B12 gets deficient, and this accumulation has been linked with increased risk of Alzheimer's disease, cardiovascular disease, chronic fatigue syndrome/fibromyalgia and multiple sclerosis among other conditions.

Folic acid deficiency can also lead to increased homocysteine levels – that's because folate and B12, in their active 'coenzyme' forms, are both necessary cofactors for the enzymatic conversion of homocysteine to methionine. Until recently it's been thought that the availability of folate was the most important determinant of the body's ability to remethylate homocysteine. New research has revealed that vitamin B12 is more important for homocysteine disposal than previously believed. In particular, a study conducted among dialysis patients with kidney failure showed that a monthly shot of B12 plus conventional oral folate was more effective than high-dose folate without B12 in lowering elevated homocysteine.

The coenzyme form of vitamin B12 is known as methylcobalamin or methyl B12. It's the only form of vitamin B12 which can directly participate in homocysteine metabolism. In addition, converting homocysteine to methionine via methyl B12 generates an increased supply of SAMe (S-adenosyl methionine), the body's most important methyl donor. Indeed, some of the benefits of methyl B12, such as protection from neurotoxicity, appear to derive from increased production of SAMe.

Methyl B12 has also been reported to be neurotrophic or growth-promoting for nerve cells, a property which may help regenerate central and peripheral nervous tissues damaged in disorders such as amyotrophic lateral sclerosis and diabetic peripheral neuropathy.

All of this scientific news is hot stuff, but it's still only half the story. The other half is that starting around 1998, methylcobalamin first became widely available in this country at an affordable price, thus offering new options for treating B12 deficiencies and lowering elevated homocysteine. Before then, methyl B12 had been enormously expensive and widely available only in Japan, where it still remains a prescription medication. Today any health-conscious American consumer can easily access the most powerful known form of vitamin B12.

Methylcobalamin and Cyanocobalamin

When most of us think of vitamin B12, the molecule we really have in mind is cyanocobalamin or cyano B12. As its name suggests, cyano B12 has a cyanide group (CN) attached, whereas methyl B12 carries a methyl group (CH3) instead. Very little of the body's natural B12 is in the cyano form under normal circumstances; exceptions are in cases of cyanide poisoning or chronic smoking, both of which can raise cyanocobalamin levels. The fact that most of our vitamin pills contain cyano rather than methyl B12 is largely an accident of history, the result of using charcoal to filter extracts during the isolation of B12. Unknown to the early researchers who first isolated B12, the traces of cyanide present in such charcoal rapidly convert all natural forms of B12, including methyl B12 into the more stable cyano form. As a result, the discovery of the B12 coenzymes and their metabolic role was delayed for years.

Whenever we swallow a conventional vitamin pill, any cyano B12 present gets carried along and absorbed by an intricate "bucket brigade" of B12-binding proteins. Operating in the stomach and small intestine, this transport system provides a very efficient mechanism for absorbing a few micrograms of B12, yet is quickly swamped by anything larger. As a result,
only about 1% of a large oral dose of any form of B12 usually makes it into the bloodstream. Fortunately, we can bypass intestinal absorption entirely by taking B12 sublingually. Sublingual administration is a simple and effective way of substantially raising blood levels by absorbing B12 through the oral mucosa. It's also unquestionably the most convenient way to take B12, especially for people taking supplements on a daily basis.

So let's say we've taken a sublingual tablet and a significant amount of B12 shows up in the bloodstream. End of story? Not if it's cyano B12. Most of the B12 naturally circulating in the blood plasma is in the methyl form. Before cyano B12 can join this metabolic pool and be properly utilized by the body, it has to be stripped of its cyano group and 'reduced' (i.e., made to gain electrons) in a time-consuming, multi-step process. The result of all this processing is a B12 molecule with its cobalt ion reduced from the +3 to the +1 oxidation state, ready to take on a methyl group and be distributed throughout the body as methyl B12.

It should be obvious that there are certain advantages inherent in taking methyl B12 as a supplement, versus 'ordinary' B12. For one thing, methyl B12 doesn't have to engage the body's resources to convert it into coenzyme form, it's already there. Even more important is the fact that methylcobalamin is the most highly reduced form of vitamin B12 possible; this makes methyl B12 a very potent reducing agent (antioxidant) indeed. In a body undergoing oxidative stress -- for example from a disease process or from a diet deficient in antioxidants -- it's possible that methyl B12 production can become impaired. A similar derangement in the cellular synthesis of adenosyl B12 (another reduced coenzyme form of B12 into which methyl B12 can be converted) is already known to occur in association with vitamin E deficiency. So it makes sense to consume B12 in a form in which it's already metabolically active and maximally reduced, and thereby put less of a strain on our body's antioxidative capacity.

How Much Is Enough?

How much methyl B12 should be taken for optimal health? In some studies on animals and humans, large doses (equivalent to 25-40 milligrams per day for an adult human) were found to halt or improve neural degeneration. The problem is, nobody knows the long-term effects of such huge doses. A more prudent approach would be to take about a tenth as much, say, 3 milligrams per day (3,000 micrograms) as a maintenance dose, with the dose increased as needed in cases of increased stress, oxidative or otherwise.

[A Note From Don Bennett: The B12 I take and recommend, and the one that's mentioned below, comes in 1,000 microgram tablets, and the bottle says "one a day", but I don't take it everyday, just when I "feel" like it, maybe every few days, and then it is usually 2,000 or 3,000 micrograms. See this article I wrote on B12 for a resource for this B12 supplement. Also, I would get a uMMA test done before beginning to take supplementary B12 (it's a urine test). This will show if you need to take any B12 or not (and this test is the gold standard for B12 utilization and should not be confused with the B12 blood test that doctors usually order). And if the test shows that you don't need to take any B12, you shouldn't. But if this test shows that you are deficient (and most people are), just how deficient you are will help determine the initial dose to take, and this is the best reason for doing this test. This test can be done at home and mailed to the lab. If you'd like a resource for this test, see my B12 article.]

So here's a belated 'Happy 50th Birthday' to B12. With all of the health and pro-longevity benefits of methyl B12 now becoming evident including warding off such age-related diseases as Alzheimer's, atherosclerosis, rheumatoid arthritis and possibly even cancer, it seems that the old vitamin's got some new life in it. May it and we continue in partnership for many birthdays yet to come.

Methylcobalamin in a Small Sample of Vegans

Note: µg = microgram, mg=milligram (1 milligram=1,000 micrograms)

Donaldson (2000, USA) studied 3 vegans with elevated urinay MMA levels who were treated with 1/2 to 1 sublingual methylcobalamin tablet (from Enzymatic Therapy, Green Bay, WI), 2 times/day for 3 weeks. Correspondence with the author (March 21, 2002) verified that these tablets contain 1,000 micrograms (1 milligram) methylcobalamin each.

Two of the subjects' urinary Methyl Malonic Acid (uMMA) normalized while the remaining subject's stayed slightly elevated at 4.1 µg/mg creatinine (normal is < 4.0 µg/mg creatinine). Thus, at a rate of 1-2 milligrams/day, methylcobalamin appears to be absorbed at a high enough rate to improve B12 status in some vegans. Additionally, this indicates that the methylcobalamin was able to improve the MMA pathway which requires adenosylcobalamin (in other words, methylcobalamin was apparently converted into adenosylcobalamin in these people).
Additional Reading:

Don's very thorough article on B12, Everything You Ever Needed to Know about B12

References


