

B12 (Cobalamin)



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Cobalamin is unique among nutrients in that it straddles the divide between vitamin and mineral, containing cobalt at the center of its molecular structure and deriving its name therefrom. A member of the B-vitamin family, B12 shares functional commonalities with others of the B complex, particularly its coenzyme role in energy production and metabolic assimilation of protein, fat, and carbohydrate. This vitamin/trace-element influences daily biorhythms, melatonin secretion, and promotes reproductive health.

Vitamin B12 resides atop the list of nutrients taken in high doses based on a presumption of performance-enhancing properties, largely because it is a cofactor in production of red blood cells that carry oxygen. The fact that toxicity has not ever been recorded at any level of B12 loading - making it among the "safest" nutrients - has encouraged experimentation with megadose shots, and sublingual B12 preparations delivering doses 1000+ times greater than the paltry RDA can be found at most health food stores.

The practice of periodic B12 injection among health enthusiasts and athletes has retained an ardent following over the years, and the progressive doctors who administer this "non-medical" application of vitamin B12 report that many patients swear by it. But does it work? Well, for those folks, particularly older individuals, with B12-deficiency-related anemia or B12-deficiency-related cognitive

impairment (in some cases misdiagnosed as "Alzheimers") the subjective improvement in well-being from a shot of B12 may well verge on miraculous.

B12 is a "methyl donor," which for practical purposes means it facilitates certain important chemical reactions within the body, particularly conversion of potentially toxic homocysteine to methionine and manufacture of neurotransmitters in the brain (including S-adenosylmethionine or "SAME"). Melatonin is made from serotonin, and studies demonstrating the influence of B12 on melatonin has led an increasing number of researchers to theorize that age-related decline in melatonin output is partly caused by age-related decline in B12 absorption.¹⁻⁶

B12 deficiency is typically accompanied by some degree of cognitive impairment or lethargic depression, which parallels symptoms of age-related melatonin deficiency. One study comparing melatonin levels of young subjects (23-39), old subjects (66-94), and demented patients (68-91) found lowest melatonin levels among the demented elderly, higher levels among the healthy elderly, and the highest levels among the young. The fact that healthy centenarians exhibited substantially better melatonin status than demented or otherwise unhealthy younger subjects led the study's author to state: "the amplitude of the nocturnal peak and/or the persistence of a prevalent nocturnal secretion may be an important marker of biological age and of health status."⁷

The associations noted between melatonin, produced by the pea-sized pineal gland within the brain, and aging are not unfamiliar to those who've been following health and anti-aging developments during the last decade. A 1995 *Newsweek* cover story and extravagant claims of diverse health benefits in popular books and other media catapulted melatonin into public awareness and created a US retail market that peaked at \$300 million in the mid-1990's. Suppliers such as Genzyme were put to the task of producing enough synthetic melatonin to satisfy the sudden escalation in demand.

Public fervor was only partly grounded on melatonin's position of uppermost significance in the hormonal cascade, as a regulator of circadian rhythm, which governs the daily ebb and flow of sex hormones and other major hormonal systems. As discussed in *Natural Hormonal Enhancement*, the light-darkness cycle influences hormonal output profoundly. The pineal reacts photosensitively to daily changes in lighting, cueing melatonin release. In humans and other diurnal mammals, the highest levels of melatonin coincide with darkness and inactivity whereas the opposite is the case for nocturnal animals.

The more compelling reason for melatonin's popularity as a proposed remedy for the unwanted effects of aging stems from animal studies showing a reversal of several parameters of aging in treated subjects. Immune function, muscle tone, and fur thickness improved as a result of melatonin treatment, while visceral fat stores diminished. Clearly, the resolution of the problem of biological aging was at hand – for rats.

The carryover to humans proved problematic for many reasons not least of which was the lifespan differential between rats and humans, requiring years of observation in humans to confirm phenomena transpiring during a period of weeks in rats. In the meantime, while waiting to grow young again, human subjects were exposing themselves to the ever-present unknown dangers of exogenous hormone replacement. Opinions as to proper dosage varied widely, and then there's the tricky issue of determining individual needs. Currently, melatonin's beneficial applications mainly pertain to treating jet lag and certain types of insomnia.

Although melatonin pills have receded into the background of anti-aging therapies, there's little doubt that melatonin is - amongst DHEA, testosterone, estrogen, and growth hormone – one of the hormones that declines with advancing age and whose decline can impact adversely on well-being. Melatonin's 10-15% per decade decline may be a predominant factor in aging, given its role as biorhythmic timekeeper in synchronizing the endocrine system.

This multi-tasking hormone/neurotransmitter also activates antioxidant enzymes that help protect the central nervous system from free radical damage, which points to a role for melatonin (and B12) in neurodegenerative disorders and impaired mental function among the elderly.⁸⁻¹³ This is supported by therapeutic trials in which melatonin has been shown to arrest the progression of degenerative brain disorders, particularly early-stage Alzheimer's but not Parkinson's. Studies indicate that Alzheimer's patients have lower melatonin levels and more sleep-wake cycle disturbances than age-matched controls.¹⁴⁻¹⁷

B12, MS, and Fine Motor Control

Vitamin B12 is intimately involved in neural function. The symptoms of diabetic neuropathy are similar to classical B12 deficiency, and B12 supplementation has been used with some success in easing the pain of diabetic neuropathy.^{18,19} People with an inborn inability to metabolize B12 properly suffer from neurological problems that mimic CNS disorders such as multiple sclerosis. MS interferes with the body's ability to utilize B12, which is especially bad because B12 deficiency can severely aggravate MS. In one study of 6 MS patients, massive doses of B12 (60 milligrams every day for six months) caused an improvement in symptoms on par with those produced by the immunosuppressive and toxic drugs often used to treat MS.²⁰

B12's (and other B vitamins') contribution to improvements in neural function among the sick raises the question of whether B12 can benefit functionality in healthy individuals. One study found that elevated dosages of B1, B6, and B12 improved target-shooting accuracy in marksmen due to an improvement in fine motor control associated with reduced "physiological tremor."²¹ While this finding may certainly catch the eye of skill athletes searching for an added advantage, a single study necessarily is inconclusive and more research into the neural aspect of B vitamins' performance-enhancing potential is warranted.

B12 deficiency is more often caused by malabsorption than by dietary lack. Uptake of

B12 in the gut is highly dependent on secretion of a specific digestive enzyme known as “intrinsic factor.” Even where sufficient intrinsic factor is present, food-cobalamin malabsorption (FCM) is a separate obstacle for older folks especially. FCM refers to diminished ability to extract B12 from protein food due to decreased output of gastric acid or pepsin enzyme. In addition, there are many gastrointestinal conditions that can impair B12 absorption. Furthermore, recent research has identified “transcobalamin II” as the protein-carrier that transports B12 from the bloodstream to the cells. Low transcobalamin II represents an independent or additional limitation on B12 bioavailability, and appears largely accountable for the greater incidence of B12 deficiency among the elderly. It also has cast doubt upon the significance of serum B12 testing, raising the likelihood that cellular B12 deficiency is more widespread than conventional diagnostic technology can assess.²²⁻³²

To maintain life, the body requires tiny amounts of B12 (more often denoted in *micrograms* than milligrams) and the actual source of B12 is microorganisms that produce it. B12 can be reliably obtained from animal sources only, making vegetarianism a predisposing factor in B12 deficiency. Especially during pregnancy and lactation, folic acid supplementation should be accompanied by other B vitamins, particularly B12, which works closely with folic acid in fostering development and maintenance of neurological health.

When B12 was isolated in 1948, injectable forms were patented and an apparent bias materialized toward B12 injections over oral B12 for treating anemia. Medical texts maintained that, absent intrinsic factor, injections were necessary while research shows that even in the absence of intrinsic factor a small but constant proportion of an oral dose of B12 is absorbed through the process of diffusion.³³⁻³⁵ This means by sufficiently increasing the dose adequate intake can be attained. Thus, the relevant question is: how high of a B12 dose is high enough?

Studies in patients with pernicious anemia demonstrate an average B12 absorption rate of 1% (cyanocobalamin).³⁶ Because even in healthy individuals a low percentage of a high dose is absorbed,³⁷ 1 milligram (1000 micrograms) per day of supplemental B12 seems a reasonable bare minimum. Unfortunately, most multivitamins don't come close to this amount, and B-complex products are not much better. Some of the more commercially popular multivitamins contain less than 10 micrograms of B12, which represents an incalculably small amount actually absorbed and no discernible health benefit. In a study performed at the National Aging Institute in Victoria, Australia, 50 micrograms of oral B12 (cyanocobalamin) daily for 1 month caused a small improvement in B12 levels whereas 10 micrograms had no effect.³⁸

No less important than dosage is the form used. The problem with cyanocobalamin is not the one harmless molecule of cyanide it contains, but rather the rate at which it's absorbed. To be utilizable, cyanocobalamin must be converted to methylcobalamin or adenosylcobalamin. Methylcobalamin is the form found in food and has much higher bioavailability than the form most widely available in supplements, cyanocobalamin.*

* Oral cyanocobalamin supplementation is not without therapeutic value, as asserted in an unusually candid article in the *Journal of the American Medical Association*, “Oral Cobalamin for Pernicious Anaemia. Medicine's Best Kept Secret?”³⁹ The author cites evidence demonstrating that oral cyanocobalamin is a viable alternative to injections if a sufficiently high dose is taken. Another article, “Oral Vitamin B12 Can Change Our Practice” published in the *Postgraduate Medical Journal* by researchers and statisticians at the Yardley Green Medical Centre in Birmingham, UK, reinforces the point, suggesting that a switchover to oral B12 would both give patients a choice who prefer not to undergo injections and reduce primary care costs substantially.⁴⁰

B12 and Reproductive Health

An article published in the *International Journal of Cancer* (Jan. 2006) theorizes that: “melatonin inhibits the growth of breast cancer cells by interacting with estrogen-responsive pathways.”³⁹ A study at Johns Hopkins University finding a connection between low B12 and breast cancer described a “threshold effect”: the women in the lowest 1/5 were at greater risk

of developing breast cancer compared with the women in the upper 4/5.⁴⁰ This implies that although a higher supplemental dosage of B12 does not necessarily correspond to lower breast cancer risk, avoiding B12 deficiency is paramount to avoid incurring extra risk. Women taking oral contraceptives may be at greater risk of B12 deficiency, as they are of B6 and folic acid deficiency.

In Japan, methylcobalamin is used to treat infertility, based on limited but promising clinical research.⁴¹⁻⁴³ That cobalt can substitute for zinc in several enzymatic pathways may represent the underlying mechanism of action. In any event, nutrition-related fertility problems are best dealt with by comprehensively providing nutrients to enhance reproductive health not arbitrarily supplementing one nutrient.

Clinical trials have repeatedly shown superior results using methylcobalamin, and the MS study cited on p. 2 used this form. In a study performed at the Linus Pauling Institute of Medicine in Palo Alto, CA, methylcobalamin extended survival time in mice with cancer, whereas cyanocobalamin had no effect on survival time and was deemed “not active” by the study’s authors.⁴⁴ In another study, titled “Effects of B12 on Performance and Circadian Rhythm in Normal Subjects,” published in the journal of *Neuropsychopharmacology*, six women (mean age 35 years) and 14 men (mean age 37 years) were randomly assigned to treatment for 14 days with 3 mg of either cyanocobalamin or methylcobalamin after 9 days of pre-treatment observation. Only the group taking the methyl form of cobalamin experienced reduced sleep time and higher self-reported “sleep quality,” “concentration,” and “feeling refreshed” one week after beginning methylcobalamin supplementation.⁴⁵

Nutrient Interactions – B12 works closely with other B vitamins, particularly folic acid and B6. B12 reactivates folic acid, such that a lower dose of folic acid is more effective where B12 is present than where it is lacking. Because folic acid can resolve certain symptoms of B12-deficiency-related anemia while allowing neurological damage to proceed unchecked, folic acid supplementation is said to “mask” a

B12 deficiency. Based on this illogic, an outdated law limits folic acid supplement dosage to 800 micrograms per day. The more reasonable and effective approach is to take both B12 and folic acid (along with the other B vitamins), which work together synergistically.

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