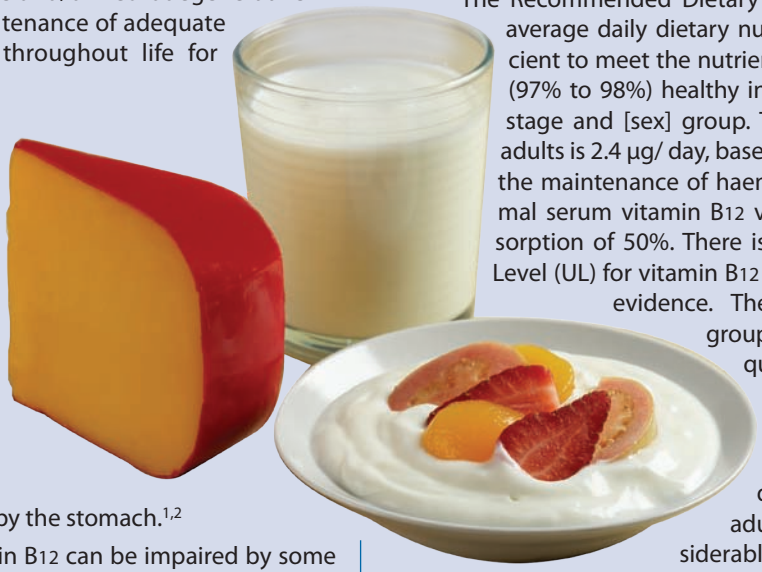
Vitamin B12 in dairy: **Vital for brain health**

Introduction

Vitamin B12, also known as cobalamin, is commonly deficient in populations which consume low amounts of animal source foods, school-age children, pregnant women and the elderly. Research has demonstrated that the vitamin B12 contained in dairy products, and particularly in milk, is more bioavailable and has the strongest correlation with blood levels of vitamin B12 compared to other animal source foods. Observational research has also shown correlations between vitamin B12 deficiency and cognitive decline and/or neurodegenerative diseases, emphasising the maintenance of adequate dietary levels of vitamin B12 throughout life for healthy brain ageing.



Absorption of dietary vitamin B12

Vitamin B12 is a water-soluble vitamin bound to protein in food, which must be released from food by pepsin digestion in the stomach. The absorption of dietary vitamin B12 also requires the formation of a complex with R-proteins (such as haptocorrins and cobalaphilin) in the stomach and linkage to intrinsic factors secreted by the stomach.[1,2]

The absorption of dietary vitamin B12 can be impaired by some medications, such as anti-convulsants, alcohol, potassium-containing products, cimetidine, ranitidine, aminosalicylic acid and proton pump inhibitors.[2]

Functions of vitamin B12

Vitamin B12 functions in two coenzyme forms: as a coenzyme for a critical methyl transfer reaction that converts homocysteine to methionine (Figure 1) and for a separate reaction that converts L-methylmalonyl-coenzyme A (CoA) to succinyl-CoA. These forms play important roles in the metabolism of propionate, amino acids, and single carbons, steps essential for the normal metabolism of cells in the gastrointestinal tract, bone marrow, and the tissues of the nervous system. An adequate supply of B12 is therefore essential for normal blood formation and neurological function. Other functions include a role in folate metabolism, biosynthesis of nucleic acids and nucleoproteins, and growth.[1,3]

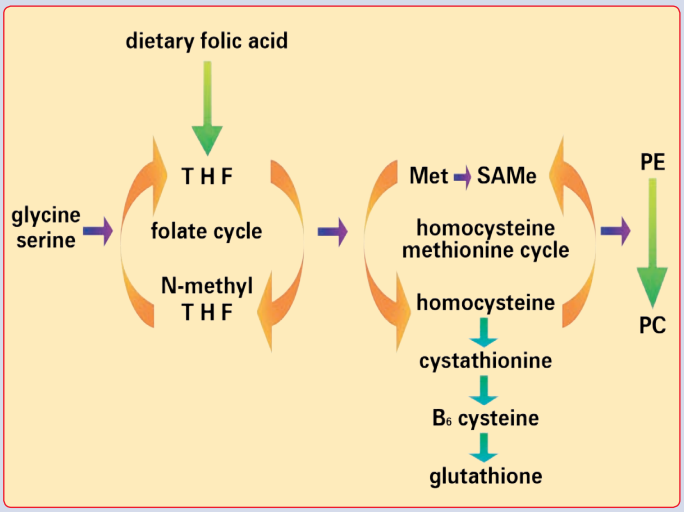


Figure 1 Homocysteine cycle[2]

Dietary Reference Intakes

The Recommended Dietary Allowances (RDAs) are the average daily dietary nutrient intakes that are sufficient to meet the nutrient requirements of nearly all (97% to 98%) healthy individuals in a particular life stage and [sex] group. The RDA of vitamin B12 for adults is 2.4 µg/ day, based on the amount needed for the maintenance of haematological status and normal serum vitamin B12 values, and an assumed absorption of 50%. There is no Tolerable Upper Intake Level (UL) for vitamin B12 due to insufficient scientific evidence. The RDAs for different age groups are given in Table 1. Adequate intakes (AI) are given for infants.[3]

Aging is one of the factors that affects vitamin B12 requirements. The RDA for adults makes provision for considerable body stores due to the prevalence of achlorhydria (decrease in gastric acidity), presence of atrophic gastritis and of bacterial overgrowth accompanied by food-bound B12 malabsorption, compromised functional and structural integrity of the B12 binding proteins, and of pernicious anaemia with ageing, especially in those older than 60 years of age.[1,3]

Table 1: Recommended intakes of vitamin B12 according to age groups[3]

Age group	RDA per day
Infants ≤ 6 months	0.4 µg (AI)
Infants 7-12 months	0.5 µg (AI)
Children 1-3 years	0.9 µg
Children 4-8 years	1.2 µg
Children 9-13 years	1.8 µg
Adults > 14 years	2.4 µg
Pregnancy	2.6 µg
Lactation	2.8 µg

RDA: Recommended Dietary Allowances; AI: Adequate Intake

Dietary sources and vitamin B12 content

Although vitamin B12 is synthesized by microorganisms in the colon, this vitamin B12 is not absorbed from the colon. Animal sources should therefore be consumed to obtain sufficient vitamin B12 from the diet to meet the daily requirement. Animal

products are the richest sources of vitamin B12 in the human diet, especially liver and kidney, milk, eggs, fish, cheese and muscle meats (Table 2). Foods of plant origin contain no vitamin B12 beyond that derived from contamination or bacterial synthesis.[1]

Table 2: Vitamin B12 content and bioavailability of dietary sources[4]

Foods	Bioavailability	Content (µg/100g)
Animal meats		
Mutton, cooked	56%–89%	2.6
Chicken, cooked	61%–66%	9.4
Dairy		
Cow's milk	65%	0.4
Eggs	9%	1.3
Shellfish		
Oyster		46.3, 28.1
Mussel		15.7, 10.3
Short-necked clam*		37.0, 52.4
Fish meats		
Skipjack, dark muscle*		158.5
Yellow fin tuna, dark muscle		52.9
Rainbow trout, cooked	42.0%	4.9

* Foods that are not well known in South Africa

Bioavailability of vitamin B12 in cow's milk

Although the vitamin B12 content of milk is not high compared to other animal sources (Table 2), the vitamin B12 in milk has been found to be highly bioavailable.[5,6]

A study by Matte *et al.*[5] used pigs as a model to estimate the bioavailability of vitamin B12 in humans. The digestive system of the pig resembles that of humans in terms of anatomy, physiology, absorption and metabolism. These authors concluded that vitamin B12 naturally present in cow's milk, is more available than cyanocobalamin, the most commonly used synthetic form of vitamin B12. Zittoun[7] also reported that the bioavailability of the synthetic form of vitamin B12 is poor (<4%) in humans and animals. Russel *et al.*[6] directly measured vitamin B12 absorption from milk in adult subjects by using extrinsically (58Co) labeled vitamin B12. Mean absorption from milk was reported as 65%, ranging from 48 to 88%.

Vitamin B12 status and dairy consumption

Observational studies in humans not only show high correlations of vitamin B12 status with dairy product intake but also suggest a higher bioavailability of the vitamin from dairy products.[8-11]

Tucker *et al.*[8] examined the association between vitamin B12 status and intake source among 2999 subjects aged 26–83 years participating in the Framingham Offspring Study. Results showed that the group in the highest tertile of vitamin B12 intake from dairy foods consumed about twice the average total vitamin B12 than did the group in the lowest tertile. The study also found that the relationship between plasma concentrations of vitamin B12 and its intake from dairy products was higher than the relationship with the intake from meat, poultry or fish.[8]

A cross-sectional, population-based study investigated the relation of dietary intake of different food items with plasma vitamin B12 concentrations in the Norwegian population. Plasma vitamin B12 was associated with intakes of increasing amounts of vitamin B12 from dairy products or fish but not with intakes of vitamin B12 from meat or eggs. For the same content of vitamin B12, intake from dairy products led to the greatest increase in plasma vitamin B12. Total intake of vitamin B12, particularly from milk and fish, decreased the risk of vitamin B12 concentrations <200 pmol/L and impaired vitamin B12 function in the total group and in 71–74-year-old subjects.[9]

Vitamin B12 status among vegetarians was also correlated with dairy intake. Vitamin B12 status was assessed in a group of 110 adults and 42 children from a macrobiotic community in New England. Vitamin B12 status of vegetarians was positively correlated with their intake of dairy products, especially milk, but not of eggs or seafood.[10]

A cross-sectional study in low- and middle-income Colombian children aged 5–12 years, showed that plasma vitamin B12 was strongly, positively associated with a pattern that included frequent intake of beef, chicken, and dairy products in a dose-response manner. The researchers concluded that low vitamin B12 status is associated with marginal intake of animal food.[11]

Experimental studies support the associations found in observational studies, showing that the consumption of milk and milk products significantly increased vitamin B12 intake[12] and blood levels[13] of vitamin B12 in adults and undernourished children, respectively.

In the study by Bar *et al.*12 adults consuming 3 cups of milk per day for 12 weeks significantly increased their vitamin B12 intakes. Milk (200–250 mL/d) given to undernourished school children (aged 5–14 years) during one school meal daily in a rural malaria-endemic area of Kenya, also significantly increased their vitamin B12 concentrations after one year. The prevalence of severe, plus moderate deficiency, also fell from 71.6 to 45.1%.[13]

Vitamin B12 deficiency

Vitamin B12 deficiency is a common cause of megaloblastic anaemia, which is related to a secondary folate deficiency. Vitamin B12 deficiency also produces neurologic abnormalities with the following symptoms: numbness, tingling and burning of the feet, stiffness and generalized weakness of the legs, neurologic disorders including impaired mentation, and depression. Prolonged deficiency can cause permanent nerve damage.[1] The causes of vitamin B12 deficiency are summarised in Table 3.

Vitamin B12 and Cognition

Methyl acceptors such as myelin, neurotransmitters, and membrane phospholipids are essential for maintaining the integrity of the nervous and haematopoietic system. Methyl acceptors receive their methyl group (CH_3) when methionine, an essential amino acid, is activated to S-adenosyl-methionine in the methionine cycle. Vitamin B12 is required for the methylation of homocysteine to methionine (Figure 1). Insufficient vitamin B12 disrupts this cycle resulting in intracellular accumulation of homocysteine which is potentially toxic to neurons.[2]

Homocysteine can cause neuronal death or vascular

Table 3: Causes of vitamin B12 deficiency[14]

At risk groups	Cause of vitamin B12 deficiency	Prevalence of vitamin B12 deficiency
Achlorhydria	Inadequate release from food	20% of those aged above 65 years
Vegetarianism	Inadequate dietary intake	53% of lacto-ovo-vegetarians
Crohn's disease	Disease or resection of the distal ileum causing poor absorption	41.9% of patients having undergone surgical alteration
H.pylori infection	Gastritis affecting the parietal cells or bacterial absorption of the vitamin	40% of patients having gastritis with *H.pylori* infection
Metformin use	Malabsorption at the distal ileum due to drug interaction	10%–30% of metformin users
Pernicious anaemia	Malabsorption due to an autoimmune reaction against intrinsic factor or the parietal cells	15% of those aged over 65 years who have vitamin B12 deficiency
Pregnancy >28 days	Haemodilution of serum vitamin B12 in pregnancy	10.1% of women after 28 days of pregnancy
Genetic predisposition	Aberrant proteins involved in the absorption, distribution, cellular uptake, chemical re-arrangement, or enzyme activities	Prevalence of MTHFR 677TT polymorphism was estimated at 10.4% in Austrian children and adolescents (2–17-year-olds)

damage that can affect cognitive function.[15] Hyperhomocysteinaemia has been shown to be an independent risk factor for cognitive dysfunction.[16] Both vitamin B12 deficiency and raised homocysteine levels have been associated with cognitive decline and neurodegenerative diseases.[2,16-18] A recent systematic review concluded that low serum vitamin B12 levels are associated with neurodegenerative diseases (Alzheimer's disease, vascular dementia, and Parkinson's disease) and cognitive impairment.[14] However, experimental trials have not yet provided any clear evidence repetition that supplementation with vitamin B12 and / or folate improves dementia or slows cognitive decline, even though it might normalise homocysteine levels.[2,15-18]

The evidence thus far implicates vitamin B12 as an important vitamin for maintaining proper metabolism of homocysteine. As an important dietary source of vitamin B12, dairy products are likely to play an important role in ensuring adequate homocysteine metabolism, particularly during ageing.[17]

Conclusion

Milk and dairy products provide a highly bioavailable source of vitamin B12 which can significantly contribute to dietary vitamin B12 intakes. The dairy recommendation of "three servings a day" is sufficient to meet the recommended dietary allowance for normal healthy people, while possibly providing additional protection against low plasma vitamin B12 status and decreasing the risk of neurodegenerative diseases.

REFERENCES:

1. Gallagher ML. 2012. Intake: the nutrients and their metabolism. In Mahan LK, Escott-Stump S, Raymond JL. Krause's food and the nutrition care process. 13th Ed. Philadelphia: W Saunders.
2. Malouf R, Areosa SA. 2009. Vitamin B12 for cognition. Cochrane database of systematic reviews. Issue 1.
3. Institute of Medicine (IOM). 1998. Vitamin B 12 In: Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline. Washington, DC: Institute of Medicine, National Academy Press, pp306–356, 1998.
4. Watanabe F. 2007. Vitamin B12 sources and bioavailability. *Exp Biol Med*. 232:1266-1274.
5. Matte JJ, Guay F, Girard CL. 2012. Bioavailability of vitamin B12 in cow's milk. *BJN*. 107:61-66.
6. Russell RM, Baik H, KehayiasJJ. 2001. Older Men and Women Efficiently Absorb Vitamin B-12 from Milk and Fortified Bread. *J Nutr.* 131: 291–293.
7. Zittoun J. 1996. Cobalamins: an update of fundamental and clinical data. Hematologie 2, 119–129.
8. Tucker KL, Rich S, Rosenberg IH, Jacques P, Dallal G, Wilson WFP, Selhub J. 2000. Plasma vitamin B12 concentrations relate to intake source in Framingham offspring study. *AJCN*. 71:514-522.
9. Vogiatzoglou A, Smith AD, Nurk E, Berstad P, Drevon CA, Ueland PM, Vollset SE, Tell GS, Refsum H. 2009. Dietary sources of vitamin B12 and their association with plasma vitamin B12 concentrations in the general population: the Hordaland Homocysteine Study. *AJCN*. 89:1078-1087.
10. Miller DR, Specker BL, Ho ML, Norman EJ. 1991. Vitamin B12 status in a macrobiotic community. *AJCN*. 53:524-529.
11. Villamor E, Mora-Plazas M, Forero Y, Lopez-Arana S, Baylin A. 2008. Vitamin B-12 status is associated with socioeconomic level and adherence to an animal food dietary pattern in Colombian school children. *J Nutr*. 138:1391-1398.
12. Barr SI, McCarron DA, Heaney RP, Dawson-Hughes B, Berga SL, Stern JS, Oparil S. 2000. Effects of increased consumption of fluid milk on energy and nutrient intake, body weight, and cardiovascular risk factors in healthy older adults. *J Am Diet Assoc*. 100:810-817.
13. SiekmannJH, AllenLH, Bwibo NO, Demment MW, Murphy SP, Neumann CG. 2003. Kenyan school children have multiple micronutrient deficiencies, but the increased plasma vitamin B-12 is the only detectable micronutrient response to meat or milk supplementation. *J Nutr*.133:3972S-3980S.
14. Moore E, Mander A, Ames D, Carne R, Sanders K, Watters D. 2012. Cognitive impairment and vitamin B12: a review. *International Psycogeriatrics*. 24(4):541-556.
15. McCracken C. 2010. Challenges of long term nutrition intervention studies on cognition: discordance between observational and intervention studies of vitaminB12 and cognition. *Nutrition Reviews*. 68(Suppl. 1):S11–S15.
16. Miller AL (2003).The methionine–homocysteine cycle and its effects on cognitive diseases. *Altern Med Rev* 8, 7–19.
17. Camfield DA, Owen L, Scholey AB, Pipingas A, Stough C. 2011. Dairy constituents and neurocognitive health in ageing. *BJN*. 106, 159–174.
18. Vogel T, Dali-Youcef N, Kaltenbach G, Andres E. 2009. Homocysteine, vitamin B12, folate and cognitive functions: a systematic and critical review of the literature. *Int J Clin Practice*. 63, 1061–1067.

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