Vitamin B12 is a water-soluble vitamin naturally present in some foods, added to others as a dietary supplement. Vitamin B12 exists in several forms and contains mineral cobalt. Compounds with Vitamin B12 activity are collectively called cobalmins and active forms are Methylcobalamin and 5-deoxyadenosylcobalamin.

Key words
Methylcobalamine, Megaloblastic anemia, Crohn’s disease, Homocysteine, achlorhydria.

Introduction
Vitamin B12 is required for proper red blood cell formation, neurological function and DNA synthesis. Vitamin B12 functions as a cofactor for methionine synthase and L-methylmalonyl-CoA mutase.

Source of Vitamin B12
- Vitamin B12 is naturally found in animal products, fish, meat, poultry, eggs, milk and milk products [1].
- Vitamin B12 is generally not present in plant foods, but fortified breakfast cereals are a readily available source of vitamin B12 with high bioavailability.
- Some nutritional yeast products also contain vitamin B12 [2].
- Vitamin B12 is usually present as cyanocobalamin [3], a form that the body converts to the active forms methylcobalamin and 5-deoxyadenosylcobalamin. Dietary supplements can also contain methylcobalamin and other forms of vitamin B12.
- Body’s ability to absorb vitamin B12 from dietary supplements is limited by the capacity of intrinsic factor. Only about 10 mcg of a 500 mcg oral supplement is actually absorbed in healthy people.
- Deficiency linked to improper absorption rather than low consumption [4]

Foods rich in B12
- Animal products (meat, fish, poultry)
- Not usually denatured by cooking
- Great sources: Liver, Kidney [5]
Important functions of Vitamin B12

- It works with the B vitamin folate to make our body’s genetic material.
- It helps keep levels of the amino acid homocysteine in check, which may help decrease heart disease risk.
- It is essential in the production of red blood cells, which carry oxygen through the blood to the body’s tissues.
- Aids in tissue growth
- Allows body to use certain nutrients
- Facilitates numerous chemical reactions
- Human body normally contains 5000-10000 µg Vitamin B12
- A healthy person needs 3-5 µg per day [6].

Levels

Vitamin B12 is accessed via serum or plasma vitamin B12 levels. Values below approximately 170-250 pg/mL for adults indicate a vitamin B12 deficiency. Serum vitamin B12 concentrations not accurately reflect intracellular concentrations. An elevated serum homocysteine level (values >13 micromol/L) also suggest a vitamin B12 deficiency. Elevated methylmalonic acid levels (values >0.4 micromol/L) is a reliable indicator of vitamin B12 status because they indicate a metabolic change that is highly specific to vitamin B12 deficiency [7].

Guidelines for the interpretation of serum vitamin B12 and urinary methylmalonic acid concentrations

<table>
<thead>
<tr>
<th></th>
<th>Serum B12 (pg/ml)</th>
<th>Methylmalonic acid (mg per 24 hour urine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>200 – 900</td>
<td>1.3 – 2.0</td>
</tr>
<tr>
<td>B12 deficiency</td>
<td>&lt; 100</td>
<td>&gt; 300</td>
</tr>
</tbody>
</table>

Causes of Vitamin B12 deficiency

Vitamin B12 malabsorption from food, pernicious anemia, post surgical malabsorption and dietary deficiency are the main causes.

- Atrophic gastritis, a condition affecting 10%-30% of older adults, decreases secretion of HCL in the stomach, resulting in decreased absorption of Vitamin B12. Decreased HCL also increase the growth of normal intestinal bacteria that use vitamin B12 further reducing the amount of vitamin B12 available to the body.
- Many people can absorb the synthetic vitamin B12 added to fortified foods and dietary supplements that adults older than 50 years obtain most of their vitamin B12 from vitamin supplements or fortified foods.
- Elderly patients with atrophic gastritis require doses much higher to avoid subclinical deficiency.
- Surgery in which part of the stomach and/or small intestine is removed.
- Long term use of acid reducing drugs.
- Small intestine causes: Crohn’s disease, celiac disease, bacterial growth, or parasite.
- Excessive alcohol consumption.
- Autoimmune disorders, such as: Graves disease, Systemic lupus erythematosus (SLE) [8]

Pernicious anemia

- Pernicious anemia, a condition that affects 1-2% of older adults, is characterized by a lack of intrinsic factor. Individuals with pernicious anemia cannot properly absorb vitamin B12 in gastrointestinal tract (GIT). Pernicious anemia is treated with IM Vitamin B12. Approx 1% of oral vitamin B12 can be absorbed passively in the
absence of intrinsic factor, suggesting that high oral doses of Vitamin B12 might be effective.

- Individuals with gastrointestinal disorders may be unable to absorb enough vitamin B12.
- Individuals with stomach and small intestine disorders, such as celiac disease and Crohn’s disease may be unable to absorb enough vitamin B12 from food to maintain healthy body stores followed by megaloblastic anemia and dementia [9].

**Individuals who have had gastrointestinal surgery**

- Bariatric surgery or surgery to remove all or part of the stomach, often result in a loss of cells that secrete HCL and intrinsic factor. This reduces the amount of Vitamin B12. Surgical removal of the distal ileum also can result in the inability to absorb vitamin B12.

**Vegetarians**

- Strict vegetarians are at greater risk than non-vegetarians of developing vitamin B12 deficiency because natural food sources of vitamin B12 are limited to animal foods. Fortified breakfast cereals are one of the few sources of vitamin B12 from plants and can be used as a dietary source of strict vegetarians [10].

**Pregnancy and lactation**

- Vitamin B12 crosses the placenta during pregnancy and is present in breast milk.
- Breastfed infants of women who consume no animal products have limited reserves of Vitamin B12 and can develop vitamin B12 deficiency within months of birth.

- Understand and untreated vitamin B12 deficiency in infants result in severe and permanent neurological damage.
- The ADA recommends supplemental vitamin B12 for vegans during pregnancy and lactation to ensure that enough vitamin B12 is transferred to the fetus and infant [11].

**Who’s at risk?**

- Strict vegetarians (who eat no animal products) and their infants
- Certain elderly people (B12 uptake ability decreases with age)

**High risk diets ...... vegetarian**

- Some nutrients only occur in animal products
- Major concern is that B12 comes from bacteria (which is only found in meat products)
- Restricting diet makes it difficult to get all nutrients
- Vegetarians may resort to non-complete nutrient sources [12]

**Other causes**

- Low intestinal B12 uptake [13]
- Low intrinsic factor in the stomach
- Deficiency of HCL in gastric juices
- Laxatives
- Low uptake in central nervous system (CNS)
- Lack of calcium

**Features of Vitamin B12 deficiency**

- Megaloblastic anemia, fatigue, weakness, constipation, loss of appetite, and weight loss.
- Neurological changes, such as numbness and tingling in the hands and feet.
- Difficulty maintaining balance, depression, confusion, dementia, poor
memory and soreness of the mouth or tongue.

- **Infancy**: failure to thrive, movement disorders, developmental delays and megaloblastic anemia.
- Common initial sign of B12 deficiency – The red sore tongue, with atrophy of the papillae is often present in pernicious anemia, angular stomatitis is also present.
- As the anemia worsens it may causes symptoms such as Weakness, tiredness or light – headedness, Rapid heartbeat and breathing, Pale skin, Sore tongue, Easy bruising or bleeding, including bleedings gums, Stomach upset and weight loss, Diarrhea or constipation
- Deficiency of vitamin B12 causes an accumulation of homocysteine in the blood and decrease levels of substances needed to metabolize neurotransmitters positive associations between elevated homocysteine levels and the incidence of Alzheimer’s disease and Dementia [14]
- Low vitamin B12 status has been associated with cognitive decline
- Damage the nerve cells results in Tingling or numbness in fingers and toes [15, 16]
- Difficult walking
- Mood changes or depression
- Memory loss, disorientation and dementia
- B12 deficiency in infants, can lead to severe and permanent damage to the nervous system [17].
- Mothers who follow a vegetarian diet should have their babies B12 levels checked.
- Most people can prevent vitamin B12 deficiency by consuming enough meat, poultry, seafood, milk, cheese and eggs.

If you don’t eat animal products or you have a medical condition that limits your absorption of nutrients, experts recommend taking a B12 containing multivitamin and eating breakfast cereal fortified with vitamin B12.

- If you experience symptoms of B12 deficiency, speak to your doctor about a blood test to check B12 levels [18].

### Consequences of deficiency

A variety of conditions may occur

- Anemia
- Fatigue
- Nerve damaged [3]
- Smooth Tongue
- Sensitive skin
- Loss of memory, exhaustion, loss of muscle strength [17]

### B12 and sleep

- Can help those with sleep disorders
- Releases Melatonin (sleep hormone) [14]
- Works in presence of sunlight and is beneficial to jetlag [14].

### Treatment

- **Injectable**: Vitamin B12 deficiency is treated with injections [19, 20] (since this method bypasses potential barriers to absorption).
- High doses of oral Vitamin B12 may also be effective.
- In most hospitals, the practice of using intramuscular (IM) Vitamin B12 to treat Vitamin B12 deficiency has remained unchanged.
- **B12 Deficiency without neurological involvement**: 1 mg Hydroxocobalamin 3 times a week for 2 weeks then every 3 months.
B12 Deficiency with neurological involvement: 1 mg Hydroxocobalamin every other day until no further improvement then every 2 months.
- Oral supplements – low success rate
- Intramuscularly proven more successful
- Active form is most successful
- Must be supplied with folic acid
- Fish should be emphasized in diet
- 6 months – one year to recover [21]

Interactions with medications
- Chloramphenicol can interfere with the red blood cell response to supplemental vitamin B12.
- Proton pump inhibitors, such as omeprazole and lansoprazole, interfere with vitamin B12 by slowing the release of gastric acid into the stomach. One should monitor vitamin B12 status in patients taking proton pump inhibitors for prolonged periods.

Folic acid and Vitamin B12
- Large amounts of folic acid mask the damaging effects of Vitamin B12 deficiency by correcting the megaloblastic anemia caused by Vitamin B12 deficiency without correcting the neurological damage.
- Permanent nerve damage can occur if Vitamin B12 deficiency is not treated.
- So, folic acid intake should not exceed 1000 mcg daily in healthy adults [21].

References
Vitamin B12 – A brief overview


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