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## Know: The Emerging Hero Vitamin: B12

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### ABSTRACT

Vitamin are essential for proper body functioning. Vitamin B12 is the last vitamin to be discovered, and is one among the water soluble vitamin B. Till last few years, it remained associated with certain type of anaemia i.e Pernicious anaemia, only. In recent years, its several new roles have been identified, and it has been considered vital for DNA synthesis, maintenance of RBC, protein metabolism, maintenance and regulation of the nervous system, promotion of activity of hormones and neurotransmitter, energy production, detoxification mechanism and many more. Apparently, it seems to be affecting every cell of the body. Vitamin B12 deficiency symptoms can lead to neurological changes such as numbness and tingling in the hands and feet, mood disorders, anxiety, insomnia, restlessness, night terror, fatigue, weakness, nausea, constipation, flatulence (gas), loss of appetite and weight, bone loss, eye disorders, hallucinations and migraine headaches etc. Sever B12 deficiency can cause very extreme symptoms, including mental dullness, coma, and even death. Prevention, early detection, and treatment of vitamin B12 deficiency are important to public health issues because they are essential to prevent development of irreversible neurologic damage which can impact quality of life. The purpose of the article is to generate awareness about Vitamin B12.

**Keywords:** Vitamin B12, Public health issue, irreversible damage.

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## INTRODUCTION

*'It is the first time that something in the blood which is related to our diet has been shown to be related to brain shrinkage.'*  
— Prof. David Smith

Human body is a very complicated system. Its physiological reactions are very complex and interlinked. Vitamins are the substances which are very much needed and essential for proper functioning of the body. Since, the thiamine, the first of the vitamin isolated, was an amine, so, the term vitamin has originated considering the vitality of such substances.

The major classification of vitamin is based on solubility. Vitamin A, E, D3, and K are fat soluble, and vitamins B and C are water soluble. Vitamin B which was considered to be a single substance initially was rather found to be group of vitamins, and vitamin B12 is one of the major B vitamins. The other vitamin includes thiamine(B1), riboflavin(B2), niacin(B3), adenine(B4), pantothenic acid (B5), pyridoxine (B6), biotin(B7), and folic acid (B9). Each of these vitamins has its specific role, and the deficiency may lead to specific disorder or group of disorders.

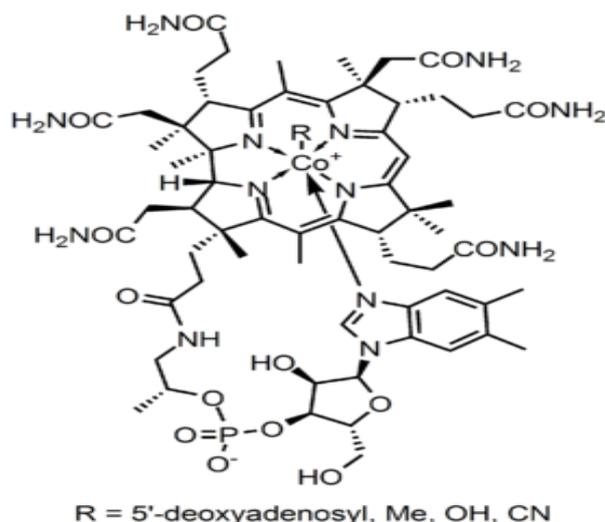
Vitamin B12 is the last vitamin to be discovered. For discovering life saving properties of vitamin B12, in relation with anaemia, three researchers (George Richards Minot, William Perry Murphy and George Whipple) won the Nobel Prize in 1934. For a very long time, in the medical literature, the vitamin B12 languished as a vitamin that cures a particular type of anaemia, the pernicious anaemia (PA). Since vitamin B12 was only associated with anaemia, doctors and nutrition experts alike tend to ignore vitamin B12 deficiency symptoms. In the last few years scenario regarding vitamin B12 has changed and it has crossed the boundaries beyond treating a particular form of anaemia. It has emerged as a vitamin that has vital role blood formation, the normal functioning of the brain and nervous system, protein metabolism and many more. It is also essential in the kinds of chemical reactions that "turn on" detoxification mechanisms. It affects every cell of the body. As per an emerging new opinion if there is any undiagnosed symptoms, that may have some association with a deficiency of vitamin B12. Considering these crucial facts, we present this article regarding vitamin B12, its role, deficiency, symptoms etc. The purpose of the article is to generate an awareness regarding Vitamin B12. However, consultation with a medical expert would be required in case someone experiences vitamin B12 deficiency symptoms listed in this article.

### **Structure and stability of vitamin B12**

#### **Structure**

Vitamin B12 is red in colour and structurally the most complicated. It is the only vitamin which contains metal ion *viz* biochemically rare element cobalt (trivalent), which accounts for its red colour. Chemically, vitamin B12 is termed as cobalamines.

In Cobalamin [cobal(t) + (vit)amin] there is a substituted corrin ring (polyaromatic ring consisting of 4 pyrrole subunits which are joined by methylene links on opposite sides and the two of the pyrroles are joined directly) attached with aglycon, the 5,6-dimethylbenzimidazole; through a glycosyl link between the two (Fig. 1).



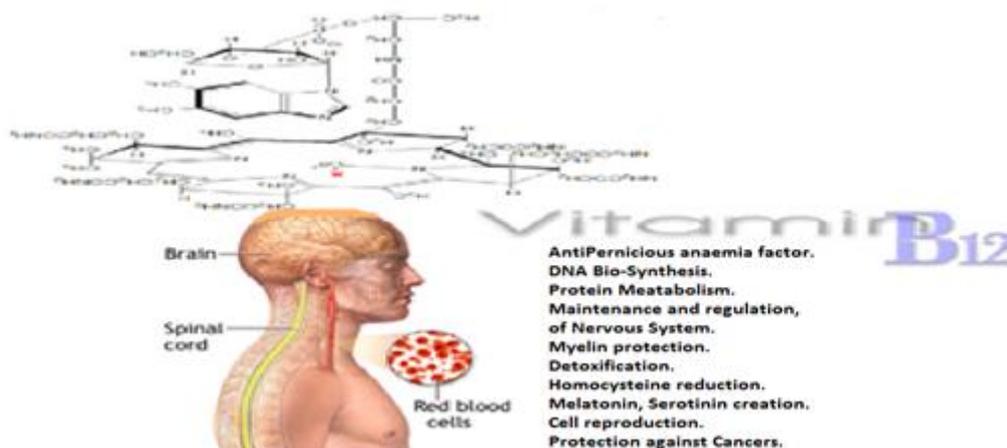
**Figure 1: Vitamin B12 (Cobalamin)**

Cyanocobalamin and Hydroxocobalamin are the most common medicinal forms of vitamin B12 (cobalt mineral at 6 position). 5'-deoxyadenosylcobalamin (adenosylcobalamin—AdoB12) and methylcobalamin (MeB12) are two naturally occurring cofactor forms of B12; these are the cofactor of Methylmalonyl Coenzyme A mutase (MUT) and 5-methyltetrahydrofolate-homocysteine methyltransferase (MTR), respectively.

**Stability**

It is heat-stable. It loses activity when exposed to light, oxygen and acid or alkali-containing environments. Sunlight, alcohol, sleeping pills and estrogen destroy vitamin B12.

**Role of Vitamin B12**



**vitamin B<sub>12</sub>**

- AntiPernicious anaemia factor.
- DNA Bio-Synthesis.
- Protein Metabolism.
- Maintenance and regulation, of Nervous System.
- Myelin protection.
- Detoxification.
- Homocysteine reduction.
- Melatonin, Serotonin creation.
- Cell reproduction.
- Protection against Cancers.

**Figure 2: Nutshell Role of Vitamin B12.**

Vitamin B12 has crossed its roles, beyond curing a specific type of anaemia. It has come up with the roles previously not associated with it. It affects every cell in the body, but its deficiency is most severely felt in the tissues (such as in the blood-forming-tissue of the bone marrow and in gastro-intestinal tract) where the cells normally divide rapidly.

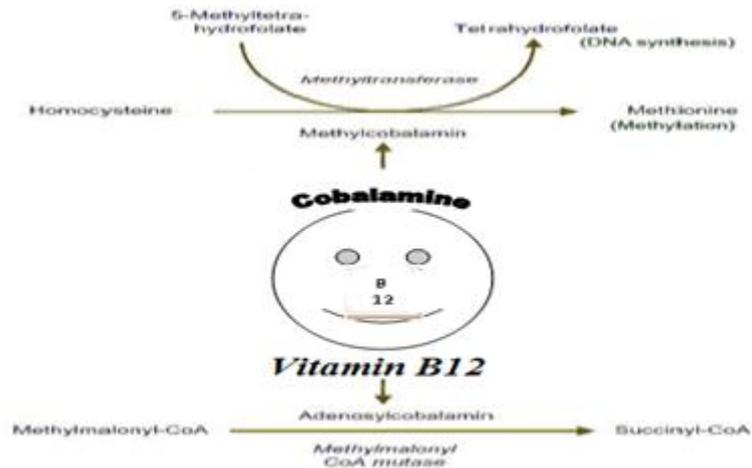


It directly or indirectly influences and regulates two very important processes in the body i.e DNA biosynthesis and protein metabolism. The following key features, in association with its role can be assigned:

- It is essential in various body processes including the DNA synthesis.
- It is important to the survival of the nerves, the maintenance and healthy regulation of the nervous system.
- Methylcobalamin (one of the cobalamine) protects myelin, the "insulation" for nerve cells throughout the central nervous system. Degeneration of the myelin layer is implicated in most cases of memory loss and progressive diseases like multiple sclerosis, lougehrig's disease (amyotrophic lateral sclerosis), and degeneration of the spinal cord. The information on vitamin B12 recently discovered by French scientists is that the methylcobalamin form of the nutrient promotes regeneration of the insulating myelin and slows the progression of these diseases.
- It is essential in the kinds of chemical reactions that "turn on" detoxification mechanisms. These methylation reactions are especially important for detoxifying heavy metals such as arsenic, antimony, and lead.
- It is the antipernicious anaemia factor. It has vital role in the formation and maintenance of red blood cells. It is used to treat the absence of intrinsic factor which is responsible for the absorption of B12 from the intestine; including particularly pernicious anaemia and other megaloblasticanemias and associated neuropathy.
- In humans, vitamin B12 functions primarily as a coenzyme in intermediary metabolism, especially in cells of the nervous tissue, bone marrow and gastrointestinal tract.
- Vitamin B12 is an important cofactor required for nucleotide and amino acid metabolism.
- Vitamin B12 promotes activity of hormones and neurotransmitters affecting mood. It is critical in the creation of the sleep hormone melatonin and the mood hormone serotonin, and helps reducing depression, stress, and brain shrinkage.
- It supports synthesis of the amino acid "*methionine*", a crucial building block of proteins.
- Vitamin B12 supports synthesis of "*SAM-e*". The amino acid "*SAM-e*" is required for over 100 enzymatic reactions required for normal metabolic activity within body.
- Vitamin B12 helps reduce dangerous levels of a toxic amino acid "*homocysteine*" , which is associated with significant cardiovascular risk/artiery damage.
- It is involved in fat and carbohydrate metabolism.
- It helps maintain a healthy digestive system. Vitamin B12 also protects against heart disease.
- It is essential for healthy skin, hair, and nails. It helps in cell reproduction and constant renewal of the skin.

- Vitamin B12 helps protect against cancers including breast, colon, lung, and prostate cancer.

In Figure 3, we present the Major vitamin B12-dependent metabolic processes that includes the formation of methionine from homocysteine, and the formation of succinyl coenzyme A from methylmalonyl coenzyme A



**Figure 3. Vitamin B12-dependent metabolic processes: the formation of methionine from homocysteine, and the formation of succinyl coenzyme A from methylmalonyl coenzyme A**

## Deficiency

### Causes

Men and women can equally be affected by the vitamin B12 deficiency. Vitamin B-12 deficiency is relatively common – thought to affect approximately 15% of the general population. That percentage goes much higher among people with chronic illness. Its occurrence is more pervasive, in those over 50 years. In western countries percentage of Vitamin B12 deficient person is higher than the third world countries. Vegans are at the higher risk.

Apart from directly determining vitamin B12 concentration in the blood, elevated levels of both methylmalonic acid (MMA) and homocysteine may indicate a vitamin B12 deficiency.

Vitamin B12 deficiency may be caused due to many reasons. Following may be some of the probable reasons :

1. **Not proper intake of the vitamin:** The vitamin B12 is rarely found in vegetables. It is mainly in animal products meat, eggs and dairy products etc. Therefore, vegan should ensure proper intake of the vitamin as some supplement. In eggs, there are factors present which hinder the proper absorption of the vitamins.



2. **Irregular replenishment of the vitamin:** The vitamin B12 is water soluble. Therefore, excess amount get passed in the urine. So, a regular replenishment is required.
3. **Chronic illness:** Chronic illness leads to depletion in the body concentration of vitamin B12.
4. **Age:** Gastrointestinal absorption of vitamin B12 occurs in the small intestine by an active process requiring the presence of intrinsic factor, another glycoprotein, which the gastric parietal cells secrete after being stimulated by food. This ability to process the food diminishes as the age increases.
5. **Lack of gastric intrinsic factor:** The gastric intrinsic factor is protein that is required for the absorption of B12 from the food in the stomach. The lack of this factor may be due to some genetic defect or due to age..
6. **Gastric atrophy:** Gastric atrophy is a chronic inflammation of the stomach resulting in decreased stomach acid production. Because this (acid production) is necessary for the release of vitamin B12 from the proteins in food, vitamin B12 absorption is reduced.
7. **Multiple sclerosis:** In multiple sclerosis (or MS), nerve myelin gets destroyed. In order to replace the lost myelin more vitamin B12 is required.
8. **Geographical reasons:** Western countries, where hygiene is top concern, more people have the deficiency, than in the third world countries people.

## Symptoms

The deficiency symptoms of vitamin B12 remain unnoticed and undiagnosed for a very long time. The symptoms may be associated with some other disease. Deficiency of vitamin B12 affects every cell in the body, but is most severely felt in the tissues where the cells normally divide rapidly, as in the blood-forming -tissues of the bone marrow and in the gastro-intestinal tract. The deficiency can also lead to neurological changes such as numbness and tingling in the hands and feet. It also includes mood disorders, anxiety, insomnia, restlessness, night terror etc. It can also include irregular/rapid heartbeat, cold skin fatigue and apathy, weakness, nausea, constipation, flatulence (gas), loss of appetite and weight, back pain, bone loss, tinnitus, eye disorders, hallucinations and migraine headaches, dementia, Alzheimers and many more. Extreme B12 deficiency can cause very extreme symptoms, including mental dullness, coma, and even death.

## Disease prevention and therapeutic use

### Pernicious anaemia

Pernicious anaemia has been one of the earliest concerns of vitamin B12. Patients with lack of intrinsic factor secretion can be effectively treated using oral vitamin B12 but require lifetime vitamin B12 therapy. When used alone, oral doses of at least 150 µg/day are required. Combinations of vitamin B12 and intrinsic factor may be used.



## Hyperhomocysteinaemia

Homocysteine (a sulfur-containing amino acid) appears to be a nerve and vessel toxin. It promotes mortality, cardiovascular disease (CVD), stroke, Alzheimer's disease, birth defects, recurrent pregnancy loss, and many more disorders. Adequate amounts of vitamin B12, folic acid and B6 intake is required for keeping homocysteine at levels associated with lower rates of these disease. Supplementation with one or more of these vitamins can lower plasma levels of homocysteine, regardless of the cause of the elevation.

Caution: Elevated homocysteine levels can be caused by vitamin B12 deficiency due to impaired absorption of vitamin B12 caused by gastric atrophy. Vitamin B12 deficiency leads to anemia and, if not corrected in time, will permanently damage the nervous system. Folic acid supplements will correct the anemia (which can serve as a warning sign before nerve damage develops), but they do not prevent the damage. For this reason, people over 50 years who take folic acid supplements should also take at least 25 micrograms of vitamin B12 per day, a dose large enough to enable adequate amounts to be absorbed. Dr. Herbert believes that everyone over the age of 50 years, should take B12 supplements anyway because gastric atrophy is common as people age. Some doctors recommend the intake of 400–1,000 mcg of folic acid per day, 10–50 mg of vitamin B6 per day, and 50–300 mcg of vitamin B12 per day.

## Cancer

Vitamin B12 deficiency may lead to an elevated rate of DNA damage and may alter Methylation of DNA. These are obvious risk factors for cancer. In a recent study, chromosome breakage was minimized in young adults by supplementation with 700µg of folic acid and 7 µg of vitamin B12 daily in cereals for two months.

## RDA and Sources of vitamin B12

*“The . . . Recommended Dietary Allowance (RDA) (2.4mcg/day) for B12 for adults ages 51 and older are the same as for younger adults but with the recommendation that B12–fortified foods (such as fortified ready-to-eat cereals) or B12–containing supplements be used to meet much of the requirements.”*

Institute of Medicine

Vitamin B12 is rarely found in vegetables. Infact, the vitamin B12 can only be made by the bacteria e.g *Aerobacter*, *Agrobacterium*, *Alcaligenes*, *Azotobacter*, *Bacillus*, *Clostridium*, *Corynebacterium*, *Flavobacterium*, *Micromonospora*, *Mycobacterium*, *Nocardia*, *Propionibacterium*, *Protaminobacter*, *Proteus*, *Pseudomonas*, *Rhizobium*, *Salmonella*, *Serratia*, *Streptomyces*, *Streptococcus* and *Xanthomonas* as they have the enzyme required for its synthesis; which is why vegetarians and vegans should ensure B12 is included in their daily vitamin supplement

Most people simply who suffer vitamin B12 deficiency symptoms simply don't get the recommended daily dosage (RDA) of vitamin B12. Its **RDA** is 2 to 3 micrograms. The dosage of up to 200 micrograms a day, from diet and supplements, of the vitamin B12 is needed to

reverse the deficiency conditions. Supplements may be in the form of tablet, liquid and injections.

Following are some examples where one can naturally source vitamin B-12:

Sources of Vitamin B12				
Excellent sources	Very Good Sources	Good sources	Natural sources	
<ul style="list-style-type: none"> <li>• Calf's liver, braised, 4 oz-wt</li> <li>• Sardines, 3.25 oz can - excellent source</li> <li>• Snapper, baked/broiled, 4 oz-wt</li> </ul>	<ul style="list-style-type: none"> <li>• Venison,</li> <li>• Shrimp, steamed/boiled,</li> <li>• Scallops, baked/broiled,</li> <li>• Salmon, chinook, baked/broiled,</li> <li>• Crab, Lobster and Oysters</li> <li>• Beef tenderloin, lean, broiled,</li> </ul>	<ul style="list-style-type: none"> <li>• Lamb loin, roasted,</li> <li>• Cod, baked/broiled,</li> <li>• Halibut, baked/broiled,</li> <li>• Yogurt, low-fat</li> <li>• Cow's milk,</li> <li>• Egg, whole, boiled</li> </ul>	<ul style="list-style-type: none"> <li>• Beef Liver</li> <li>• organic eggs</li> <li>• fish</li> <li>• clams</li> <li>• blackstrap molasses</li> <li>• sardines</li> <li>• oysters</li> <li>• lamb</li> </ul>	<ul style="list-style-type: none"> <li>• yogurt</li> <li>• milk products</li> <li>• Nuts-rich in complete b complex</li> <li>• pecans</li> <li>• almond</li> <li>• walnut</li> <li>• filberts</li> </ul>

**Side effects, contraindications, negative interaction, and warnings**

Although there is no known toxicity of vitamin B12 and any excess is passed in urine. But, care should be taken while dealing with the vitamin. Following may be some of probable points of attention:

**Dermatologic:** Itching, rash, transitory exanthema, and urticaria have been reported. Vitamin B12 (20 micrograms/day) and pyridoxine (80 mg/day) has been associated with cases of rosacea fulminans, characterized by intense erythema with nodules, papules, and pustules.

**Gastrointestinal:** Diarrhea has been reported.

**Hematologic:** Peripheral vascular thrombosis has been reported. Treatment of vitamin B12 deficiency can unmask polycythemiavera, which is characterized by an increase in blood volume and the number of red blood cells. The correction of megaloblastic anaemia with vitamin B12 can result in fatal hypokalemia and gout in susceptible individuals, and it can obscure folate deficiency in megaloblasticanemia. Caution is warranted.

**Anticonvulsants:** The metabolism of cobalamins in the cerebrospinal fluid (CSF) can be altered by a number of anticonvulsants such as phenobarbitone, primidone, phenytoin and ethylphenacemide. This can lead to neuropsychic disturbances.



## **CONCLUSION**

Vitamin B12 has emerged as a vitamin that has vital role in blood formation, the normal functioning of the brain, maintenance and regulation of nervous system, protein synthesis, promotion of activity of hormones and neurotransmitter, energy production and many more. It is also essential in the chemical reactions that "turn on" detoxification mechanisms. It is involved in metabolism of every cell of the body. Vitamin B12 (cobalamin) deficiency should be on watch. Prevention, early detection, and treatment of vitamin B12 deficiency are important to public health issues because they are essential to prevent development of irreversible neurologic damage which can impact quality of life.