7.3H: Vitamin B₁₂ (Cobalamin)

Vitamin B₁₂, also called cobalamin, is a water-soluble vitamin that has a key role in the normal functioning of the brain and nervous system, and the formation of red blood cells. It is one of eight B vitamins. It is involved in the metabolism of every cell of the human body, especially affecting DNA synthesis, fatty acid and amino acid metabolism.[1] No fungi, plants, nor animals (including humans) are capable of producing vitamin B₁₂. Only bacteria and archaea have the enzymes needed for its synthesis. Proven sources of B₁₂ are animal products (meat, fish, dairy products) and supplements. Some research states that certain non-animal products possibly can be a natural source of B₁₂ because of bacterial symbiosis. B₁₂ is the largest and most structurally complicated vitamin and can be produced industrially only through a bacterial fermentation-synthesis. This synthetic B₁₂ is used to fortify foods and sold as a dietary supplement.
Vitamin B₁₂ consists of a class of chemically related compounds (vitamers), all of which show pharmacological activity. It contains the biochemically rare element cobalt (chemical symbol Co) positioned in the center of a planar tetrapyrrole ring called a corrin ring. The vitamer is produced by bacteria as hydroxocobalamin, but conversion between different forms of the vitamin occurs in the body after consumption.

### Dietary Reference Intake

The Food and Nutrition Board of the U.S. Institute of Medicine (IOM) updated Estimated Average Requirements (EARs) and Recommended Dietary Allowances (RDAs) for vitamin B₁₂ in 1998. The current EAR for vitamin B₁₂ for women and men ages 14 and up is 2.0 μg/day; the RDA is 2.4 μg/day. RDAs are higher than EARs so as to identify amounts that will cover people with higher than average requirements. RDA for pregnancy equals 2.6 μg/day. RDA for lactation equals 2.8 μg/day. For infants up to 12 months the Adequate Intake (AI) is 0.4-0.5 μg/day. and for children ages 1–13 years the RDA increases with age from 0.9 to 1.8 μg/day. Because 10 to 30 percent of older people may be unable to effectively absorb vitamin B₁₂ naturally occurring in foods, it is advisable for those older than 50 years to meet their RDA mainly by consuming foods fortified with vitamin B₁₂ or a supplement containing vitamin B₁₂.

For U.S. food and dietary supplement labeling purposes the amount in a serving is expressed as a percent of Daily Value (%DV). For vitamin B₁₂ labeling purposes 100% of the Daily Value was 6.0 μg, but as of May 2016 has been revised downward to 2.4 μg.
Deficiency

Vitamin B₁₂ deficiency can potentially cause severe and irreversible damage, especially to the brain and nervous system. At levels only slightly lower than normal, a range of symptoms such as fatigue, lethargy, depression, poor memory, breathlessness, headaches, and pale skin, among others, may be experienced, especially in elderly people (over age 60) who produce less stomach acid as they age, thereby increasing their probability of B₁₂ deficiencies.

Vitamin B₁₂ deficiency is most commonly caused by low intakes, but can also result from malabsorption, certain intestinal disorders, low presence of binding proteins, and use of certain medications. Vitamin B₁₂ is rare from plant sources, so vegetarians are most likely to suffer from vitamin B₁₂ deficiency. Infants are at a higher risk of vitamin B₁₂ deficiency if they were born to vegetarian mothers. The elderly who have diets with limited meat or animal products are vulnerable populations as well. Vitamin B₁₂ deficiency may occur in between 40% to 80% of the vegetarian population.

Vitamin B₁₂ is a co-substrate of various cell reactions involved in methylation synthesis of nucleic acid and neurotransmitters. Synthesis of the trimonoamine neurotransmitters can enhance the effects of a traditional antidepressant. The intracellular concentrations of vitamin B₁₂ can be inferred through the total plasma concentration of homocysteine, which can be converted to methionine through an enzymatic reaction that uses 5-methyltetrahydrofolate as the methyl donor group. Consequently, the plasma concentration of homocysteine falls as the intracellular concentration of vitamin B₁₂ rises. The active metabolite of vitamin B₁₂ is required for the methylation of homocysteine in the production of methionine, which is involved in a number of biochemical processes including the monoamine neurotransmitters metabolism. Thus, a deficiency in vitamin B₁₂ may impact the production and function of those neurotransmitters.

Dietary Sources

Foods having rich content of vitamin B₁₂ include clams, organ meats (especially liver) from lamb, veal, beef, and turkey, fish eggs, mackerel, and crab meat. B₁₂ is synthesized by some gut bacteria in humans and other animals, but humans cannot absorb the B₁₂ made in their guts, as it is made in the colon which is too far from the small intestine, where absorption of B₁₂ occurs.

Animals store vitamin B₁₂ in liver and muscle and some pass the vitamin into their eggs and milk; meat, liver, eggs and milk are therefore sources of the vitamin for other animals, including people. For humans, the bioavailability from eggs is less than 9%, compared to 40% to 60% from fish, fowl and meat. Insects are also a source of B₁₂. Foods fortified with B₁₂ are also dietary sources of the vitamin. Foods for which B₁₂-fortified versions are widely available include breakfast cereals, soy products, energy bars, and nutritional yeast.

Vitamin B₁₂ is an ingredient in multi-vitamin pills and in some countries used to enrich grain-based foods such as bread and pasta. In the U.S. non-prescription products can be purchased providing up to 5000 µg/serving, and it is a common ingredient in energy drinks and energy shots, usually at many times the recommended dietary allowance of B₁₂. The vitamin can also be a prescription product via injection or other means.
Absorption and Distribution

Methyl-B\textsubscript{12} is absorbed by two processes. The first is an intestinal mechanism using intrinsic factor through which 1-2 micrograms can be absorbed every few hours. The second is a diffusion process by which approximately 1% of the remainder is absorbed. The human physiology of vitamin B\textsubscript{12} is complex, and therefore is prone to mishaps leading to vitamin B\textsubscript{12} deficiency. Protein-bound vitamin B\textsubscript{12} must be released from the proteins by the action of digestive proteases in both the stomach and small intestine.

Absorption of food vitamin B\textsubscript{12} thus requires an intact and functioning stomach, exocrine pancreas, intrinsic factor, and small bowel. Problems with any one of these organs makes a vitamin B\textsubscript{12} deficiency possible. Individuals who lack intrinsic factor have a decreased ability to absorb B\textsubscript{12}. The total amount of vitamin B\textsubscript{12} stored in body is about 2–5 mg in adults. Around 50% of this is stored in the liver. Approximately 0.1% of this is lost per day by secretions into the gut, as not all these secretions are reabsorbed. Bile is the main form of B\textsubscript{12} excretion; most of the B\textsubscript{12} secreted in the bile is recycled via enterohepatic circulation. Excess B\textsubscript{12} beyond the blood's binding capacity is typically excreted in urine. Owing to the extremely efficient enterohepatic circulation of B\textsubscript{12}, the liver can store 3 to 5 years’ worth of vitamin B\textsubscript{12}; therefore, nutritional deficiency of this vitamin is rare. How fast B\textsubscript{12} levels change depends on the balance between how much B\textsubscript{12} is obtained from the diet, how much is secreted and how much is absorbed. B\textsubscript{12} deficiency may arise in a year if initial stores are low and genetic factors unfavorable, or may not appear for decades. In infants, B\textsubscript{12} deficiency can appear much more quickly.

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