Introduction

Vitamins are essential nutrients that are sourced from food. They are required for their vital physiological functions, and are significant contributors to the maintenance of optimal health.1 The B-group (or B-complex) vitamins, specifically, assist with the production of energy and the biosynthesis of many physiologically vital molecules in cells. They are water soluble and are not stored in the body. Therefore, daily replenishment is possible through dietary intake.1 Cereals, mainly in their purest and unrefined form, are a common source of these vitamins.2 However, the practice of excessively refining and polishing cereals strips them of a significant amount of vitamin B.3 Multiple B-vitamin deficiencies are quite common. Therefore, a balanced diet, including a full spectrum of B vitamins, is usually needed when any of them are found to be deficient. Conversely, their therapeutic value is limited to supplementation during states of deficiency since they have no additional benefits in the presence of an adequate dietary intake. In general, their active supplementation should only be used to correct deficiencies. This article provides an overview of B-complex vitamin deficiencies and their supplementation.

What are vitamins?

Vitamins are organic compounds that are characterised by high levels of potency. Therefore, they are only required in very small amounts. They are classified as nutrients, and most of them are obtained via dietary intake (hence the reason why several vitamins become depleted in patients with a poor nutritional status). Some of the B vitamins are also synthesised by the intestinal bacteria, but in insufficient quantities. Vitamins are typically categorised as either being water soluble or fat soluble, as shown in Table I.5 6

Abstract

Vitamins are either fat- or water-soluble micronutrients that are derived from a healthy, well-balanced diet. The B-complex vitamins are well-known examples of water-soluble nutrients that are readily absorbed from a healthy gut, and easily eliminated via renal excretion. They are required for their vital physiological functions and are significant contributors to the maintenance of optimal health. Multiple B-vitamin deficiencies are quite common. Therefore, a balanced diet, including a full spectrum of B vitamins, is usually needed when any of them are found to be deficient. Conversely, their therapeutic value is limited to supplementation during states of deficiency since they have no additional benefits in the presence of an adequate dietary intake. In general, their active supplementation should only be used to correct deficiencies. This article provides an overview of B-complex vitamin deficiencies and their supplementation.

Table I: Water-soluble versus fat-soluble vitamins6-7

<table>
<thead>
<tr>
<th>Water-soluble vitamins</th>
<th>Fat-soluble vitamins</th>
</tr>
</thead>
<tbody>
<tr>
<td>B complex</td>
<td></td>
</tr>
<tr>
<td>• Vitamin B&lt;sub&gt;1&lt;/sub&gt; (thiamine)</td>
<td>• Vitamin A (retinol)</td>
</tr>
<tr>
<td>• Vitamin B&lt;sub&gt;2&lt;/sub&gt; (riboflavin)</td>
<td>• Vitamin D (ergocalciferol and cholecalciferol)</td>
</tr>
<tr>
<td>• Vitamin B&lt;sub&gt;3&lt;/sub&gt; (niacin)</td>
<td>• Vitamin E (α-tocopherol)</td>
</tr>
<tr>
<td>• Vitamin B&lt;sub&gt;5&lt;/sub&gt; (pantothenic acid)</td>
<td>• Vitamin K (phytonadione)</td>
</tr>
<tr>
<td>• Vitamin B&lt;sub&gt;6&lt;/sub&gt; (pyridoxine)</td>
<td></td>
</tr>
<tr>
<td>• Vitamin B&lt;sub&gt;7&lt;/sub&gt; (biotin)</td>
<td></td>
</tr>
<tr>
<td>• Folic acid (vitamin B&lt;sub&gt;9&lt;/sub&gt;)</td>
<td></td>
</tr>
<tr>
<td>• Para-aminobenzoic acid</td>
<td></td>
</tr>
<tr>
<td>• Choline</td>
<td></td>
</tr>
<tr>
<td>• Inositol (vitamin B&lt;sub&gt;3&lt;/sub&gt;)</td>
<td></td>
</tr>
<tr>
<td>• Biotin (vitamin B&lt;sub&gt;7&lt;/sub&gt;)</td>
<td></td>
</tr>
<tr>
<td>Vitamin C (ascorbic acid)</td>
<td></td>
</tr>
</tbody>
</table>

Notes

• The water-soluble vitamins are readily absorbed from the gastrointestinal tract, and merely require passage in conjunction with water. (The notable exception is vitamin B<sub>12</sub>, which also needs to bind to intrinsic factor that is derived from the stomach)
• These vitamins are excreted in the urine and are not stored in the body in any significant quantities. Therefore, hypervitaminosis is quite rare.

• These vitamins require binding to ingested lipids to facilitate their absorption from the gastrointestinal tract. It is important to note that any condition that interferes with fat absorption will necessarily also interfere with the absorption of the fat-soluble vitamins
• These vitamins are stored in the body, with the noteworthy exception of vitamin K, and toxicities are well-known, e.g. hypervitaminosis A.
The various B vitamins

Vitamins are essential for normal growth, metabolism and reproduction. However, their therapeutic value is limited to supplementation during states of deficiency since they have no additional benefits in the presence of an adequate dietary intake. In general, their active supplementation should only be used to correct deficiencies, after which a well-balanced diet should be able to provide all of the necessary nutrients.5

As already mentioned, the B-complex vitamins are water soluble, and the vitamins in this group are easily eliminated from the body via renal excretion. Typical members of this complex are thiamine (vitamin B1), riboflavin (vitamin B2), niacin (vitamin B3), pantothenic acid (vitamin B5), pyridoxine (vitamin B6), biotin (vitamin B7), folic acid (vitamin B9) and cobalamin (vitamin B12).6 Some authors also include inositol, para-aminobenzoic acid and choline in this group.7 Among a diverse array of functions, they act as important co-factors or co-enzymes in a wide variety of metabolic processes in the body. It is noteworthy that many different vitamins play a role in the formation and normal functioning of red blood cells.8 Furthermore, vitamin C and E act as antioxidants, and vitamin A and D as hormones.5

Vitamin B1 (thiamine)

Thiamine is essential for glucose metabolism in the body.9 It functions as a co-enzyme in the metabolism of carbohydrates and branched-chain amino acids.2 It is also essential for a normal appetite and plays a crucial role in maintaining the proper functioning of the nervous system.1

A thiamine deficiency may manifest itself in any of the following:2-10

- Beriberi, which can be wet (oedematous) or dry (paralytic)
- Wernicke’s encephalopathy, which is characterised by confusion, ataxia and nystagmus
- Korsakoff’s psychosis, which is characterised by confabulation, lack of insight, retrograde and anterograde amnesia, and apathy.10 The latter two are also referred to as the Wernicke-Korsakoff syndrome. Korsakoff’s psychosis is associated with chronic alcoholism, following a thiamine deficiency in these patients.5

Treatment is invariably via thiamine supplementation (Table II).11 Table II provides a summary of B-complex vitamin functions, deficiencies and the treatment thereof. Also refer to Figure 1.

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Functions</th>
<th>Results of a deficiency</th>
<th>Treatment of deficiency</th>
</tr>
</thead>
</table>
| Vitamin B1 (thiamine) | Functions as a co-enzyme in the metabolism of carbohydrates and branched-chain amino acids in the body. It catalyses the decarboxylation of α-ketoacids. | Beriberi, polyneuritis and Wernicke-Korsakoff syndrome | Thiamine is given as follows:  
- For mild polyneuropathy: 10-20 mg orally, once daily, for 2 weeks  
- For moderate or advanced neuropathy: 20-30 mg once daily, continued for several weeks after the symptoms disappear  
- For congestion and oedema due to cardiovascular beriberi: 100 mg intravenously, once daily, for several days  
- For Wernicke-Korsakoff syndrome: 50-100 mg intramuscularly or intravenously, twice daily, usually for several days, followed by 10-20 mg once daily, until a therapeutic response is obtained11  
- Neuropathy will not respond to treatment if the nerve cells have died off  
- Prophylactic thiamine should be used in patients with chronic diarrhoea and those who have undergone intestinal resection11  
- 100 mg of thiamine should be given intravenously before the administration of intravenous glucose* to alcoholic patients, or to any other patients who are at risk of having a thiamine deficiency11 | 
| Vitamin B2 (riboflavin) | Functions as a co-enzyme in several oxidation and reduction reactions in the body. | Cheilosis, angular stomatitis, lip fissures and dermatitis (fissures may become infected with *Candida albicans*), as well as normochromic or normocytic anaemia | Riboflavin 5-10 mg orally, once daily, until recovery. Other B vitamins should also be administered11  
- Dosages up to 50 mg orally or intravenously may need to be considered5 |
| Vitamin B3 (niacin, nicotinic acid or nicotinamide) | Functions as a co-substrate or co-enzyme for hydrogen transfer with several dehydrogenases. | Pellagra with dermatitis, diarrhoea and dementia, as well as secondary to diarrhoea, cirrhosis of the liver, alcoholism and carcinoid syndrome | Nicotinamide 250-500 mg daily orally, in divided dosages 3-4 times a day or 100 mg 8 hourly,5,11 |
| Vitamin B5 (pantothenic acid) | Functions as a component of co-enzyme A and phosphopantetheine and is involved in fatty acid metabolism. | Fatigue, sleep disturbances, impaired coordination and nausea | The recommended daily allowance has not been established with certainty, but 5-10 mg daily provided by a balanced diet is probably adequate12 |
Vitamin B2 (riboflavin)

Riboflavin functions as a co-enzyme in several oxidation and reduction reactions in the body. It is essential for the release of energy from food and the conversion of the amino acid, tryptophan, into niacin.

A riboflavin deficiency may lead to cheilosis (fissuring and dry scaling of the vermilion surface of the lips and angles of the mouth), angular stomatitis (inflammation of the corners of the mouth, associated with a wrinkled or fissured epithelium that does not involve the mucosa), and dermatitis (inflammation of the skin), mucosal crusts and even a magenta-coloured tongue. Treatment is usually via riboflavin supplementation (Table II).

Vitamin B3 (niacin)

Also known as nicotinic acid, niacin is a vitamin that is mainly involved in energy production, normal enzyme functioning, digestion, and the promotion of a normal appetite, healthy skin and nerves. It functions as a co-substrate or co-enzyme for hydrogen transfer with several dehydrogenases. A niacin deficiency may result in pellagra, which is characterised by dermatitis, diarrhoea and dementia (the so-called three “Ds” of pellagra). Nicotinamide is usually used for treatment because unlike nicotinic acid, the most common form of niacin, it does not cause flushing, itching, burning, or tingling sensations, owing to intense vasodilatation (Table II).

Table II: A summary of B-complex vitamin functions, deficiencies and their treatment

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Functions</th>
<th>Results of a deficiency</th>
<th>Treatment of deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin B6 (pyridoxine, pyridoxal phosphate or pyridoxamine)</td>
<td>Functions as a co-enzyme (pyridoxal phosphate) in the metabolism of amino acids, glycogen and sphingoid bases</td>
<td>Nasolateral seborrhoea, glossitis and peripheral neuropathy (and epileptiform convulsions, especially in infants, which may be refractory to treatment with anticonvulsive agents), as well as normocytic, microcytic or sideroblastic anaemia</td>
<td>• Specific causes, e.g. the use of pyridoxine-inactivating drugs, such as isoniazid, and malabsorption, should be corrected for secondary deficiency. • Pyridoxine 50-100 mg orally, once daily. • Dosages may be as low as 2 mg per day. • An amount larger than the daily recommended intake may be required for deficiency due to increased metabolic demand. • High dosages of pyridoxine may be effective in most cases of inborn errors of metabolism.</td>
</tr>
<tr>
<td>Vitamin B7 (biotin)</td>
<td>Has co-enzyme functions in bicarbonate-dependent carboxylation reactions</td>
<td>Fatigue, conjunctivitis, alopecia, nausea, dermatitis, muscular pain, depression, hallucinations and paraesthesia of the extremities</td>
<td>Biotin 150 µg intramuscularly, once daily. Symptoms should begin to resolve within 3-5 days, and should be absent within 3-5 months. Biotin 5-20 mg per day. The symptoms may resolve much faster with a larger dosage.</td>
</tr>
<tr>
<td>Vitamin B8 (inositol)</td>
<td>Functions include cell membrane synthesis, the maintenance of healthy hair, control of oestrogen levels and cholesterol metabolism</td>
<td>Atherosclerosis, alopecia, eczema, increased blood cholesterol levels, skin disorders, eye disorders, declining brain function, mood swings and constipation</td>
<td>Treatment is difficult to establish as inositol is not recognised as a true vitamin, but a recommended dietary allowance of approximately 1 000 mg can be given.</td>
</tr>
<tr>
<td>Vitamin B9 (folic acid, folate and folacin)</td>
<td>Functions include aiding protein metabolism, promoting red blood cell formation and maturation, and purine and pyrimidine synthesis</td>
<td>Megaloblastic anaemia and neural tube defects</td>
<td>Folate 400-1 000 µg orally, once daily. The normal requirement is 400 µg per day.</td>
</tr>
<tr>
<td>Vitamin B12 (cobalamin)</td>
<td>Functions include aiding in nucleic acid metabolism, methyl transfer, myelin synthesis and repair, as well as red blood cell production</td>
<td>Megaloblastic anaemia, fatigue, neurological disorders and the degeneration of nerves, resulting in peripheral neuropathy</td>
<td>Cobalamin 1 000-2 000 µg orally, once daily, in patients who do not have severe deficiency or neurological symptoms or signs. Cobalamin 1 mg intramuscularly, 1-4 times per week, for several weeks, until the haematological abnormalities are corrected, then given once per month for severe deficiency.</td>
</tr>
</tbody>
</table>

*: Intravenous glucose can worsen a thiamine deficiency.
REVIEW

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

Vitamin B5 (pantothenic acid)

Pantothenic acid is important for the production of energy, hormone synthesis and the metabolism of fat, protein and carbohydrates. It functions as a component of co-enzyme A and phosphopantetheine, and is involved in fatty acid metabolism. Deficiency occurs very rarely, but if it does occur, it is typically accompanied by deficits in other nutrients. Deficiency is usually characterised by fatigue, sleep disturbances, impaired coordination, irascibility (a bad temper), postural hypotension, a rapid heart rate on exertion, epigastric distress with anorexia, constipation and nausea, as well as numbness and tingling of the hands and feet (so-called burning feet syndrome). The recommended daily allowance has not been established with certainty, but 5-10 mg daily provided by a balanced diet is probably adequate (Table II).

Vitamin B6 (pyridoxine)

Pyridoxine, also known as pyridoxal phosphate or pyridoxamine, is required for the synthesis of the neurotransmitters, serotonin and noradrenaline, and for myelin formation. It functions as a co-enzyme, as pyridoxal phosphate, in the metabolism of amino acid, glycogen and sphingoid bases. Deficiency is also rarely seen, and is usually associated with a deficiency in other B-complex vitamins. Deficiency is associated with anaemia, abnormalities on the electroencephalograph, dermatitis with cheilosis and glossitis (a swollen tongue), nasalateral seborrhea, depression, confusion, weakened immune function, peripheral neuropathy and seizures, especially in infants, which may be refractory to treatment with anticonvulsant agents, as well as normocytic, microcytic or sideroblastic anaemia.

Treatment usually involves the elimination of risk factors, where possible, and the administration of pyridoxine (Table II).

Vitamin B7 (biotin)

Biotin is required for the release of energy from carbohydrates and for the metabolism of fat, protein and carbohydrates. Deficiency presents with fatigue, conjunctivitis, alopecia, nausea, dermatitis (the erythematous and seborrhoeic types), muscular pain and central nervous system abnormalities, such as hypotonia, lethargy and stunted development in children; and depression, hallucinations and paraesthesia of the extremities in adults. Treatment is usually via biotin supplementation, and in cases where there is a secondary cause, e.g. eating raw eggs (owing to the fact that avidin, a glycoprotein contained in raw egg white, binds to biotin and effectively prevents its absorption from the gastrointestinal tract) or anticonvulsant therapy, e.g. phenobarbital, phenytoin and primidone. The secondary cause should be eliminated, where possible, or substituted in the case of anticonvulsant therapy (Table II).

Vitamin B8 (inositol)

Strictly speaking, inositol is not a true vitamin because it is biosynthesised in the body. It is involved in cell membrane synthesis, the maintenance of healthy hair, the control of oestrogen levels and in cholesterol metabolism. Deficiency, although rare, may result in atherosclerosis, alopecia, eczema, increased blood cholesterol levels, skin disorders, eye disorders, declining brain function, mood swings and constipation. Treatment is with the recommended dietary allowance, which is quite difficult to establish, of approximately 1 000 mg (Table II).

Vitamin B9 (folic acid)

Folic acid, also known as folate or folacin, is a vitamin that assists with protein metabolism, the promotion of red blood cell

A vitamin B12 deficiency is also rarely seen, and is usually associated with a deficiency in other B-complex vitamins. Deficiency is associated with anaemia, abnormalities on the electroencephalograph, dermatitis with cheilosis and glossitis (a swollen tongue), nasalateral seborrhea, depression, confusion, weakened immune function, peripheral neuropathy and seizures, especially in infants, which may be refractory to treatment with anticonvulsant agents, as well as normocytic, microcytic or sideroblastic anaemia.
formation and maturation (folic acid is a haematogenic, together with iron, vitamin B_{12}, vitamin B_{6}, ascorbic acid and epoietin), and the synthesis of purines and pyrimidines.\textsuperscript{3,4} It also lowers the risk for neural tube birth defects, e.g. spina bifida, and helps to control homocysteine levels, thus potentially reducing the risk of coronary heart disease.\textsuperscript{1} Deficiency causes megaloblastic anaemia, which cannot be distinguished from that caused by vitamin B_{12} deficiency.\textsuperscript{6} Maternal deficiency increases the risk of neural tube birth defects (there is an increased demand for folate during pregnancy). Folic acid is converted to folinic acid, a metabolically active folate, which may also be used to treat folic acid deficiency in patients taking dihydrofolinic acid reductase inhibitors, such as methotrexate, trimethoprim and pyrimethamine.\textsuperscript{5} General treatment is with folate supplements (Table II).

**Vitamin B_{12} (cobalamin)**

Cobalamin is another vital haematogenic agent. It is also important in nucleic acid metabolism and methyl transfer, as well as myelin synthesis and repair.\textsuperscript{1} Deficiency most commonly affects strict vegetarians, infants of vegan mothers and the elderly.\textsuperscript{1} It is characterised by fatigue, megaloblastic anaemia, neurological disorders and the degeneration of nerves which results in peripheral neuropathy, i.e. numbness and tingling.\textsuperscript{4} Treatment is with suitable cobalamin supplementation, for which hydroxocobalamin is preferred over cyanocobalamin because the former is excreted more slowly than the latter (Table II).\textsuperscript{3,5}

### A few important points to ponder

A specific B-vitamin deficiency is not likely to occur in isolation. When megaloblastic anaemia is detected, both vitamin B_{12} and folic acid should be supplemented. Medicines that could deplete folic acid include methotrexate, trimethoprim and pyrimethamine. Those that could potentially hamper its absorption from the gut include cholestyramine and certain anticonvulsants, such as phenytoin. Folic acid is essential for normal cell proliferation and erythropoiesis, and is in increased demand during pregnancy.\textsuperscript{3,8,12}

Lifelong parenteral supplementation is required in patients who develop pernicious anaemia, secondary to a deficiency in intrinsic factor, and therefore also a deficiency in vitamin B_{12}. Lastly, vitamin B_{6} prophylaxis is recommended in high-risk patients, i.e. those at high risk of the development of neurotoxicity, who need to take isoniazid to treat tuberculosis. Such patients include those who are malnourished, alcoholics, pregnant women or those who suffer from diabetes mellitus or human immunodeficiency virus infection. A dose of 10-25 mg per day is sufficient in these patients. However, higher dosages should be considered in those who already have an established neuropathy.\textsuperscript{3,12}

### Conclusion

The B-complex vitamins play a vital role in the maintenance of an optimal health status. A diverse group of micronutrients that are normally derived from the intake of a healthy and well-balanced diet is included within this group of water-soluble vitamins. However, when a deficiency is detected or diagnosed, the likelihood exists that multiple B vitamins are actually lacking. The B-complex vitamins are essential for normal growth, metabolism and reproduction. However, their therapeutic value is limited to supplementation during states of deficiency since they have no additional benefits in the presence of an adequate dietary intake. In general, their active supplementation should only be applied to correct actual deficiencies.

Several disease states are associated with one or more B-vitamin deficiency, including a nutritional deficit, i.e. beriberi and pellagra, various forms of anaemia, suppressed metabolic and nervous system functioning and a weakened immune system. Therefore, their major areas of physiological functioning extend to metabolism, including the normal metabolic conversion of homocysteine to methionine, as well as neurological and blood-forming effects. Furthermore, there are a number of medicines that contribute to B-vitamin depletion. For example, methotrexate and trimethoprim, as well as cholestyramine, may cause a folic acid deficiency. Knowledge of the B-complex vitamins contributes to an understanding of their role, individual functions, deficiency states and the judicious use of their supplementation.

### References