

Vitamin B deficiencies and treatment

Vitamins are organic compounds that are essential for normal physiological functions and the maintenance of optimal health. They cannot be synthesised by the body and hence are required in small quantities in the diet. A deficiency thereof may cause specific nutritional medical disorders.1,2

The B-group (or B-complex) vitamins act as important co-enzymes in numerous metabolic processes and help the body convert carbohydrates into glucose for energy production, as well as to metabolise proteins and fats. B vitamins are also needed for the maintenance of healthy skin, hair, eyes, the liver and nervous system.3-7 Some of the B vitamins are involved in the synthesis of red blood cells, neurotransmitters and nucleic acids such as RNA and DNA.4,5 Refer to Figure 1. There are eight essential B vitamins that cannot be synthesised in the body and hence need to be ingested daily. Of these, deficiencies in the so-called BIG 5 (B1, B3, B6, B9, and B12), can result in serious medically defined disorders.2 See Table 1.

A well-balanced diet, including both plant and animal-based foods, will prevent the occurrence of Vitamin B deficiencies.1 However, there are certain conditions that may predispose a person to the development of a vitamin B deficiency by either decreasing their intake or absorption of the B vitamins and/or increasing their need for or excretion of the B vitamins. Vitamin B deficiencies seldom occur in isolation.1 Active supplementation of vitamins should generally only be used to correct documented deficiencies, after which a well-balanced diet should be resumed to provide all necessary nutrients.1 Daily requirements of some of the B vitamins is listed in Table 2.

Table 2. Daily requirements of Vitamins B1, B2, B3, B6, B9, and B123-7

<table>
<thead>
<tr>
<th>Vitamin B</th>
<th>Daily requirements</th>
<th>Adult males</th>
<th>Adult females</th>
<th>Pregnant females</th>
</tr>
</thead>
<tbody>
<tr>
<td>B1 (thiamine)</td>
<td>1,2mg</td>
<td>1,1mg</td>
<td>1,4mg</td>
<td></td>
</tr>
<tr>
<td>B2 (riboflavin)</td>
<td>16mg</td>
<td>14mg</td>
<td>18mg</td>
<td></td>
</tr>
<tr>
<td>B5 (pyridoxine)</td>
<td>1,3-1,7mg*</td>
<td>1,5mg</td>
<td>1,9mg</td>
<td></td>
</tr>
<tr>
<td>B6 (folic acid)</td>
<td>400µg</td>
<td>400µg</td>
<td>600µg</td>
<td></td>
</tr>
<tr>
<td>B12 (cobalamin)</td>
<td>2,4µg</td>
<td>2,4µg</td>
<td>2,6µg</td>
<td></td>
</tr>
</tbody>
</table>

* 1,3mg up to age 50 years, 1,7 mg from 51 years

Conditions that predispose to vitamin B deficiencies

The elderly

In the elderly, pathophysiological changes, multiple comorbidities and increasing dependency can lead to malnutrition due to the inadequate intake and malabsorption of nutrients, vitamins and minerals.8 See Table 3. B vitamin deficiencies, even subclinical deficiencies, in the elderly are important, as they have been linked to cognitive impairment, memory loss, depression, and dementia.10-14

Table 1. Vitamin B complex1,8

<table>
<thead>
<tr>
<th>Vitamin B complex</th>
<th>Essential Vit B’s</th>
<th>BIG 5</th>
<th>Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin B1 (thiamine)</td>
<td>Thiamine</td>
<td></td>
<td>Beriberi, polyneuritis, Wernicke-Korsakoff syndrome</td>
</tr>
<tr>
<td>Vitamin B2 (riboflavin)</td>
<td>Riboflavin</td>
<td></td>
<td>Pellagra (dermatitis, dementia, diarrhoea)</td>
</tr>
<tr>
<td>Vitamin B3 (niacin)</td>
<td>Niacin</td>
<td></td>
<td>Anaemia, dermatitis, depression, confusion, peripheral neuropathy</td>
</tr>
<tr>
<td>Vitamin B5 (pantothenic acid)</td>
<td>Pantothenic acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin B6 (pyridoxine)</td>
<td>Pyridoxine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin B7 (biotin)</td>
<td>Biotin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin B8 (inositol)</td>
<td>Folic acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin B9 (folic acid)</td>
<td>Cobalamin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin B12 (cobalamin)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Para-aminobenzoic acid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Choline</td>
<td></td>
<td></td>
<td></td>
</tr>
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</table>
Neurotropic B Vitamins (B₁, B₆ and B₁₂) are all necessary for healthy nerve function, and symptoms** of a Vitamin B deficiency may include: ¹⁻⁴

- Forgetfulness, confusion
- Mood disturbance
- Pins-and-needles, numbness or weakness (hands & feet)
- Difficulty walking, maintaining balance and ataxia

The elderly are at risk of Vitamin B deficiencies⁵⁻⁶

Pathophysiological changes, multiple comorbidities and increasing dependency can lead to malnutrition and vitamin deficiencies in the elderly⁵

- Poor intake ⁶⁻⁷
- Poor absorption ⁶⁻⁷
- Increased requirements ⁷
- Increased excretion ⁷

Other patients at risk of Vitamin B deficiency and/or neuropathy include: ⁹⁻¹¹

- Vegetarians and vegans
- Patients who consume excessive amounts of alcohol

Neurobion® - the market-leading Vitamin B complex product in 74 countries worldwide. **¹²

** Symptoms may be related to another medical condition.

** Neurobion® is the market-leading Vitamin B complex product/ Vitamin B combination product for the last two-year period, based on a combined market of 74 countries worldwide.


Medication
Certain chronic medications can increase risk for a Vitamin B deficiency.3-7,9-11 These medications can decrease absorption, deplete stores, and increase clearance of the B vitamins.3,7-9,11 See Figure 2. Higher doses and prolonged administration (> 3 years) of metformin has been significantly associated with an increased risk of Vitamin B12 deficiency.18 Although the exact mechanism is unknown, metformin is thought to compete with Vitamin B12 at the ileal receptor sites and thus decrease its absorption.18 Gastric acid suppressive agents, such as H2-receptor blockers and proton pump inhibitors, are another group of medications that are often used long-term and that have been linked to Vitamin B12 deficiency.19 These medications cause a hypochlorhydric state, which results in malabsorption of protein-bound B12.19

Table 3. Causes of Vitamin B deficiencies in the elderly

<table>
<thead>
<tr>
<th>Poor intake</th>
<th>Poor health and increasing dependency1,5</th>
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<tbody>
<tr>
<td>Poor absorption</td>
<td>Increased comorbidities and use of chronic medications that interfere with Vitamin B12 absorption e.g. metformin, H2-receptor blockers, PPIs, antacids, cholestyramine10</td>
</tr>
<tr>
<td>Increased prevalence of Pernicious Anaemia with advancing age9</td>
<td></td>
</tr>
<tr>
<td>Atrophic gastritis (20-50% of elderly) with decreased acid-pepsin secretion and decreased release of protein bound Vitamin B129</td>
<td></td>
</tr>
<tr>
<td>Overgrowth of bacteria, due to hypochlorhydria associated with atrophic gastritis, which bind Vitamin B12 for their own use9</td>
<td></td>
</tr>
<tr>
<td>Increased requirements</td>
<td>Age-related metabolic changes and health problems can lead to increased requirements of B vitamins e.g. Vitamin B612,15,16</td>
</tr>
<tr>
<td>Increased excretion</td>
<td>Use of diuretics can lead to the increased excretion of B vitamins e.g. Vitamin B17</td>
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Excessive alcohol intake
Malnutrition and micronutrient deficiencies are common in chronic alcoholics.30-32 30-80% of alcoholics have thiamine deficiency, 50% have pyridoxine deficiency, 35% have niacin deficiency and 6-80% have folic acid deficiency.32 Severe vitamin deficiencies (Vitamin B1, B3, B6, and B12) in chronic alcoholics may result in severe functional impairment and tissue damage, particularly in the brain.32 Excessive alcohol consumption not only decreases the intake and absorption of B vitamins, but it also interferes with the storage, metabolism, utilisation and excretion of these vitamins.32 See Figure 4.

HIV/AIDS
B vitamin deficiencies are widely seen in HIV, even in asymptomatic patients.24,25 See Table 4. The B vitamin deficiencies in these patients are most likely due to the cachexia and catabolic state characteristic of AIDS.26 In fact, HIV-infected patients require levels of B vitamins in multiples of the recommended

Figure 1. Simplified summary of some of the B-complex vitamins and their major areas of physiological functioning

Figure 2. Medications that increase the risk of Vitamin B deficiencies.
dietary allowance (RDA) to achieve normal plasma levels.

Malabsorption of Vitamin B₁₂ occurs in HIV/AIDS patients and is due to many mechanisms including AIDS-related inflammation of the small intestine, gastric acid hyposcretion and production of antibodies to intrinsic factor.

### Diagnosis of vitamin B deficiencies

Severe deficiencies of some of the B vitamins may result in recognised disease entities such as pellagra, Beriberi and Wernicke's encephalopathy, megaloblastic anaemia and peripheral neuropathy. However, the non-specific symptoms of milder deficiencies such as headache, confusion, weight loss, and fatigue may require a high index of suspicion to make an accurate diagnosis. See Figure 5 for symptoms of B vitamin deficiencies. Multiple Vitamin B deficiencies are quite common. Therefore, if at least one B vitamin is found to be deficient, other B vitamin deficiencies should be considered and excluded. Also, a simple 'gold standard' diagnostic test may not be available – as is the case with Vitamin B₁₂.

When a B₁₂ deficiency is suspected, the initial laboratory assessment includes serum B₁₂ concentrations, a full blood count and a blood film examination to check for megaloblastic anaemia (which is often not seen in mild cases of B₁₂ deficiency). There is also no universally accepted serum Vitamin B₁₂ cut-off to define deficiency – the WHO recommends the value of < 150 pmol/L, however, higher levels of 220 to 258 pmol/L based on more sensitive indicators of B₁₂ status (raised homocysteine and MMA levels) have been suggested.

Refer to Table 5 for diagnostics measurements for Vitamin B deficiencies.

### Treatment

Active replacement treatment should be instituted in documented/diagnosed vitamin deficiencies. Since Vitamin B deficiencies

<table>
<thead>
<tr>
<th>B Vitamin</th>
<th>Incidence of deficiency in clinical studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>B₁ (thiamine)</td>
<td>23% of patients with AIDS or AIDS-related complex&lt;sup&gt;36&lt;/sup&gt; 10% of patients with AIDS had Wernicke’s encephalopathy at autopsy&lt;sup&gt;35&lt;/sup&gt;</td>
</tr>
<tr>
<td>B₂ (pyridoxine)</td>
<td>34% of asymptomatic HIV patients&lt;sup&gt;34&lt;/sup&gt; 53% of CDC Stage III patients&lt;sup&gt;34&lt;/sup&gt;</td>
</tr>
<tr>
<td>B₉ (folic acid)</td>
<td>41% of HIV-infected patients&lt;sup&gt;37&lt;/sup&gt; 64% of HIV-infected individuals at all stages of infection&lt;sup&gt;34&lt;/sup&gt;</td>
</tr>
<tr>
<td>B₁₂ (cobalamin)</td>
<td>10%-35% of patients with HIV/AIDS&lt;sup&gt;34&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

CDC = Centres for Disease Control and Prevention

*Only at high alcohol intake levels

PLP = pyridoxal-5-phosphate (a coenzyme and active form of pyridoxine)
NUTRITION

Table 5. Diagnosing Vitamin B deficiencies

<table>
<thead>
<tr>
<th>B Vitamin</th>
<th>Measurements</th>
</tr>
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| B1 (thiamine) 28, 38 | • TDP effect*: 15-25% for marginal deficiency >25% for deficiency  
• Direct measurement of erythrocyte TPP: <70nmol/L |
| B3 (niacin) 39 | • Serum niacin <0,5µg/L |
| B6 (pyridoxine) 16, 24 | • Most common measure of vitamin B6 status is serum PLP  
• PLP <20nmol/L |
| B9 (folic acid) 31 | • Serum folate** <3ng/ml  
• Erythrocyte folate <140ng/ml  
• Increased homocysteine >16nmol/L |
| B12 (cobalamin) 9, 30 | • Serum B12 <150pmol/L  
• Increased homocysteine >13mmol/L  
• Full blood count and blood film examination showing megaloblastic anaemia |

* TDP effect reflects the extent of unsaturation of transketolase enzyme with thiamine diphosphate, the main metabolically active form of thiamin (also known as thiamine pyrophosphate). Now considered an inadequate method as it is nonspecific and less sensitive than erythrocyte TPP.  
** Sensitive to diet, so may not reflect long-term status. Not specific to Vitamin B12 deficiency as affected by low Vitamin B3 and B6 levels. TPP = thiamine pyrophosphate, PLP = pyridoxal 5’ phosphate, MMA = methylmalonic acid

Table 6. Treating Vitamin B deficiencies

<table>
<thead>
<tr>
<th>B Vitamin</th>
<th>Replacement Therapy</th>
</tr>
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</table>
| B1 (thiamine) 1 | Mild polyneuropathy  
• 10-20mg orally, once daily, for two weeks  
Moderate or advanced polyneuropathy*  
• 20-30mg orally, once daily, for several weeks after the symptoms disappear |
| B3 (niacin) 1 | Cardiovascular beriberi  
• 100mg IV, once daily for several days  
Wernicke-Korsakoff syndrome  
• 50-100 mg IM or IV, twice daily, for several days  
• Then 10-20mg orally, once daily, until therapeutic response obtained |
| B6 (pyridoxine) 1 |  
• 50-100mg orally, once daily |
| B9 (folic acid) 1 |  
• 400-1000µg orally, once daily  
• The normal requirement is 400µg per day |
| B12 (cobalamin) 1 |  
Mild deficiency or no neurological symptoms and signs  
• 1000-2000 mg orally, once daily  
Severe deficiency or neurological symptoms and signs  
• 1 mg IM, 1-4 times per week for several weeks, then given once a month for severe deficiency |

IV = intravenously, IM = intramuscularly  
* Neuropathy will not respond to treatment if the nerve cells have died off

Figure 5 Symptoms of Vitamin B deficiencies.

Conclusion

B vitamins are essential for important physiological functions and are significant contributors to the maintenance of optimal health. Generally, a well-balanced diet will prevent Vitamin B deficiencies; however certain conditions and/or the use of chronic medication may predispose patients to low vitamin levels. Active treatment should be instituted in documented/diagnosed vitamin deficiencies. In cases where underlying conditions or chronic medicine usage places patients at continued risk, there should be ongoing vitamin replacement therapy. References available on request.

References available on request. 16

Table 6 for guidelines.
NUTRITION

1. The B-group (or B-complex) vitamins act as important co-enzymes in numerous metabolic processes and help the body convert carbohydrates into glucose for energy production, as well as to metabolise proteins and fats.
   a. True  
   b. False

2. Some of the B vitamins are involved in the synthesis of RNA and DNA.
   a. Red blood cells, nerve transmitters and nucleic acids
   b. White blood cells, neurotransmitters and stomach acids
   c. White blood cells, neurotransmitters and nucleic acids
   d. Red blood cells, neurotransmitters and nucleic acids

3. There are _______ essential B vitamins that cannot be synthesised in the body and hence need to be ingested daily.
   a. Eight  
   b. Seven  
   c. Five  
   d. Ten

4. A well-balanced diet, including both plant and animal based foods, will prevent the occurrence of Vitamin B deficiencies.
   a. True  
   b. False

5. Increased comorbidities and use of chronic medications that interfere with Vitamin B12 absorption e.g. ________________, H2-receptor blockers, PPIs, antacids, cholestyramine.
   a. Magnesium  
   b. Metformin  
   c. Potassium  
   d. Methadone

6. Gastrointestinal absorption of the B vitamins takes place mainly in the large intestine and there are many disorders that can negatively impact their uptake and result in deficiencies.
   a. True  
   b. False

7. ____________ of alcoholics have thiamine deficiency
   a. 30-50%  
   b. 20-50%  
   c. 30-80%  
   d. 20-80%

8. Severe deficiencies of some of the B vitamins may result in recognised disease entities such as pellagra, Beriberi and Werner’s encephalopathy, megaloblastic anaemia and peripheral neuropathy.
   a. True  
   b. False

9. There is also no universally accepted serum Vitamin B12 cut-off to define deficiency – the WHO recommends the value of <_________ pmol/L.
   a. 150  
   b. 200  
   c. 220  
   d. 300

10. B vitamin deficiencies are widely seen in HIV, even in asymptomatic patients.
    a. True  
    b. False

This is to state that I have participated in the CPD-approved programme and that these are my own answers.

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