CYTOPLAN

THE TECHNICAL INFORMATION SERIES

Vitamin B12

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What is B12?

B12 is one of the eight B vitamins and is a class of chemically related compounds, also called cobalamins that contain cobalt. It is considered the most important factor in the maintenance of nerves and also has a number of other important functions within the body, however deficiency and depletion of B12 are prevalent around the world[1]. Estimations are that some level of deficiency is present in 10-40% of the population; deficiency is frequently missed and contributes to cognitive decline, stroke and many other chronic diseases[2,3]. In food, B12 occurs bound to animal proteins.

Functions of B12

Vitamin B12 is involved in the metabolism of every single cell in the human body and it also plays an important role in the synthesis and formation of the body's genetic material, DNA and RNA. It's needed for red blood cell formation, the synthesis of choline, brain and normal nerve cell function, normal psychological function, homocysteine metabolism, functioning of the immune system and it also contributes to protein, fat and carbohydrate metabolism. B12 helps to promote optimal utilisation of iron in the body.

Symptoms of B12 deficiency

B12 deficiency can affect many bodily systems including neurologic, hematologic, immunologic, vascular, gastrointestinal, musculoskeletal and genitourinary. Symptoms include – extreme tiredness/lack of energy, pins and needs, a sore and red tongue, muscle weakness, difficulty walking (staggering, balance problems), depression, problems with memory, understanding and judgement, paranoia or hallucinations and many more[4,5].

Vitamin B12 deficiency and with it the possibility of raised homocysteine levels can lead to brain atrophy (shrinkage). Brain shrinkage usually occurs alongside the normal process of ageing however it is accelerated in the presence of neurodegenerative diseases such as Alzheimer's disease. Research that suggests a lack of B12 contributes significantly to brain atrophy:

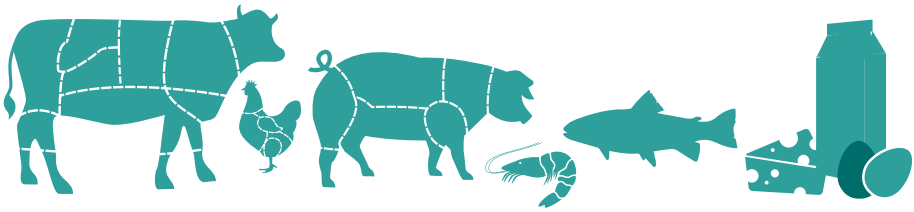
Christine C Tangney, PhD and team carried out a study with 121 individuals aged at least 65 years from the south side of Chicago. They underwent blood tests to check their levels of B12 and B12 related metabolites which can give an indication of a B12 deficiency. They were also assessed for memory and other cognitive skills. About 4.5 years later MRI scans of their brains were taken to see how big their brains were, as well as identifying some other signs of brain damage. Those with four of five markers for vitamin B12 deficiency were found to have a higher risk of getting lower cognitive test scores and smaller total brain volumes[6].

Absorption of B12

Even an adequate consumption of vitamin B12 can sometimes result in the possibility of deficiency because of the complexity of the absorption and methylation process. The absorption of B12 begins with gastric acid and the enzyme pepsin releasing the B12 from animal protein; it then binds firstly to R-protein which transports it through the stomach and into the small intestine. The parietal cells of the stomach also produce another protein called Intrinsic Factor which also travels to the small intestine. When the B12-R protein complex reaches the small intestine it is released from this complex and attaches to Intrinsic Factor (IF) which protects it from digestion and assists with absorption in the ileum (ie small intestine). Once in the bloodstream it is transported bound to another protein called Transcobalamin II which takes it to various tissues in the body and takes the excess to the liver for storage[5,7]. Inside the cell it is converted to two active cofactors – adenoyslcobalamin and methylcobalamin.

Factors that can contribute to low levels of B12

The liver stores enough vitamin B12 to last several years, and any conditions that may lead to vitamin B12 deficiency are likely to have been ongoing for around 2 or 3 years before symptoms appear[7].



Factor that can contribute to low levels[5]	Reason
Vegan or vegetarian diets	B12 is bound to animal protein. Vegetarians will obtain some B12 eg from eggs and dairy.
Damage to parietal cells (eg high alcohol intake, gastritis, autoimmunity versus parietal cells)	Parietal cells in the stomach produce intrinsic factor. IF is needed for B12 absorption so low levels will reduce absorption. High alcohol intake, gastritis and autoimmunity (ie as seen in pernicious anaemia).
Low stomach acid (eg due to antacid medication, PPIs, H2 blockers, ageing, zinc deficiency)	Stomach acid releases B12 from food. Antacid medication (eg proton pump inhibitors) reduce stomach acidity so can lead to low levels of B12 if taken long-term. As we age, levels of stomach acid decrease. Zinc deficiency can lead to low stomach acid.
Nitrous oxide (used in some surgical operations, including dental surgery)	Active vitamin B12 contains cobalt in its reduced form. Nitrous oxide produces irreversible oxidation that renders vitamin B12 inactive[5].
Genetics eg TCN, MTR, MTRR mutations	These genetic polymorphisms or mutations affect the transport (TCN), use and recycling (MTR / MTRR) of B12 and can lead to increased needs[8].
Malabsorption eg Crohns, ulcerative colitis or coeliac disease	Damage to cells of small intestine where absorption occurs.
Surgery eg stomach or small intestine	Gastric bypass: Loss of cells that produce hydrochloric acid and intrinsic factor. Intestinal surgery – loss of part or all of ileum will result in reduced surface area for absorption of B12.
Other drugs	In addition to antacids discussed above, some other prescription medications can impair B12 absorption eg metformin, colchicine, neomycin and others[5].

Forms of Vitamin B12

The most commonly found 'forms' of vitamin B12 used in supplements are cyanocobalamin, methylcobalamin, hydroxycobalamin and adenosylcobalamin. The last three forms also occur in food along with another form called sulphitocobalamin[9]. In supplements, cyanocobalamin is the most commonly used form, despite methylcobalamin and hydroxycobalamin being better absorbed, retained and used by the body[5].

The inactive cyanocobalamin and hydroxycobalamin forms can be converted to the active cofactor forms – methylcobalamin in the cytoplasm of cells and adenosylcobalamin in the mitochondria. Rare inborn errors can affect cobalamin cofactor synthesis[10].

Cyanocobalamin is an inactive form of vitamin B12 and exists only via chemical supplementation. It is not present in nature, meaning the body does not metabolically recognise it and absorption is much less efficient. The cyano- compound found in cyanocobalamin is not needed by the body, so it quickly looks to convert it into active methylcobalamin. Not only does this mean that cyanocobalamin is a much less efficient form of supplementation of vitamin B12, but the body also has to 'deal' with a cyanide group that is liberated during conversion into methylcobalamin.

Despite the levels of cyanide being rarely at a level to have a detrimental impact to health, it is vital that it is removed from the body as quickly as possible. This could be a particular problem for those with detoxification enzyme errors as when the cyanide component is not removed and accumulates it can lead to toxic overload. Cyanocobalamin is the cheapest of the forms.

Hydroxycobalamin is a natural inactive form of vitamin B12, attached to a hydroxyl group. This form can be converted into active methylcobalamin and adenosylcobalamin in the body. For some people this form may be indicated rather than the active methylcobalamin. Hydroxycobalamin has high affinity to plasma proteins. This property helps to retain the hydroxyl-protein complex in the blood stream for a much longer period of time, compared to cyanocobalamin[5].

Hydroxycobalamin may be indicated where high nitric oxide levels are suspected as it is an effective nitric oxide scavenger[11]. Too much nitric oxide can contribute to oxidative stress. Hydroxycobalamin may also be recommended for people who do not tolerate methyl groups.

Methylcobalamin is the active form of B12 where the cyanide group is replaced by a methyl group. It occurs in the cytoplasm of cells and can be synthesised from hydroxycobalamin by the addition of a methyl group. It is needed for vital cellular processes including methylation and DNA synthesis. Thus methylcobalamin is a cofactor in the methionine cycle. The purpose of this cycle is to regenerate SAM (S-adenosyl methionine), the universal methyl donor. In the process homocysteine is converted to methionine. Methylation reactions using SAM occur over a billion times per second!

Methylcobalamin is the only form able to across the blood-brain barrier without further metabolism, other forms need to be reduced[5]. This form of B12 may be recommended to provide 'methyl' groups or for people with specific genetic polymorphisms that can result in less effective recycling of B12. It would also be indicated where an active form is required, for example if it is suspected that there are conversion issues from the inactive hydroxycobalamin form. Disturbances in methylcobalamin levels can result in elevated homocysteine which is linked to many health conditions including cardiovascular disease, stroke and dementia.

Studies have shown benefit in terms of helping with pain reduction and promoting regeneration of injured nerves. It has been used as a therapy for a number of disease conditions including Alzheimer's and rheumatoid arthritis[12].

Adenosylcobalamin is the mitochondrial form of B12 which acts as a co-factor for a metabolic enzyme involved in energy production. It can be synthesised from hydroxycobalamin or methylcobalamin. People with certain genetic polymorphisms may have a reduced capacity to synthesise adenosylcobalamin. This can result in elevated levels of methylmalonic acid (MMA) which can be measured in blood or urine and which provides an indirect measure of B12 status. Due to its importance in energy production, adenosylcobalamin is a form useful for people with severe fatigue.

Testing B12 levels

There is no gold standard test for B12 deficiency because as B12 deficiency occurs blood serum values may be maintained while B12 tissue levels are depleted. Thus B12 serum values within the normal range do not necessarily indicate adequate B12 status. Other tests include measurement of methylmalonic acid – this test may be oversensitive especially in the elderly; and holotranscobalamin or plasma total homocysteine[2].

Our products

Vitamin B12 methylcobalamin – 500 mcg per sublingual tablet

(New Improved available later in 2016 with both methylcobalamin 500 mcg and adenosylcobalamin 500 mcg)

Order code 1039

Vitamin B12 Hydroxycobalamin – 1000 mcg per sublingual tablet

Order code 1036

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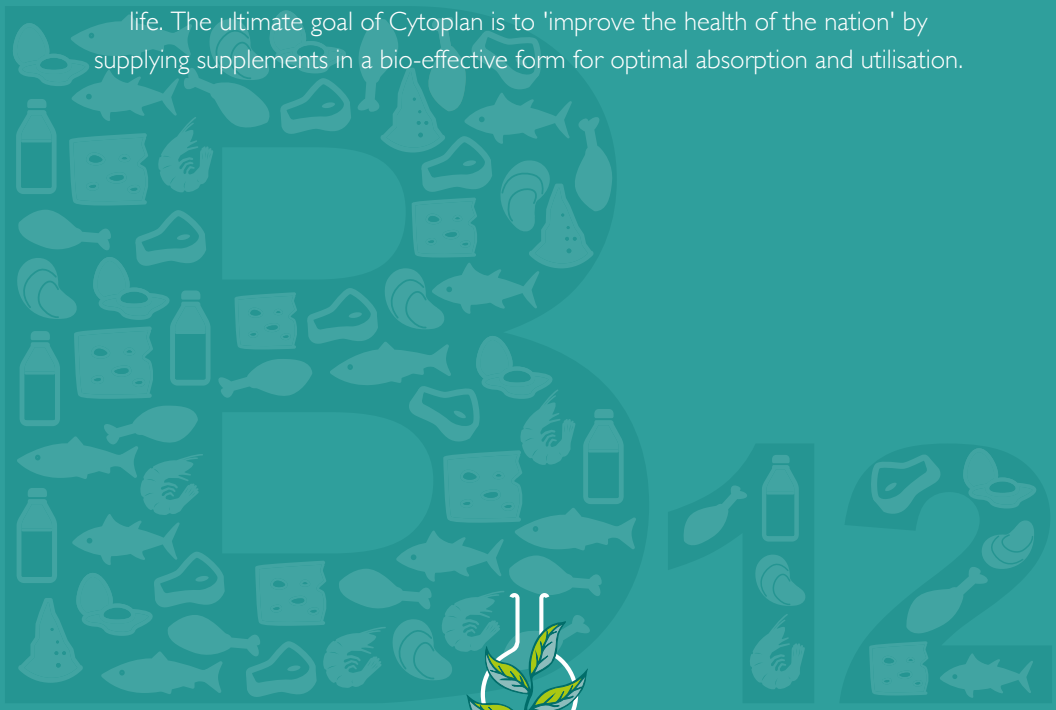
Cytoplan celebrates 25 years in the field of food-based supplementation and from the moment of conception to the present day we have promoted the philosophy that nutrients are best delivered to the body "in the same form as food".

The philosophy and message of Cytoplan was founded on the simple logic that our bodies are designed to eat food and utilise its components for the maintenance of life. The ultimate goal of Cytoplan is to 'improve the health of the nation' by supplying supplements in a bio-effective form for optimal absorption and utilisation.



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