16

Vitamins and vitamin-like compounds

Mark L. Wahlqvist and Naiyana Wattanapenpaiboon

OBJECTIVES

- To understand the historical and contemporary bases for the designation 'vitamins' for a class of essential nutrients.
- To know the food sources of vitamins.
- To know the functions and toxicities of vitamins.
- To introduce a range of phytochemicals and vitamin-like compounds being recognised as conditionally essential for health.
- To appreciate the place and limitations of food supplementation with vitamins.

WHAT ARE VITAMINS AND ARE THEY UNIQUE?

A vitamin is an organic compound that occurs in small concentrations in food. Each of the thirteen known vitamins has certain specific and vital functions in the cell and tissues of the body so that one vitamin cannot replace or act for another; nevertheless, there may be functions, like antioxidation, which may overlap with other compounds or among vitamins. The lack or deficiency of one vitamin can also interfere with the function of another and consumption of excessive amounts of one vitamin can lead to vitamin imbalances (Machlin 1984).

The body needs only small amounts each day, measured in micrograms or milligrams, of each vitamin to sustain the normal metabolic processes of life. Vitamins cannot be synthesised by the body (except vitamin D, which can be made in the skin upon adequate exposure to sunlight) and the continued lack of one vitamin in the diet, or its improper absorption or utilisation by the body, results in a vitamin deficiency disease. Bacteria in the human intestine can synthesise certain vitamins, but usually not in quantities large enough to meet the body's needs with the exception of vitamin K; bacteria, however, are usually

considered to represent an exogenous or 'outside source', rather than an endogenous source. An organic compound must be required in the diet to prevent a deficiency disease (such as scurvy, rickets or beri-beri) in order to be considered as a vitamin. In fact, vitamins were discovered while searching for the cause of such diseases. Frank vitamin deficiency diseases are rare in developed societies, like Australia, Japan, New Zealand or Singapore, but whether vitamin status is optimal is being vigorously debated. Subclinical deficiency represents a state of 'nutritional risk', but is hard to measure and whether it impairs overall health is uncertain. To do this only on the basis of clinical biochemistry of nutrients (for example, more than two standard deviations below the population mean) remains a statistical rather than a functional definition of subclinical deficiency. More recently, functional markers of subclinical deficiency have become available, like the increase in the vascular toxin serum homocysteine with low blood folate status.

Primary deficiency states due to dietary inadequacies are probably less common than secondary deficiency states, which may be induced by some other factor or disease in the face of an apparently adequate dietary intake. In the Asia–Pacific region, however, people and communities with vitamin A, thiamin (B-1), riboflavin (B-2) and folacin deficiency are still to be found. The possibility of an excessive and potentially harmful intake of certain vitamins has also been identified with the consumption of large doses of certain vitamins by some individuals. Such a condition is referred to as hypervitaminosis. *Hypervitaminosis is a toxic condition that occurs as a result of the excessive consumption of quantities of certain vitamins.* Healthy individuals usually meet their vitamin requirements by eating a varied diet (Kant et al. 1993). The extent to which the diet meets the average person's needs is often measured against the recommended dietary intakes prepared by the Nutrition Committee of the National Health and Medical Research Council (NH&MRC) in Australia or similar bodies in other countries (see Chapter 36).

VITAMIN CLASSIFICATION

Vitamins are usually classified according to their solubility in either fat or water. The four vitamins A, D, E and K are soluble in fat, whereas vitamin C and B-complex vitamins are water soluble. They also may be classified according to their function in the body: for example, some of the B-complex vitamins (vitamins B-1, B-2, niacin, B-6, pantothenic acid and biotin) function as co-enzymes in many and varied metabolic reactions involving the release of energy for cellular activity; vitamin B-12 and folate are involved in the synthesis of the gene-containing material of the cells, deoxyribonucleic acid (DNA); and others are anti-oxidants (vitamins A, E, C and carotenoids). *A co-enzyme is a small molecule that combines with a particular protein molecule to make an enzyme, and an enzyme is a protein molecule that acts as a catalyst to facilitate chemical reactions.*

As vitamins were discovered they were designated by letters assigned in alphabetical order. After they had been chemically identified, it became apparent that the vitamins were not single compounds but mixtures of compounds. For example, several different compounds all with vitamin A activity have been isolated. In the case of vitamin B, numerical subscripts were added to distinguish between individual vitamins as they were discovered (vitamin B-1, B-2, B-6, and so on). Many vitamins exist in food in several different forms, some of which (precursors and provitamins) require conversion into vitamin active compounds in the body before they can function. *A precursor is a compound that can be converted to a nutrient in the body. Provitamins are chemical compounds closely related to vitamins in their structure; in the body the inactive provitamin is converted to the active form of the vitamin, for example, β-carotene is a provitamin of vitamin A.* Some vitamins may not be completely available for absorption from the human gut and therefore have reduced bioavailability. The term biological activity, when applied to a nutrient, takes into account factors that may affect its absorption and utilisation and it is therefore a measure of the nutritional effectiveness of the particular nutrient.

FAT SOLUBLE VITAMINS

Fat soluble vitamins are present in a wide variety of foods. The mechanism of digestion and absorption follows a similar pathway to the dietary fats and any condition that hinders the function of the intestine or interferes in any way with fat absorption (such as malabsorption syndrome—a condition in which there is faulty absorption of nutrients) will also limit the

absorption of fat soluble vitamins. They can be stored, mainly in the liver, and consequently the clinical symptoms of deficiency develop more slowly than for water soluble vitamins which are rapidly excreted or metabolised but which may also have effective long-term storage mechanisms. If taken in excessive amounts, some fat soluble vitamins accumulate in the body and may produce undesirable toxic effects. In contrast to water soluble vitamins, fat soluble vitamins are not easily destroyed by usual cooking methods and they do not dissolve into the cooking water.

Vitamin A (retinol)

Vitamin A is present in food in two main forms: as preformed vitamin A (the vitamin itself); and, more commonly, as a precursor of vitamin A, namely provitamin A (the carotenes and similar substances, the

Table 16.1 Food sources of vitamin A, functions, deficiency states, benefits and toxicity

Food source	Retinol (μg/100 g)	Carotene (μg/100 g)	Notes	RDI
High				
cod liver oil	28 400	1050	1 Maximum of 30% to 40% loss in cooking.	Adults (over 11 years) 750 μg RE
palm oil	0	7000	2 Both retinol and carotene are sensitive to light and oxygen.	
lambs' liver (fried)	20 600	10		
Medium				
carrots	0	2000		
spinach	0	1000		
sweet potato	0	670*		
egg yolk	660	100		
Low				
bread	0	0		
potato*	0	trace		
chicken	trace	trace		

Functions
1 Vision. An essential component of rhodopsin (visual purple) which is present in the retina of the eye and is responsible for vision in dim light.
2 Epithelial surfaces. Essential for the maintenance of specialised epithelial surfaces of the body.
3 Bone growth. Essential for normal bone formation.

Deficiency (Hypovitaminosis A)
Clinical signs include:
1 Night blindness. The inability to see in dim light is usually the first symptom.
2 Keratinisation of epithelial surfaces: normal secretory epithelium is replaced by dry, hard, keratinised epithelium which is more susceptible to infection. When this process occurs in the cornea of the eye it can lead to xerophthalmia and if deficiency continues it can rapidly lead to blindness.
3 Poor dental health can be the result of deficiency.
Deficiency is rare in Australia but may occur secondary to:
1 Malabsorption syndromes, including cystic fibrosis and coeliac disease.
2 Severe liver disease can result in inadequate reserves.
3 Zinc deficiency, which can occur in alcoholics, may reduce utilisation of vitamin A. In Australia zinc deficiency rather than deficiency of vitamin A is more likely to cause night blindness.

Possible benefits
1 May reduce the risk of breast, lung, colon, prostate and cervical cancer.
2 May reduce the risk of heart disease and stroke.
3 May retard macular degeneration (a common cause of blindness among the elderly).

Toxicity (Hypervitaminosis A)
Chronic intakes in excess of 1000 μg/kg body mass (approx. 100 x RDI) can induce symptoms of toxicity in adults, less for children.
Clinically characterised by loss of appetite, headache, blurred vision, irritability, hair loss, general drying and flaking of skin, bony growths or exotoses, haemorrhages, bone fractures, liver damage and death.
Congential abnormalities in offspring observed when hypervitaminosis occurs in pregnancy.
Carotene in large amounts is not toxic but causes a yellowing of skin which disappears when carotene is metabolised.

* Amount varies with variety

carotenoids). Vitamin A is the generic description for at least seven different active forms of the vitamin. It is found almost exclusively in animal sources, usually in association with fats in foods such as dairy products and liver. Food derived from animals provide compounds that are converted to retinol in the intestine. Most of the provitamin A in a mixed diet is supplied in the form of carotenoids mainly in deep yellow and green coloured plants (Table 16.1). Only 50 of approximately 600 carotenoids found in nature are converted into vitamin A. The most important and most known of these carotenoids is β-carotene, which can be split by an enzyme to release retinal (oxidised retinol) in the intestine and liver. It is the most abundant in food and possesses the highest vitamin A activity of the carotenoids. One microgram of β-carotene is estimated to have one-sixth of the biological activity of one microgram of retinol, at least as a source of vitamin A, but not insofar as other functions are concerned. However, it is less efficiently utilised by the body than is preformed vitamin A. This difference is partly attributable to the lower absorption of carotenoids, affected by the presence or absence of other components in the diet such as dietary fat and protein and by bile salts. The 'one-sixth' evidence for β-carotene is also being challenged (Solomons and Bulux 1993). Vitamin A activity used to be measured in international units (IU), but nowadays retinol equivalents (RE) are used because of the need to take into account not only the absorption of carotenoids, but also the degree of conversion to vitamin A. The equivalents are listed in Table 16.2.

In the blood, retinol-binding protein (RBP), a protein produced by the liver, combines with retinol and carries it to tissues as the RBP–retinol complex. The amount of circulating retinol is set by the amount of RBP. Any dysfunction of the liver, such as protein energy malnutrition or alcoholic liver disease, can affect vitamin A status. Apart from its role in visual function, vitamin A plays a part in other basic physiological processes, such as growth, reproduction, immunity and epithelial tissue maintenance. It is essential throughout the entire life span, yet its influence is particularly critical during periods in which cells proliferate rapidly and differentiate, such as during pregnancy and early childhood. Each form of vitamin A performs specific tasks. Retinol supports reproduction and is the major transport and storage form of the vitamin. Retinal, the reduced form, is active in vision and is also an intermediate in the oxidative conversion of retinol to

Table 16.2 Conversion factors for retinol equivalents

1 retinol equivalent	= 1 microgram retinol
	= 6 micrograms β-carotene
	= 12 micrograms other provitamin A carotenoids
	= 3.33 IU vitamin activity from retinol
	= 10 IU vitamin activity from β-carotene

Note: International Units: the measure traditionally used for vitamins A and D. The amount of the vitamin comprising a unit was determined by its biological activity in rats, i.e. the amount required to cure or prevent the specific vitamin deficiency disease.

Retinol equivalents: a measure of vitamin A activity that has replaced IU, and accounts for dietary variances in retinol and its precursor, carotene. To calculate the retinol equivalents in a diet or food item, the following formula is used:

$$\mu g \text{ retinol} + \frac{\mu g \text{ β-carotene}}{6} + \frac{\mu g \text{ other carotenoids}}{12} = \text{retinol equivalents}$$

retinoic acid. Retinoic acid acts as an intracellular hormone and binds with an intercellular protein, retinoic acid receptor, to form a complex that can bind to DNA to act as a modulator of gene expression, controlling mRNA synthesis. It is thus involved in cell differentiation, growth and embryonic development, and this explains why excess vitamin A is both toxic and teratogenic (producing birth malformation).

The function of retinol in black and white (dim light) vision is as a component of rhodopsin (visual purple) which is bleached to visual yellow by contact with light arriving at the retina (see Figure 16.1). This reaction triggers an electrical impulse that is conducted through the optic nerve to the brain; this signal is recognised as part of a visual image. Rhodopsin can be regenerated so that the process can be repeated. Failure to adapt visually to the dark is an early manifestation of vitamin A deficiency, but this can also be seen with zinc deficiency (because zinc is required for synthesis of RBP and conversion of retinol to retinal) and with vitamin E deficiency. Megadoses of β-carotene in the form of supplements have been positively linked to lung cancer (see Chapter 32).

Vitamin A deficiency remains one of the world's major nutritional problems (Chapter 30), leading to blindness through xerophthalmia, but also increasing the risk of infections. Fortunately, progress is being made towards its eradication in Asia. Clinical deficiency of vitamin A is virtually never seen in Australia. Vitamin A is retained in the body more extensively than most other vitamins and the average amount stored (mostly in the liver) can satisfy the normal requirement for between one and two years. Toxicity from excessive and

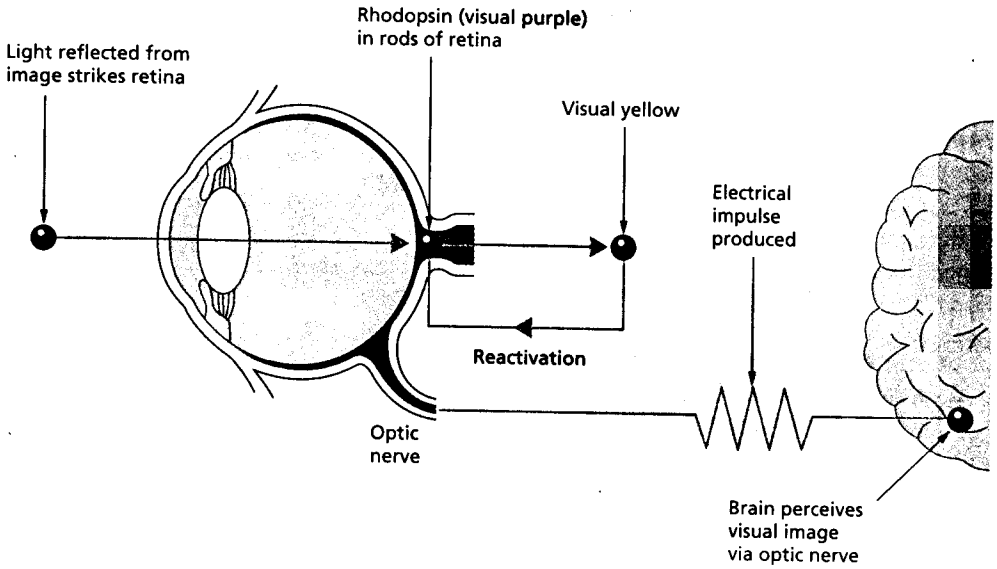


Figure 16.1 **The function of retinol in black and white (dim light) vision is as a component of rhodopsin (visual purple) which is bleached to visual yellow by contact with light arriving at the retina. This reaction triggers an electrical impulse that is conducted through the optic nerve to the brain; this signal is recognised as part of a visual image. Rhodopsin can be regenerated so that the process can be repeated.**

prolonged intakes of vitamin A, usually in the form of supplements, is rare, but has been reported both in adults and children owing to the mistaken belief that large amounts are beneficial and safe. Vitamin A taken in excessive and repeated doses can be hazardous, especially during pregnancy (see Table 16.1).

Vitamin D

Of the several forms of vitamin D that exist in nature, the two most important for humans are vitamin D-2 (ergocalciferol, plant origin), and vitamin D-3 (cholecalciferol, animal origin). Vitamin D could be classified as a hormone rather than as a vitamin because although it is an essential nutrient for humans, it can be produced by the body and, like a hormone, is then carried by the bloodstream from its site of production to act elsewhere. Both these vitamins are formed by the ultraviolet irradiation of two provitamins: provitamin D-2 (ergosterol), found in yeasts and fungi, and provitamin D-3 (7-dehydrocholesterol), synthesised from cholesterol in the liver and then transported to the skin (Figure 16.2). Vitamin D formed in the skin is transported to the liver, where it is converted to 25-hydroxy cholecalciferol (calcidiol), the major circulating form in the plasma. 1,25-dihydroxy cholecalciferol (calcitriol), the active form of vitamin D, is formed from calcidiol in the kidney.

Only a few natural food sources of vitamin D are known to exist; small amounts are found in fatty fish, butter, eggs and fortified foods such as margarine (Table 16.3). Those who receive adequate exposure to sunlight do not need additional dietary vitamin D. The amount of vitamin D-3 synthesis in skin is determined by the length and intensity of exposure to sunlight and the amount of melanin (colour pigment) in the skin. There is a risk of vitamin D deficiency in infants living in cold climates, especially during the winter months (Table 16.3). This can cause rickets (Figure 16.3). The bones fail to calcify normally, causing growth retardation and skeletal abnormalities. The bones become so weak that they bend when they have to support the body's weight. Those who wear clothes which exclude sunlight (as with Islamic women), the elderly and those institutionalised for long periods are also at risk of osteomalacia, the adult form of rickets.

Vitamin D acts in conjunction with parathyroid hormone (PTH) to control calcium and phosphorus balance. Vitamin D raises blood concentrations of these minerals in three ways: it stimulates their absorption in the small intestine, their reabsorption in the kidney, and their withdrawal from the bones into the blood (Figure 16.2). The formation of calcitriol is strictly controlled according to the body's calcium needs. The main controlling factors are the existing levels of calcitriol itself, and the blood level of PTH, calcium

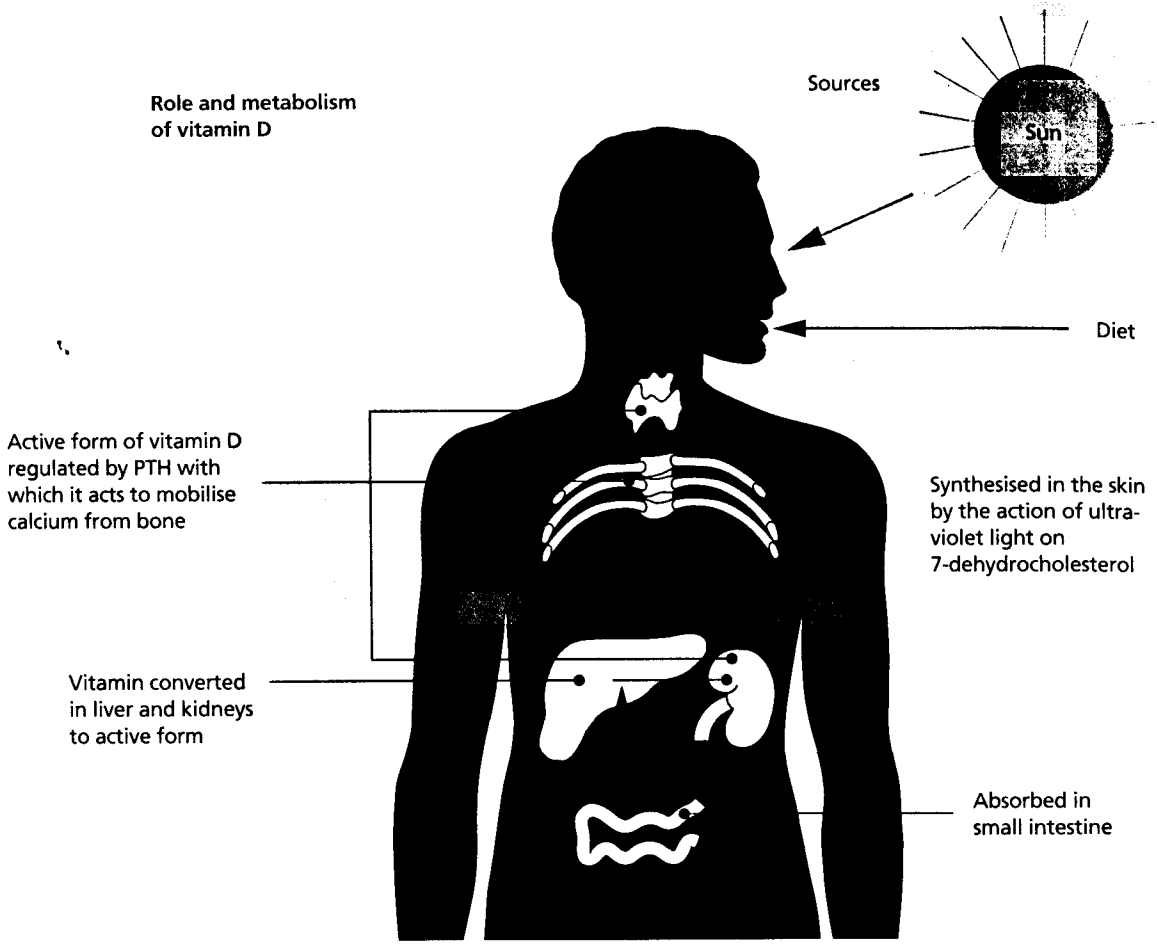


Figure 16.2 The role and metabolism of vitamin D are complex processes. The vitamin may be available in food or formed in the skin by the action of sunlight. It acts in conjunction with parathyroid hormone (PTH) to control calcium and phosphorus balance. The activated vitamin has hormone-like properties and acts on the intestine and kidney as well as on bone. It is known now to induce differentiation of cells (and presumably to reduce the risk of tumour formation) and to regulate some aspects of immune function

and phosphorus. The vitamin D receptor is known to be present in most cells of the body. Not only can presumption of vitamin D function in most cells help to explain some of the abnormalities in vitamin D deficiency, but these abnormalities may also help to identify whether calcitriol plays a general role in all cells. The muscle weakness in vitamin D deficiency could be related to some regulatory role of calcitriol in skeletal muscle. Likewise, the apparent increase in susceptibility to infection of vitamin D deficient children could be evidence for a defect in the expression of vitamin D in the immune function. It now has been proposed that vitamin D is also important for insulin and prolactin secretion, stress responses and cell differentiation.

Vitamin E

Vitamin E exists in at least eight different tocopherol and tocotrienol forms. Tocopherol is an oily liquid compound found in seeds and fish oils. The structure of vitamin E consists of two carbon rings joined together and a carbon side chain. The number and position of the carbon side chain on the ring differentiate one form from another (α-, β-, γ-, δ-), while tocotrienols have three double bonds in the side chain. The

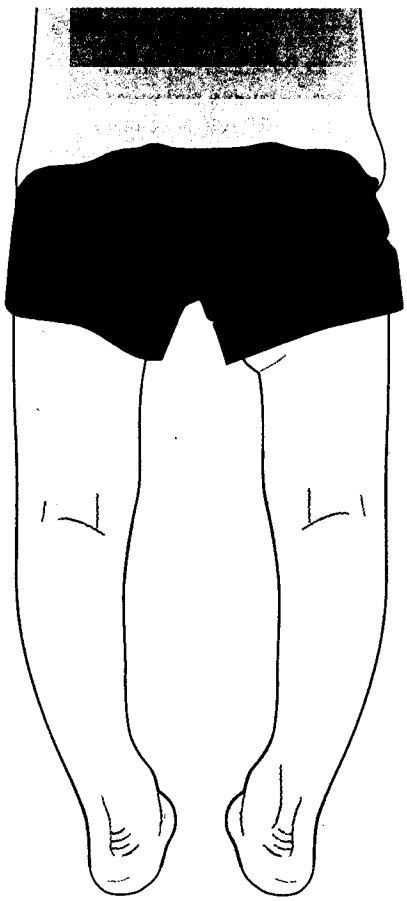


Figure 16.3 Bow legs characteristic of rickets

compound d-α tocopherol is the most widely distributed and has the highest biological activity. One way of calculating the total vitamin E activity of a varied diet is to multiply the α-tocopherol value (in milligrams) by 1.2 (this accounts for the other tocopherols present). This calculation gives an approximation of total vitamin E activity expressed as 'milligrams of α-tocopherol equivalents', but is not a complete statement about the vitamin E content.

The richest dietary sources of vitamin E are the commercially available vegetable oils. These are also the richest sources of polyunsaturated fatty acids (PUFAs), which vitamin E protects from oxidative breakdown. The fundamental characteristic of vitamin E is as an antioxidant (that is, preventing or inhibiting oxidation by vitamin E itself being oxidised). Nuts are the next best source, while almost all vegetables and meats have small amounts (Table 16.4). The requirement for vitamin E in the body is difficult to estimate since it is influenced by the amount and type of fat eaten in the diet; that is, a high PUFA intake increases the vitamin E requirement. However, since foods that are good sources of PUFA are also generally good sources of vitamin E, the intake of the vitamin automatically increases as the intake of unsaturated oils increases; the problem may arise with extensive refining of edible oils and fats. Furthermore, most of the vitamin E in PUFA oils is committed (depending on the degree of refinement of the oil) and little may be available for other metabolic functions. One advantage of a mono-unsaturated fat source (such as peanuts, olives) may be that it has less of a requirement for vitamin E to protect it against oxidation. It is worth remembering that, historically, humans obtained most of their fat from unrefined sources like seeds (grains and nuts) and lean land animals, fish or other aqua-food. It seems almost impossible to induce a vitamin E deficiency through the consumption of a vitamin E deficient diet. However, evidence of vitamin E deficiency is sometimes seen in intestinal malabsorption syndromes and in low birth weight infants whose blood levels are low for the first month or so of life. Because these conditions are rare, however, it is assumed that under normal circumstances enough vitamin E is supplied by the normal diet and that there is no need for a supplement (Table 16.4).

Accumulating evidence suggests that vitamin E may reduce the risk of heart disease by protecting low density lipoprotein (LDL) against oxidation. The oxidative modification of LDL, which carries cholesterol to the tissues, appears to play an important part in the process of atherosclerosis. Oxidised LDL is taken up more readily than native LDL by macrophages to create foam cells. Vitamin E can inhibit the oxidative modification of LDL *in vitro* and *in vivo*. Recent studies of cohorts of men and women health care professionals in North America have raised the possibility that up to 100 mg of vitamin E a day (which cannot be obtained from food alone) may reduce the risk of death from coronary heart disease. Other studies on less well advantaged individuals are not supportive of these findings. Most prospective epidemiological studies suggest that vitamin E intake is in itself not related to overall risk of cancer, but that low serum levels of vitamin E, particularly when coupled with low serum levels of selenium, may increase the risk of some cancers, namely lung and cervical cancers (Knekt 1994).

Table 16.3 Food sources of vitamin D, functions, deficiency states, benefits and toxicity

Food source	Vitamin D (μg/100 g)	Notes	RDI
High		1 Maximum of 40% loss in cooking.	Infants and young children: 400 IU (10 μg). No dietary recommendation is made for normal healthy adults in Australia because their needs seem to be satisfied by the action of sunlight. In the USA a recommendation for vitamin D is given of 5 μg per day for both men and women.
cod liver oil	210	2 Stable to heat, ageing and storage.	
Medium			
fatty fish	5–25		
margarine	8		
Low			
egg yolk	5		
butter	1		
cheese	0.2		
milk	0.01		

Functions

1. Absorption of calcium and phosphorus. Aids the absorption of calcium from the small intestine and bone and reabsorption from the kidney; increases the permeability of the cell to both calcium and phosphorus.
2. Bone formation. Increases the rate calcium and phosphorus form and maintain bone. (Vitamins A and C are also involved in bone formation.)
3. Cellular differentiation—reduces excessive cell division (Jordan et al. 1993).
4. Modulates immune function.

Deficiency (Hypovitaminosis D)

Clinical signs include:

Rickets in children. Mineralisation of bone matrix is impaired and collagen synthesis is defective (largely due to inadequate absorption of calcium and phosphate). When this condition occurs in the adult it is known as *osteomalacia*.

Deficiency rarely occurs in Australia since exposure to sunlight is not a problem, but infants, young children, the elderly or invalids may be at risk if not exposed to sunlight, especially in the winter months. In adults deficiency is usually secondary to:

1. Malabsorption syndromes.
2. Gastrectomy. Osteomalacia can occur as a complication of removal of the stomach.
3. Diseases of the liver and kidney. Activation of vitamin D requires a functioning liver and kidney.
4. Skin disorders.
5. Medication. Prolonged treatment with phenobarbitone (sedative) may induce deficiency.

Possible benefits

1. May help prevent osteoporosis.
2. May reduce cancer risk and enhance immunity.

Toxicity (Hypervitaminosis D)

Excessive intake can be hazardous. Most reports of toxicity induced in children range from 25 000 to 60 000 IU/day for 1 to 4 months. Clinically characterised by loss of appetite, headache, nausea, vomiting, intense thirst and polyuria, calcification of soft tissues such as lung and kidney, bone disease and death.

Vitamin K

Two forms of vitamin K occur naturally: vitamin K-1 or phylloquinone, which is found in green plants, and vitamin K-2 or menoquinone, which is synthesised by the intestinal bacteria and is also found in small amounts in animal tissue. A third form of the vitamin, vitamin K-3, menadione, is a synthetic product. It has been estimated that approximately half of the vitamin K needed by the body can be obtained from the bacteria inhabiting the gut, while the remainder can be obtained from the diet. Vitamin K is widely distributed in food; good sources include green leafy vegetables, soy beans and wheat bran. Fruit and most animal products contain little vitamin K. A recommended dietary intake of vitamin K has generally not been available, because it is difficult to establish the amount required from food since the amount produced by gut bacteria is likely to vary. Deficiency is extremely rare, however, except under the conditions indicated in Table 16.5. An adequate vitamin K status is probably ensured both because the intestinal bacteria constantly produce a supply and the amount the body needs is very small. A diet consisting of a wide variety of foods would provide approximately 300 μg to 500 μg of vitamin K daily, and this compares well with the estimated safe and adequate range of uptake which is from 70 μg to 140 μg for men and women.

Table 16.4 Food sources of vitamin E, functions, deficiency states, benefits and toxicity

Food source	Vitamin E* (mg/100 g)	Notes	RDI
High		1 Maximum 55% loss in cooking.	Adults and children 8 years and over 7–10 mg/day. A daily diet consisting of a wide variety of food would provide 8–11 mg of α-tocopherol equivalents. An alternative recommendation taking into consideration the polyunsaturated fat content of the diet is 0.4 mg vitamin E/g polyunsaturated fat.
wheatgerm oil	140	2 Sensitive to heat, oxygen and decomposes in sunlight.	
polyunsaturated vegetable oils	20–80	3 Some loss during freezer storage.	
Medium		4 Presence retards spoilage of unsaturated fats and β-carotene.	
peanut oil	15–20		
olive oil	5		
nuts, seeds wholegrains	1–20		
Low			
milk	0.02		

Functions

1 In the body.
   (a) Acts as a tissue antioxidant protecting the lipid membrane of cells against oxidant damage. In the same way it preserves the integrity of red blood cells and protects β-carotene and unsaturated fatty acids from oxidative breakdown.
   (b) May be involved in the formation of haemoglobin.
2 In food. Acts as an antioxidant by preventing the oxidation and breakdown of PUFA. Effective synthetic antioxidants appear to eliminate the need for vitamin E as an antioxidant in food.

Deficiency (Hypovitaminosis E)

There is the possibility of haemolytic anaemia in low birthweight infants and in malabsorptive states. Deficiency has not been reported in Australian adults but may occur in:
1 Low birthweight infants given formula feeds low in vitamin E. They may develop a form of haemolytic anaemia associated with low blood levels of vitamin E.
2 Possibly in malabsorption syndromes such as cystic fibrosis.

Possible benefits

1 May reduce risk of angina and heart attack.
2 May slow macular degeneration.
3 May prevent spinal cord damage in patients with cystic fibrosis.

Toxicity (Hypervitaminosis E)

Relatively non-toxic, though some adverse effects have been observed with daily intakes of 300 mg of synthetic α-tocopherol. Symptoms include severe influenza, malaise, fatigue and gut disturbances. An unbalanced ration of vitamin E and K may lead to impairment of blood coagulation in humans.

* Total vitamin E activity estimated to be 80% α-tocopherol and 20% other tocopherols

WATER SOLUBLE VITAMINS

Thiamin (vitamin B-1)

Thiamin (vitamin B-1) is widely distributed in a large variety of animal and vegetable sources, but is present only in relatively small amounts in most of them. Yeast and the yeast extract (for example, Vegemite) are the richest food sources, but are usually eaten in small amounts. Because refining cereal products removes thiamin, restoration to bread and cereals is permitted in Australia to ensure that daily requirements are met (Table 16.6).

Since thiamin is a water soluble vitamin, storage in the body is limited and this leads, therefore, to a constant requirement for the vitamin; compared with fat soluble vitamins, only short periods of deprivation will lead to deficiency. The principal role of thiamin in the body is as a co-enzyme in reactions that release energy from carbohydrates and trap it in the energy-laden compound ATP (adenosine triphosphate). The daily thiamin requirement, therefore, is proportional to the amount of energy consumed (particularly from carbohydrate sources). The recommended daily intake is usually expressed in terms of energy intake, that is, 0.1 mg/1000 kJ for all age groups. There are bacteria in the large intestine with the ability to synthesise thiamin but its absorption into the body is minimal.

The group most likely to develop a thiamin deficiency in Australia is those who chronically drink alcohol to excess (a regular daily intake of at least 40 g alcohol) and who eat little or no food for extended periods of time (Table 16.6). Where rice is a staple and not parboiled, thiamin deficiency is also a risk.

Table 16.5 Food sources of vitamin K, function, deficiency states, benefits and toxicity

Food source	Vitamin K (μg/100 g)	Notes	RDI
High		1 Maximum 5% cooking loss.	No recommendation for vitamin K intake has been made in Australia. Estimate of daily requirement is about 2 μg/kg body mass (half of this may be supplied by gut bacteria). In the USA the safe and adequate range of intake for vitamin K is estimated to be between 70 μg to 140 μg/day for men and women.
spinach	240	2 Sensitive to light, oxygen and both acid and alkaline conditions.	
soy beans	190		
cabbage	100	3 Also found in corn and soy bean oils.	
Medium			
bran (wheat)	80		
green beans	20		
pork liver	20		
Low			
oranges	less than		
apples	5		
Function	Clotting of blood. 1 Involved in the synthesis of certain blood clotting factors in the liver (clotting factors II, VII, IX and X are vitamin K dependent proteins). 2 Through the action of these clotting factors, vitamin K may influence calcium metabolism in various parts of the body.		
Deficiency (Hypovitaminosis K)	Haemorrhage. The time that blood takes to clot is delayed and may result in a tendency to bleed; if this occurs in the infant it is called haemorrhagic disease of the newborn. Deficiency in Australian adults is rarely seen but may occur in: 1 Newborn and low birthweight infants which have limited stores of vitamin K (due to low vitamin K stores in the mother). Since the intestinal tract is sterile, haemorrhage may occur during the immediate postnatal period. 2 Malabsorption syndromes such as diseases of the pancreas, intestines or alcohol abuse may prevent adequate absorption. 3 Liver diseases may reduce synthesis of clotting factors despite adequate vitamin K. 4 Medications. Certain antibiotics (neomycin) can reduce the content of bacteria in the gut (but is rare as a cause of deficiency). 5 Anticoagulant therapy (warfarin) can lead to a bleeding tendency if dietary vitamin K is poor or supply from the gut bacteria is reduced or both.		
Possible benefits	1 Possible role in cancer prevention. 2 Regulation of bone metabolism.		
Toxicity (Hypervitaminosis K)	Potentially toxic if given in large doses over a prolonged period of time.		

Riboflavin (vitamin B-2)

Riboflavin is found in small amounts in a wide variety of animal and vegetable food sources. The most important in the Australian diet are milk and dairy products. Other good sources include breakfast cereals, organ meats and nuts (Table 16.7). Once absorbed from the small intestine, riboflavin must be converted (by the addition of phosphate) into its active form. It is a constituent of all metabolising cells but, as with thiamin, there is limited storage in the body. Excess riboflavin is excreted by the kidneys in the urine, a possible explanation for its low toxicity. (See Figures 16.4 and 16.5, and Table 16.7.)

Niacin (vitamin B-3)

Two forms of this vitamin have been identified: niacin (nicotinic acid) and niacinamide (nicotinamide). The best dietary sources of niacin are foods rich in protein, such as organ and muscle meats, poultry, legumes and peanuts (Table 16.8). Niacin can also be made in the body from tryptophan, an amino acid obtained from animal and vegetable protein sources. It has been estimated that approximately 60 mg of the precursor tryptophan is needed to produce 1 mg of niacin in the body. This relationship between niacin and tryptophan has been taken into account in the development of the unit known as the niacin equivalent (NE). The niacin equivalent of a diet is calculated as follows:

Table 16.6 Food sources of thiamin, function, deficiency states and toxicity

Food source	Thiamin (mg/100 g)	Notes	RDI
High		1 Maximum loss during cooking is 80% (usual loss in cooking of mixed diet is about 25%, e.g. toasting bread, but if the cooking water is discarded the loss is greater). 2 Sensitive to heat, light and alkaline conditions. In refining cereal products some of the vitamin can be lost. 3 Some foods contain thiamin antagonists (tea, coffee, etc.) and enzymes that break down thiamin (raw fish).	Expressed in terms of energy intake: 0.1 mg/1000 kJ for all ages. Varies from 0.4 mg per day for infants to 1.1 mg per day for adults.
brewers yeast	12.0		
Vegemite	9.7		
Medium			
lean pork (raw)	0.9		
legumes	0.4		
wholemeal bread	0.26		
white bread	0.18		
Low			
polished rice	trace		
Function	Functions as a coenzyme in at least 24 enzyme systems, many of which are involved in the release of energy from carbohydrate, protein and fat.		
Deficiency (Hypovitaminosis B-1)	Frank deficiency is known as beri-beri. Clinical effects are reflected in: 1 Gastrointestinal symptoms, such as loss of appetite, indigestion, vomiting, loss of muscle tone. 2 Nervous system symptoms called dry beri-beri. Results in impairment of sensation, loss of reflexes, difficulty in movement, partial paralysis. When symptoms are accompanied by oedema it is termed wet beri-beri. Brain involvement is termed Wernicke's encephalopathy, with symptoms of involuntary eye movement, muscular uncoordination and mental deterioration, which may progress to Korsakoffs psychosis if untreated. This is characterised by memory defect and confabulation (making up stories to cover loss of memory). 3 Cardiovascular symptoms: cardiac failure unlike that caused by other forms of heart disease. Deficiency in Australia occurs mainly among chronic alcoholics and is probably one of the most common vitamin deficiencies. Other causes of deficiency include: 1 Kidney disease (renal dialysis patients in particular). 2 Long-term intravenous feeding with a nutrient formula inadequate in thiamin. 3 Consumption of large amounts of thiamin antagonists or large amounts of food containing thiaminase (e.g. raw fish).		
Toxicity (Hypervitaminosis B-1)	Large doses taken orally appear safe, but large doses administered intravenously have produced symptoms of shock.		

dietary niacin + (0.16 x dietary protein in grams) expressed as milligrams = niacin equivalent (mg).

The roles of niacin and riboflavin in cell metabolism are closely related and clinical evidence of both deficiencies is often seen in the same individual (see Table 16.8). The niacin deficiency disease pellagra produces the symptoms of diarrhoea, dermatitis, dementia and eventually death.

Vitamin B-6

Vitamin B-6 occurs naturally in food in three forms: pyridoxine, pyridoxal and pyridoxamine. It is widely distributed in a variety of animal and plant food sources: legumes, nuts, potatoes and bananas are among the best sources of pyridoxine; pork, fish and organ meats are the richest sources of pyridoxal and pyridoxamine. The bioavailability of vitamin B-6 varies with the type of food and losses can occur during storage and preparation. As vitamin B-6 is involved in protein metabolism, the need for it varies with protein intake; consumption of a high protein diet increases the need for vitamin B-6. The amount of vitamin B-6 required is small and deficiency is rare. Symptoms of deficiency resemble those of pellagra and can lead to niacin deficiency, since vitamin B-6 is required for the conversion of tryptophan to niacin as well as for folate metabolism. The present recommendation for Australian adults allows for an intake of 100 g or more of protein daily.

Unlike other water soluble vitamins, vitamin B-6 is stored in muscle tissue. It is not safe to consume large amounts of this vitamin. The recommended upper limit in Australia should probably not exceed 10 mg daily on a regular basis (see Table 16.9). A 'sensory neuropathy'

Table 16.7 Food sources of riboflavin, function, deficiency states and toxicity

Food source	Riboflavin (mg/100 g)	Notes	RDI
High		1 Maximum loss during cooking is 75%.	Expressed in terms of energy intake: 0.12 mg/1000 kJ for all ages. Varies from 0.5 mg/day for infants to 1.4 mg/day for adults.
Vegemite	14.3	2 Sensitive to light and alkaline conditions. Milk, an important source, if exposed to light for about 2 hours may lose at least half of its riboflavin content.	
lamb's liver (fried)	4.4		
cornflakes	2.1		
Medium			
milk	0.2		
cheese (cheddar)	0.5		
Low			
potato (boiled)	0.03		
apple	0.02		
Function	Functions as part of a group of enzymes called flavoproteins, which are involved in: 1 Cell respiration. 2 Release of energy from carbohydrate, protein and fat.		
Deficiency	Deficiency causes damage to a variety of body tissues, clinically characterised by: 1 Pallor and cracking of lips (cheilosis) and at the angles of the mouth (angular stomatitis). 2 Smooth tongue (glossitis). 3 Failure of growth in children. 4 Eye and visual disturbances. 5 Conjunctivitis and greasy, scaly dermatitis affecting nasolabial folds. These features often occur in multiple deficiencies of the B complex and are not specific to riboflavin deficiency. There is no evidence of riboflavin deficiency in Australia. (Dietary deficiency of riboflavin is usually associated with a deficiency of other B-group vitamins.)		
Toxicity	Large doses taken orally appear safe.		

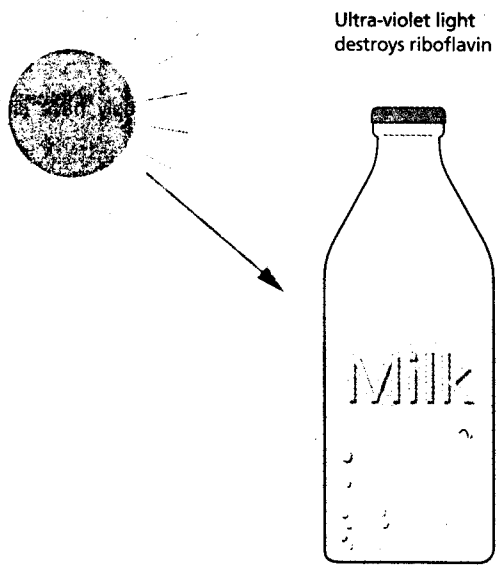


Figure 16.4 Riboflavin is one of the B-vitamins that is susceptible to destruction by the action of the ultra-violet rays in sunlight. Milk left in sunlight may lose a significant proportion of its riboflavin content

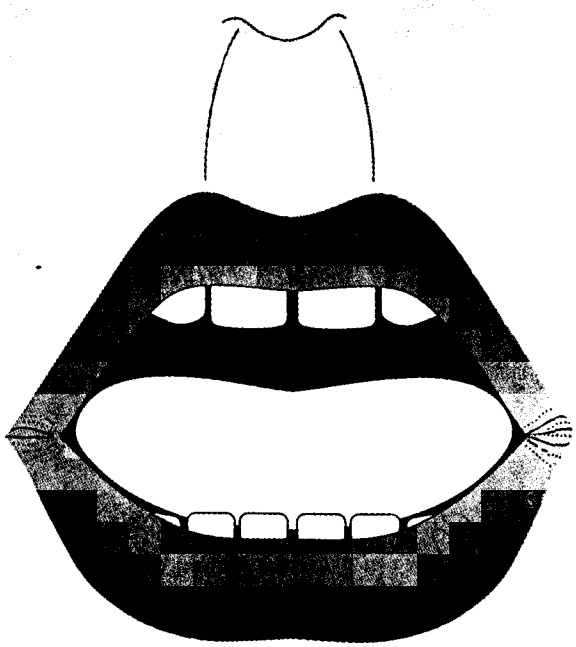


Figure 16.5 Angular stomatitis caused by riboflavin deficiency

Table 16.8 Food sources of niacin, function, deficiency states, benefit and toxicity

Food source	Niacin (mg/100g)	Notes	RDI
High		1 Maximum loss of 75% during cooking.	Expressed in terms of energy intake: 1.6 mg niacin equivalents/1000 kJ for all ages.
Vegemite	110	2 Relatively stable to heat, light and alkaline conditions.	
bran (wheat)	29.5	3 Milk is a good source of precursor tryptophan.	
Ovaltine	18	4 Niacytin (a bound form of niacin) in wheat, corn and rye is unavailable to the body for biological purposes.	
Medium			
peanut butter	15		
lambs liver (fried)	15		
beef	2.5–5.5		
Low			
vegetables	trace to		
fruit and milk	4.5		
eggs	trace		

Function	Functions as part of the co-enzyme nicotinamide adenine dinucleotide (NAD) and is involved in: 1 Cell respiration. 2 Metabolism of carbohydrate, protein and fat.
Deficiency	Frank deficiency is known as pellagra and is characterised by the three Ds: 1 Dermatitis (pigmented and scaly skin) develops on areas of the body exposed to sunlight. 2 Diarrhoea. 3 Dementia (rare). Early symptoms include: loss of appetite, indigestion, weakness, anaemia, glossitis. (All of these can be found in association with other vitamin deficiencies.)
Possible benefit	Possible cancer inhibitor.
Toxicity	Large doses of nicotinic acid (100–200 x RDI) have pharmacological effects such as: 1 Lowering of blood cholesterol and triglyceride. 2 Increasing blood high density lipoprotein, HDL (which appears to be protective against heart disease). Undesired side effects include 'flushing', gastrointestinal disturbances.

(damage to nerve fibres conducting sensation) has been described with intakes of 200 mg daily which some supplements contain. There is limited evidence that premenstrual tension may be ameliorated by vitamin B-6 supplements. It is in this situation that the individual must be careful not to take excessive amounts.

Pantothenic acid

Pantothenic acid (or pantothenate) is very widely distributed in food, primarily in the form of co-enzyme A and its derivatives; liver, kidney and eggs (especially the yolk) are among the best sources. Because of this, dietary deficiency of pantothenic acid has not been reported in humans, and only experimental deficiency, using a vitamin antagonist, has been described. A recommendation for dietary intake of pantothenic acid has therefore not been made in Australia and an average varied diet provides 5 mg to 10 mg which is regarded as being adequate for most children and adults. Intestinal bacteria synthesise this vitamin, but the availability to the body from this source is unknown (see Table 16.10).

Biotin

There are eight isomers of biotin, but only one has vitamin activity. It is present in a variety of foods and good sources include egg yolks, brewers yeast, soy beans and liver; lesser amounts occur in meat, fruit and vegetables. Significant amounts of biotin are produced by intestinal bacteria, which makes the dietary requirement uncertain. An average varied diet is likely to contain between 50 mg and 300 mg of biotin per day, and appears to meet the needs of most healthy adults (Table 16.11).

Folacin (folic acid)

Folacin is the generic name for many compounds that exhibit the biological activity of folic acid (pteroylglutamic acid or PGA). Folacin is a provitamin

Table 16.9 Food sources of vitamin B-6, function, deficiency states, benefit and toxicity

Food source	Vitamin B-6 (mg/100 g)	Notes	RDI
High		1 Maximum loss of 40% during cooking.	Adults and children 8 years and over 1.0–2.2 mg/day based on: 0.015–0.020 mg/g protein per day for all ages, from a mixed diet providing 10% to 15% of energy from protein.
Vegemite	3.0	2 Sensitive to light, air or oxygen and alkaline conditions.	
walnuts	0.7		
bananas	0.5		
lamb's liver (fried)	0.5		
Medium			
chicken/fish	0.2–0.5		
egg yolk	0.3		
potatoes	0.2		
Low			
milk	0.04		
apples	0.02		

Function

Functions as a co-enzyme for many different systems involved in:

1 Synthesis and metabolism of proteins such as serotonin; synthesis of niacin from tryptophan; and the formation and growth of red blood cells.
2 Release of energy from carbohydrate and fat.

Deficiency

Clinical symptoms of deficiency are not specific but may include:

1 Central nervous system disturbances such as irritability, mental depression, convulsive seizures, abnormal brain wave pattern and conduction of nerve impulses.
2 Dermatitis, similar to that seen in pellagra.
3 Cheilosis, angular stomatitis and glossitis.
4 Sideroblastic anaemia is responsive to vitamin B-6.
5 Immune deficiency; impaired antibody formation.
6 Renal calculi (kidney stones).

Deficiency is rare in Australia but groups at risk include:

1 Infants; the ratio of vitamin B-6 to protein may be low in some breast milk and cow's milk.
2 Alcoholics, the incidence may be in the order of 20% to 30%.
3 Women on oral contraceptives, especially those containing oestrogen.
4 Vitamin B-6 dependent syndromes, genetic abnormality requiring large amounts of vitamin B-6 to prevent convulsions, seizures, mental retardation.
5 Thyroid disease (overactive thyroid gland).
6 Certain medications inactivate vitamin B-6, including isoniazid and penicillamine.

Possible benefit

1 May protect against heart disease.

Toxicity

Toxicity is low but regular and prolonged intake of large amounts can induce:

1 Dependency on vitamin B-6.
2 Interference with the action of certain drugs such as L-dopa (used in Parkinsonism).
3 Sensory neuropathy leading to problems in walking with doses of about 200 mg per day.

which must be converted to its biologically active form by the body; folic acid is one of the active forms. The different forms of folacin vary widely in biological activity, stability and availability to the body. In animal foods, such as liver, most of the folate is present as 5-methyltetrahydrofolate or 'free form', which is readily absorbed unaltered in the duodenum and jejunum of the small intestine. In plant foods, most of the folacin is present as polyglutamates by being conjugated with the amino acid glutamic acid. This 'conjugated form' has to be hydrolysed to monoglutamate prior to absorption. Hydrolysis is carried out by the enzyme folate conjugase, probably in the lumen of the gut by intestinal bacteria. The larger the number of glutamate residues in the polyglutamate chain, the less well the compound is absorbed.

The availability of folates from foods is poorly understood, and the poor absorption of polyglutamates from the gut may have been exaggerated. The distinction between free folate and conjugated folate is now considered less useful. The recommended intake for folacin in Australia is now based on *total* folacin—this includes the 'free forms' plus the 'conjugated forms'. Small amounts of folacin are synthesised by

Table 16.10 Food sources of pantothenic acid, function, deficiency states and toxicity

Food source	Pantothenic acid (mg/100 g)	Notes	RDI
High		1 Maximum loss of 50% during cooking.	No recommendation has been made in Australia. 4 to 7 mg/day for adults have been estimated to be safe and adequate (USA). Intestinal bacteria synthesise small quantities.
lamb's liver (fried)	7.6	2 Sensitive to heat and both acidic and alkaline conditions.	
egg yolk	4.6	3 Considerable amounts are lost during the milling of cereal grains.	
broad beans (boiled)	3.8		
Medium			
lobster (boiled)	1.6		
apricots	0.7		
beef	0.5–0.8		
milk	0.4		
Low			
pear	.05		
french beans (boiled)	.07		

Function	Functions as part of the acetyl carrier co-enzyme A and acylcarrier protein (ACP) and is involved in many key chemical reactions in the body. Some of these include: 1 Energy release by metabolism of carbohydrate, protein and fat. 2 Synthesis of amino acids, fatty acids, sterols (such as cholesterol), steroid hormones and vitamin D. 3 Formation of red blood cells, haemoglobin. 4 Formation of acetylcholine (neurotransmitter).
Deficiency	Clinical signs of deficiency have been recorded only under experimental conditions and include: 1 personality changes 2 irritability, restlessness 3 fatigue Evidence of dietary deficiency has not been recognised in humans, though marginal deficiencies may exist along with deficiencies of other B-complex vitamins.
Toxicity	Toxicity is low, however some studies indicate that daily doses of 10 g to 20 g may result in diarrhoea and fluid retention.

bacteria in the human intestine. Folacin occurs widely in a variety of foods including leafy vegetables, liver, citrus fruit and nuts, which are particularly good sources. Because bread and other cereals, especially wholegrain, may be eaten in significant quantities by some people, these foods may provide the majority of folacin. Studies suggest that between 25% and 50% of folacin is absorbed from a diet containing a variety of foods (Table 16.12).

Folacin deficiency impairs cell division and protein synthesis. Without folate, DNA synthesis slows and cells lose their ability to divide. In folacin deficiency, the replacement of red blood cells and GI tract cells falters—therefore, two of the first symptoms of folacin deficiency are anaemia, characterised by large, immature blood cells (macrocytic anaemia, Figure 16.6), and GI tract deterioration. Furthermore, folacin deficiency (along with vitamin B-6 and B-12 deficiencies) may, even when marginal by usual criteria of its blood level, lead to an increase in homocysteine concentrations in the blood (homocysteinaemia), which can be toxic to blood vessels and increase the risk of thrombosis. In this way, micronutrient deficiency may contribute to a major non-communicable disease, cardiovascular disease leading to stroke and ischaemic heart disease.

Neural tube defects (NTD) may also be caused by folic acid deficiency. It is clear that up to 60% of NTD may be preventable by an adequate intake of folic acid before conception and throughout pregnancy, probably as much as 400 µg daily supplements. We do not know if fortifying the food supply will achieve the same outcome. For example, will the women whose pregnancies are at risk actually consume the fortified foods? What about those who will then consume more than 1000 µg daily? Also, in some countries, the increased intake of folic acid may increase the risk of malaria, mask vitamin B-12 deficiency and make anticonvulsant therapy less effective. Folic acid may also have a role in preventing certain cancers, notably cervical cancer in women, although not all studies agree. This is one situation in which megadoses may be required, although lesser amounts need more evaluation.

Table 16.11 Food sources of biotin, function, deficiency states and toxicity

Food source	Biotin (mg/100 g)	Notes	RDI
High		1 Maximum loss of 60% during cooking.	No recommendation has been made in Australia. 100 mg to 200 mg/day has been estimated to be safe and adequate (USA). Intestinal bacteria produce significant amounts for absorption.
brewers yeast	200	2 Sensitive to alkaline conditions as well as oxygen.	
egg (yolk)	60	3 Avidin, an anti-vitamin found in raw egg white, inactivates biotin.	
soy beans	60	4 Biotin in wheat is in a bound form and unavailable to the body.	
liver	40		
Medium			
wholemeal bread	6		
fish	6–10		
milk	2		
Low			
potatoes	trace		

Function

Functions as a co-enzyme in:

1 The fixation of CO_2 into organic molecules.
2 Linking the metabolism of carbohydrate and fat.
3 Formation of glucose (gluconeogenesis) and fatty acid systhesis.
4 May be involved in the metabolism of vitamin B-12.

Deficiency

Deficiency in humans has been characteristically associated with the consumption of avidin, which is rare. Symptoms include: lethargy, loss of appetite, nausea, vomiting, glossitis, mental depression, dry scaly dermatitis, muscle pain, hypercholesterolemia and changes in the electrocardiogram (ECG).
Groups at risk of deficiency include:

1 Infants below 6 months of age may develop seborrheic dermatitis due to dietary deficiency.
2 Leiner's disease in children, a condition resulting in dermatitis responds to large doses of biotin.
3 Long-term intravenous feeding (total parenteral nutrition).

Toxicity

Toxicity is low.

Vitamin B-12

There are three predominant forms of vitamin B-12 in food: methylcobalamin, adenosylcobalamin and hydroxycobalamin. Vitamin B-12 is supplied almost entirely by animal foods: organ meats, eggs, seafood, dairy products and fermented foods being excellent sources. The occurrence of vitamin B-12 in nature is the result of microbial synthesis, but the amount available from the intestinal bacteria of humans is not known (Table 16.13). Intestinal absorption of vitamin B-12 requires the presence of a molecule called *intrinsic factor*, which is secreted by the stomach and facilitates the transfer of vitamin B-12 into the cells lining the ileum. Calcium is also thought to be necessary for this transfer. The body has a good storage capacity for vitamin B-12, as well as a very efficient method of recycling the vitamin so that the amount needed for normal metabolism appears to be small. The onset of deficiency symptoms due to depletion may be delayed by up to ten years and is rarely seen within two years (Table 16.13).

As vitamin B-12 is required for the activation of folate, vitamin B-12 deficiency manifests as the anaemia of folate deficiency. Giving either vitamin B-12 or folate

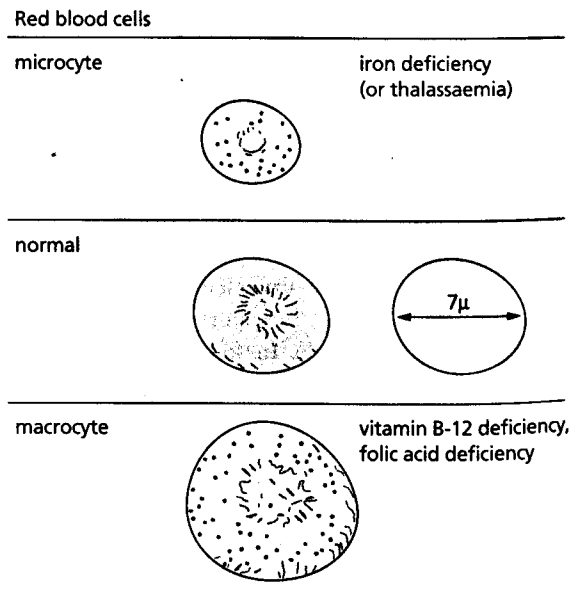


Figure 16.6 Characteristic features of red blood cells with iron, B-12 or folate deficiency

Table 16.12 Food sources of folacin, functions, deficiency states, benefit and toxicity

Food source	Folacin (μg/100 g)	Notes	RDI
High		1 One of the most unstable vitamins and considerable amounts are lost during cooking (up to 100%) either by leaching into the cooking water or destruction by heat. 2 Sensitive to light, air or oxygen. 3 Folacin antagonists in some foods may decrease its availability to the body.	200 μg *total* folacin/day for adults; 400 μg *total* folacin/day during pregnancy (bacteria in the intestines synthesise small amounts of folate for absorption).
cabbage (boiled)	230–430		
lamb's liver (fried)	260		
spinach (boiled)	140		
peanuts	110		
Medium			
peas	78		
egg yolk	52		
oranges	37		
wholemeal bread	30		
Low			
meat	3		
milk	0.3		

Functions	1 Functions as a co-enzyme in the transfer of carbon molecules to various compounds in the synthesis of key materials such as: (a) purines (essential cell components involved in cell division transmission of inherited traits); (b) thymine involved in DNA synthesis; (c) haemoglobin; (d) choline. 2 Involved in the metabolism of protein and fat (functions are closely linked with those of vitamin B-12).
Deficiency	Characteristic and early result of deficiency is macrocytic anaemia (see Figure 16.6) in which the red blood cells are abnormally large. Any frequently dividing cell in the body can be affected: 1 Small intestine defects resulting in malabsorption and deficiency of other nutrients. 2 White blood cells and platelets or during periods of rapid growth such as pregnancy. Clinical manifestation of deficiency has been reported to develop in approximately 16 weeks on low folacin diets. Probably the most common vitamin deficiency in Australia and is seen in: 1 Institutionalised elderly, chronic alcoholics and pregnant women (oral folacin supplementation appears desirable to maintain maternal stores and provide for increased needs of the fetus). 2 Malabsorption syndromes. 3 Medications such as the antitumour drug methotrexate, antimalarial drug pyrimethamine, antibiotics trimethoprim, sedatives and barbiturates.
Possible benefit	May help protect against heart disease, nerve damage, neural tube defects, cervical dysplasia.
Toxicity	Up to 15 mg/day appears to be non-toxic (some reports of aggravation of epileptic symptoms).

can treat the anaemia, but if folate is given when vitamin B-12 is needed, the blood symptoms of vitamin B-12 deficiency would be cured, but the nerve symptoms would progress. By doing so, folate masks vitamin B-12 deficiency. Therefore, the folate supplementation in cereal products may cause a problem in those at risk of vitamin B-12 deficiency, such as the elderly.

Ascorbic acid (vitamin C)

Vitamin C exists in two forms: L-ascorbic acid (most of the vitamin exists in this form) and L-dehydro-ascorbic acid. The best sources of vitamin C include readily available fruits and vegetables. Considerable amounts of the vitamin are also added to the food supply in the preservation of food and in the process of nutrient restoration. For example, ascorbic acid may be added to processed meats, flour and beverages such as fruit juices, drinks and cordials. Ascorbic acid is easily destroyed by high temperatures and exposure to air, drying, alkali and prolonged storage. It is very soluble in water and losses during the preparation and cooking of fruit and vegetables can be considerable.

Clinical scurvy is a rare disease in Australia and most other developed countries. Subclinical deficiency represents a state of 'nutritional risk', but whether it impairs overall health is uncertain. No consistent evidence supports the claims for 'megadose' vitamin C therapy, up to 1 g or more per day. Lack of protective effect of vitamin C against the common cold

Table 16.13 Food sources of vitamin B-12, functions, deficiency states, benefits and toxicity

Food source	Vitamin B-12 (μg/100 g)	Notes	RDI
High		1 Maximum loss of 10% during cooking.	2.0 μg/day for adults and children from 11 years of age. Intestinal bacteria produce vitamin B-12 but this is not absorbed to a significant extent.
lamb's liver (fried)	81	2 Sensitive to alkaline conditions but stable to heat, light, oxygen and acid.	
sardines	28		
oysters	15		
Medium			
egg yolk	4.9		
fish	1.5		
beef	1.2		
cheese	1.2–1.5		
Low			
vegetables	0		
fruit	0		

Functions	1 Functions as a co-enzyme in amino acid metabolism and in the synthesis of nucleic acids, e.g. DNA and RNA. This is especially important in the: (a) bone marrow, where the red blood cells are formed; (b) nerve tissue, where vitamin B-12 is involved in the breakdown of certain fats. 2 Vitamin B-12 acts indirectly on red blood cell formation through the activation of folacin co-enzymes.
Deficiency	Characteristic result of deficiency is: 1 Pernicious anaemia: a chronic, macrocytic type of anaemia (similar to that seen in folacin deficiency). Symptoms include lethargy, dyspnoea, loss of appetite and weight, pallor, lemon-yellow appearance of the skin. 2 Neurological disturbances. Groups at risk of nutritional deficiency: 1 Strict vegetarians (vegans) who eat no animal products, milk or eggs. 2 Newborn infant of the vegetarian (vegan) mother, where the newborn has insufficient stores of the vitamin and the breastmilk may be a poor source. 3 Methylmalonic acidaemia, an inherited defect in vitamin B-12 metabolism. 4 After surgical removal of part of the stomach which produces the intrinsic factor or part of the ileum where absorption takes place.
Possible benefits	1 May protect against heart disease and nerve damage. 2 May protect against neural tube defects in fetuses during the first six weeks of pregnancy.
Toxicity	Very low toxicity in doses up to 1000 times the RDI.

(symptoms of the cold were reduced but not frequency of events), was reported in a controlled study of twins in Sydney, in which 500 mg daily was taken at the time the infection was encountered. These amounts are within reach of the human diet without supplementation, although good sources, like papaya and plentiful orange juice, would have to be taken. Many of the original claims of beneficial effects of large doses of vitamin C have not been substantiated and since high dosages can have adverse effects, recommendations to the general public to increase intake of vitamin C to gram amounts is unjustified on the basis of the available evidence (Table 16.14). Excessive intake of vitamin C is implicated in development of diarrhoea and other gastrointestinal disturbances, kidney stones, withdrawal scurvy, dental erosion and increased toxicity of certain metals such as iron. The past two decades have seen substantial growth in interest in the role of antioxidants (for example, vitamins A, C and E) in health and disease prevention (see also Chapters 27 and 32). The antioxidant functions of vitamin C include scavenging oxygen free radicals (which can cause cellular damage), and in regenerating vitamin E from the tocopheroxyl radical. High intakes of vitamin C have been linked to a reduction in risk of certain cancers (especially gastric) and cataracts. However, intakes of vitamin C above 500 mg/day may actually be pro-oxidant and damage DNA. A limited number of reports suggest that very low intakes and poor status of vitamin C are associated with an increased risk of mortality from coronary causes (Enstrom 1992). At present the RDIs in Australia for these antioxidants may be less than adequate to

Table 16.14 Food sources of vitamin C, functions, deficiency states, benefits and toxicity

Food source	Vitamin (mg/100 g)	Notes	RDI
High		1 Maximum loss of 100% during cooking.	1 30 mg to 40 mg/day for adults.
blackcurrants	200	2 Sensitive to heat, light, oxygen and alkali such as bicarbonate of soda.	2 10 mg/day will prevent and cure clinical signs of scurvy.
green peppers	100	3 Use of copper cookware can destroy vitamin C.	
orange juice (fresh)	50		
lemon	47		
Medium			
cauliflower	20		
brussels sprouts	35		
cabbage	20		
spinach (all cooked)	20		
Low			
milk (cow's)	2		
beef	0		

Functions

1 Maintenance of body connective tissue: involved in the formation of hydroxyproline in the synthesis of collagen, a connective tissue of bone, muscle, joints, etc.
2 Brain and nerve function: involved in the formation and breakdown of noradrenaline and serotonin (neurotransmitters).
3 Muscle function through formation of carnitine.
4 Also involved in:
(a) energy release from fatty acids;
(b) increased intestinal absorption of iron;
(c) cholesterol metabolism;
(d) formation of thyroid hormone;
(e) folic acid metabolism;
(f) reduction of nitrosamine formation in the stomach;
(g) antioxidant.

Deficiency (Hypovitaminosis C)

Frank deficiency is known as scurvy and is characterised by defective collagen synthesis and a tendency of blood vessels to bleed. Other symptoms: bruising, delay in wound healing, ulcers, drying of skin and mucous membranes, susceptibility to infections, anaemia, muscle weakness and fatigue.
It takes several months on a diet deficient in vitamin C for scurvy to develop.
Scurvy is uncommon in Australia but may occur in:
1 Newborn infants of mothers who have ingested large doses of vitamin C adapt to the elevated level prenatally, and may suffer scurvy after birth.
2 Young children fed exclusively and for a prolonged period on cow's milk.
3 Institutionalised elderly: Recent studies indicate that 30% have low blood levels of vitamin C.
4 Chronic alcoholics.
5 Cigarette smokers, those on large doses of aspirin and oral contraceptive users have been reported to have low blood levels of vitamin C.
6 Nutritional ignorance combined with poor cooking and eating habits is usually associated with deficiency.

Possible benefits

1 May help reduce the risk of certain cancers and heart disease.
2 Retards macular degeneration in the eyes of the elderly.

Toxicity (Hypervitaminosis C)

Toxicity is low. Risks of megadose therapy include:
1 Rebound scurvy may occur after discontinuation of megadoses of vitamin C.
2 Oxalate stone formation in the kidney and bladder with daily intake in excess of 8 g.
3 Gastrointestinal disturbances, nausea/abdominal cramps/diarrhoea usually before meals.
4 Blood clotting.
5 Vitamin B-12 deficiency may occur if intake of vitamin C is high.
6 Toxic metal absorption such as mercury may increase.
7 Alteration of action of certain drugs such as warfarin (anticoagulant), aspirin, antidepressants and the contraceptive pill.
8 Increased absorption of iron may cause problems in individuals susceptible to iron overload.

promote optimal health. It has been suggested that intakes two to three times higher than the current RDIs for these vitamins are a useful objective for protection against these diseases. Such intakes are now commonly achieved through the liberal use of citrus fruits and drinks, along with other fruits and vegetables (and without recourse to supplements).

Vitamin C also reacts readily with nitrous acid (preservative added to cured meats such as ham and salami) and appears to act as a scavenger of nitrite in the stomach, preventing the conversion of nitrite to the carcinogenic compound nitrosamine. Exactly how important this is in the prevention of gastric cancer is uncertain.

PHYTOCHEMICALS AND VITAMIN-LIKE COMPOUNDS

Nutritional science has now focused more on the role of specific foods composed of non-nutrient factors, most of which are *phytochemicals* (*plant-based chemicals*). Although the term may include all plant chemicals, it is being applied to chemically minor components and ones that have not already been classified as nutrients for humans. In addition, the term is not being applied to naturally occurring plant toxicants, although as with all factors affecting human biology they will have a safety range (see Chapter 7). These compounds usually exist in plants as secondary metabolites used by the plant for defence and survival. However, they may also appear in animal tissue eaten by humans.

Phytochemicals may almost be regarded as pharmaceuticals rather than dietary nutrients when they are used to manage clinical conditions. This is not surprising as many important drugs available today were, at least initially, derived from plants. An alternative viewpoint is that conditions for which they are used as treatment may have occurred because of inadequate intakes from foods. In future, we may prevent or delay the onset of diseases. The emergence of new familial diseases may reflect a change in food culture, exposing genetic predisposition. The growing array of phytochemicals opens up opportunities for more healthful food choices and for the development of functional foods to serve particular physiological or pathological needs. Phytochemicals may fall into any one of several categories: non-provitamin A—carotenoids, flavonoids and isoflavonoids, polyphenols, isothiocyanates, indoles, sulforaphane, monoterpenes, xanthin and non-digestible oligosaccharides. Detailed consideration is now given to these categories which are undergoing active investigations for their health properties (Table 16.15).

In addition, there is another range of compounds being recognised as *conditionally essential*. This may be because of the following.

1 They are needed in some but not all situations, such as:
   - in early, but not later life
   - growth or tissue repair
   - where they may compensate for the depletion of other nutrients
   - where they provide an additional function for a compound. This applies to taurine, which is an amino acid involved in bile salt conjugation, excretion and turnover, but may also be required for infant retinal function.
2 They are partly synthesised in the body, but in inadequate amounts without a dietary source. This may apply to choline, carnitine and glutathione.

Those discussed here are not a complete list. They reflect a grey area of nutrition where compounds not currently regarded as nutrients, but with biological activity nevertheless, are seen to optimise health and longevity rather than simply prevent disease in the short to medium term, which is the way essential nutrients are conceptualised.

Carnitine

Carnitine may be obtained preformed in the diet or synthesised in the human body, but an exogenous source appears desirable. It is formed from the two essential amino acids lysine and methionine. It was originally found to be essential for the growth of meal worms. It facilitates the transport of fatty acids within cells to sites where they are oxidised. Some dietary carnitine seems required by humans. Good food sources include human colostrum, dairy products, meat and poultry. Because its function is to transport fats into muscle tissue for use as energy, it has been thought that its use will enhance 'fat burning'. Hence it has been suggested for endurance events such as marathons, or even simply for losing weight. Contrary to claims, supplementation with L-carnitine in normal subjects

Table 16.15 Phytochemicals and their possible roles in health

Phytochemical	Some important food sources	Possible roles in health
carotenoids	orange pigmented and green leafy vegetables, e.g. carrots, tomatoes, spinach	■ antioxidants ■ antimutagen ■ anticarcinogen ■ immuno-modulating
polyphenols	cranberries, raspberries, blackberries, rosemary, oregano, thyme	■ antioxidant ■ antibacterial ■ reduce urinary tract infection
catechins	green tea	■ antimutagen ■ anticarcinogen ■ anticariogen
flavonoids and saponins	green leafy vegetables and fruit, e.g. parsley, celery, onions, apple, tea	■ antioxidant ■ anticarcinogen
isoflavonoids	soy bean and soy products	■ oestrogen-like ■ anti-angiogenic ■ immuno-modulating
lignans	linseed, chickpea	■ oestrogen-like
isothiocyanates and indoles	cruciferous vegetables, e.g. broccoli, cabbage	■ antimutagen
allyl sulfinates	garlic, onions, leeks	■ anticarcinogen ■ antibacterial ■ cholesterol lowering
terpenoids including limonene	citrus, caraway seeds	■ anticarcinogenic against mammary tumours
phytosterols, e.g. β-sitosterol	pumpkin seeds	■ reduce symptoms of prostate enlargement
curcumin	turmeric	■ anti-inflammatory
salicylates	grapes, dates, cherries, pineapples, oranges, apricots, gherkins, mushrooms, capsicums, zucchini	■ protective against macrovascular disease ■ modulation of gene expression
L-dopa	broad beans	■ treatment of Parkinson's disease
non-digestible carbohydrates	artichokes, chicory root, murrnong, maize, garlic, oats, fruit, legumes and vegetables	■ stimulate growth of microbial flora ■ cholesterol lowering

Source: Wahlqvist et al. 1998

does not increase performance or enhance fat burning, although it may correct a deficiency in some people. Even if it did have an effect on weight loss or fat burning, this would only be in conjunction with exercise, as it is involved in fat transport during activity.

Carotenoids

Carotenoids are the most abundant and widespread pigments, responsible for many of the brilliant red, orange and yellow colours of edible fruit, vegetables and flowers, as well as the colours of certain animals, such as lobsters and trout. They are a class of hydrocarbons (carotenes) and their oxygenated derivatives (xanthophylls) consisting of eight isoprenoid units. The symmetrical structure of the molecule found in β-carotene and many carotenes has been shown to be a precursor of vitamin A in both humans and animals. Although more than 600 naturally occurring carotenoids have been characterised, only 50 show provitamin A activity. Two pathways have been proposed for the conversion of β-carotene to retinoids in mammals. One is at the central double bond (central cleavage), and the other at one or more of the other double bonds (exocentric cleavage). It has been reported that the molar ratio of retinal to β-carotene ranges from 0.9 to 1.8. Whether this is realised in practice depends on the bio-availability of the β-carotene during absorption.

Humans are not capable of carotenoid synthesis, and are dependent for their carotenoids on those found in the diet. Carotenoids are present in all photosynthetic tissues, but their colours are masked by the chlorophylls also present in the chloroplasts. The reason for the co-existence of the two pigments is that carotenoids prevent the photodynamic sensitisation of chlorophylls, which could destroy the chloroplasts. Carotenoids of fruit, vegetables and animal products are usually fat soluble and are associated with lipid fractions. During digestion, carotenoids are released from complex proteins and then incorporated into micelles and transported to the mucosal cells. Absorption efficiency of carotenoids is known to be affected by the presence or absence of other components in the diet such as dietary fat and protein and by bile salts. Therefore, carotenoids in foods are usually less well absorbed from the intestine than preformed vitamin A. After absorption, provitamin A carotenoids are cleaved in the intestinal mucosal cells to form retinal, which is then reduced to retinol (vitamin A). Some unconverted carotenoids are directly absorbed and pass into the blood where their composition reflects the diet. Major circulating carotenoids in blood are β-carotene, α-carotene, lycopene, β-cryptoxanthin, lutein and zeaxanthin. These carotenoids are transported in human plasma by lipoproteins, predominantly by low density lipoproteins (LDL). It has been suggested that LDL which carries most of the carotenoids in plasma may deliver carotenoids to peripheral cells which express the LDL receptor.

Carotenoids also possess other biological actions, including antioxidant, immuno-enhancement, antimutagenesis and anticarcinogenesis. Owing to the antioxidant property of carotenoids, the possibility exists that these compounds may contribute to protection against coronary heart disease and cataracts which are linked to oxidative stress, lipid peroxidation and free radical damage. Cells involved in the generation of specific immune responses can also be adversely affected by free radicals and products from lipid peroxidation processes. Incubation with β-carotene has been shown to protect human neutrophils against free radicals. It has also been suggested that antioxidant vitamins may play a role in reducing the risk of cancer and in cancer prevention by reducing pre-malignant lesions such as cervical dysplasia, leucoplakia and atrophic gastritis. Carotenoids may play an important role in enhancing an immune response which can lead to reduction of tumour growth, such as breast cancer. Recent studies, however, have also linked β-carotene supplementation with increased risk of certain cancers (see also Chapter 32).

The physiological functions of carotenoids may be highly specialised as indicated, for instance, by the presence of zeaxanthin and lutein in the macula area of the retina in the virtual absence of β-carotene. The macular pigment density could be raised by increasing dietary intake of lutein and zeaxanthin from spinach and corn. These carotenoids accumulated in the retina, and other antioxidant vitamins may help to retard some of the destructive processes in the retina and the retinal pigment epithelium that lead to age-related degeneration of the macula (Snodderly 1995).

Choline

Humans have been made choline deficient by leaving it out of the diet for as little as four weeks. The principal effect of choline deficiency is the development of incipient liver dysfunction (Shils et al. 1994). However, 500 mg choline per day is sufficient to prevent a decline in biochemical measures of choline deficiency. It is likely that choline deficiency increases the risk of liver cancer, perhaps because liver cell turnover increases. Fatty liver develops with choline deficiency and is a reflection of its importance as a part of the phospholipid lecithin in lipoprotein (membrane and plasma) structure, and in the turnover of the molecule carnitine, involved in free fatty acid transport in cells (see below). Choline is a 'quaternary amine' and contains four methyl groups so that it can act as an important methyl donor for many important metabolic pathways. Choline also serves as a precursor for acetylcholine, which is a neurotransmitter (chemical signal from one neurone to another or to an end organ). It is this aspect which has attracted attention in relation to its possible significance in Alzheimer's disease (pre-senile dementia due to plaque formation in the brain). Choline can be synthesised in the body from phosphatidyl-ethanolamine. It is, however, widely distributed in foods, being part of the phospholipid lecithin (Table 16.16). People generally consume about 6 g as lecithin per day. Total choline consumed (free and as lecithin) is about 600 mg to 1000 mg/day (6 mmol to 10 mmol/day). Commercially available lecithin which is used as an additive in processed foods (see Chapter 7) is mainly extracted from soy beans and eggs. When injected intravenously, lecithin has been shown to lower

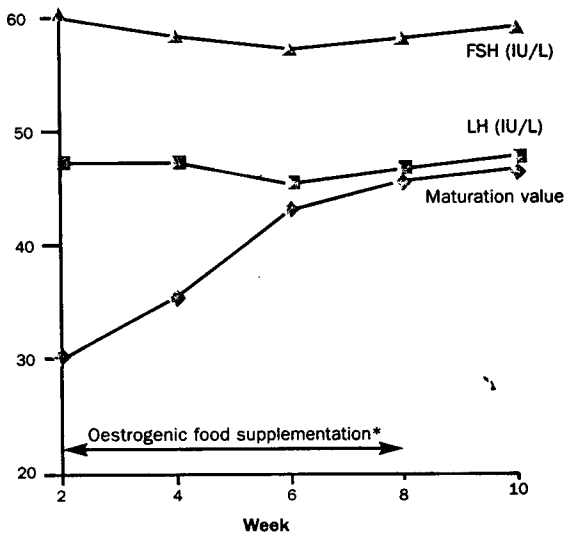
cholesterol in the blood. Taking lecithin orally, however, has not been shown to influence blood cholesterol levels. This is probably because it is not absorbed as such in the intestine. It is broken down principally to lysolecithin and fatty acid. Therefore, the individual cannot directly influence body lecithin by having it in the diet (Wahlqvist & Briggs 1991). Indirectly, the degree and kind of unsaturation of the fatty acid in lecithin may alter blood cholesterol (in soy lecithin it is mainly polyunsaturated and in egg lecithin saturated).

Flavonoids and isoflavonoids

Flavonoids are a large group of polyphenolic compounds that occur naturally in vegetables and fruit and in beverages such as tea and wine. The most important groups of flavonoids are anthocyanin, flavonols, flavones, catechins (e.g. green and black tea) and flavonones. Flavonoids have been studied in relation to their improvement of vascular fragility, their ability to increase cellular permeability and vitamin C-sparing activities. Some flavonoids such as quercetin, kaempferol and myricetin have antimutagenic and anticarcinogenic effects *in vitro* and *in vivo*. In a large number of epidemiological studies investigating relations between diet and cancer, a protective effect of the consumption of vegetables and fruit on various forms of cancer has been found. This protective effect is generally believed to be attributed to vitamin C and carotenoids present in these foods. However, the significance of other potentially protective compounds such as flavonoids present in vegetables and fruit has become an important issue. It appears that a number of the biological effects of flavonoids may be explained by their antioxidative activity and ability to scavenge free radicals. Other mechanisms for their reported anticarcinogenic potential include their capacity to inhibit the promotion phase of carcinogenesis, and to modulate the balance between activation and inactivation processes of specific enzymes in the liver. Isoflavonoids are another group of plant polyphenolic compounds having important antimicrobial activities. A small number of isoflavones, such as genistein, daidzein, display oestrogenic activity in animals and humans (Figure 16.7). This hormonal effect is attributed to the similar spatial arrangement of functional groups on both isoflavones and oestrogens, allowing those isoflavones to bind to the oestrogen receptors (see also Chapter 32). Furthermore, genistein is also found to inhibit endothelial cell proliferation and *in vitro* angiogenesis. Average intake of all flavonoids in the US is estimated to be 1 g (expressed as glycoside). Much more recently, however, it has been reported that the flavonoid intake was 25 mg/d for Dutch elderly men, using results from chemical analysis on content of flavonoids in vegetables, fruit, fruit juice, tea infusions and wines (Hertog et al. 1995). Isoflavonoids occur principally, although not exclusively, in legumes (Leguminosae family). They are at particularly high levels in certain legumes which are regularly consumed by humans and animals. Indeed many traditional human diets which have relatively high legume consumption (such as diets including soy beans, lentils

Table 16.16 Food source of choline (μmol/kg)

	Choline	Lecithin
beef liver	5800	43500
cauliflower	1300	2800
egg	42	52000
lettuce	2900	100
peanuts	4500	5000
potatoes	500	300
tomatoes	400	50
wholemeal wheat cereal	1000	300
coffee	1000	20



*Soy flour (45 g/day), red clover sprouts (10 g dry seed/day) and linseed (25 g/day), each for two weeks in turn

Figure 16.7 Oestrogenic effects of plant foods on pituitary hormones (FSH and LH) and vaginal lining cells maturation value in post-menopausal women (Wilcox et al. 1990)

and chickpeas) consequently have high isoflavone contents, particularly those with oestrogenic activity (see also Chapter 38).

Glutathione

The tripeptide glutathione (γ-L-glytamyl-L-cysteinyl-glycine; GSH) is the most important non-protein thiol present in animal cells and also in most plant and bacterial cells. It is a reducing agent and is a soluble component of the cellular plasma. Reduced glutathione reacts with oxidising agents and is itself oxidised. It has been identified as the major cellular defence against toxic compounds. The glutathione transferases, some of which have peroxidase activity, play a defensive role against oxidative and alkylating mutagens and carcinogens. An important precursor of glutathione is cysteine. Good food sources include fruit (especially oranges) and vegetables (especially potatoes). Poultry and beef also provide significant amounts of glutathione (see Table 16.17). Whey protein is also rich in two of the amino acids found in glutathione and its intake can facilitate the endogenous synthesis of glutathione in various tissues.

Inositol

Brain, heart and skeletal muscles contain large amounts of inositol. Inositol is essential for the growth of cells in tissue culture. Phosphatidyl inositol (PI) is a precursor of eicosanoids which affect a wide range of physiological responses in numerous cell systems. PI is part of phospholipid in cell membranes and gives rise to cell signalling or messenger compounds. Glucose is a precursor of inositol and, evidently, enough can be synthesised from glucose to meet the metabolic needs of humans. Food sources include meats, milk and milk products, and storage forms of phosphate in plant foods, especially wholegrain cereals, nuts, fruits and vegetables.

Table 16.17 Contribution of foods to usual dietary intakes of glutathione

Food	%
orange juice (from concentrate)	10.8
potatoes (other than fried)	7.2
potato chips	6.5
broccoli	4.1
grapefruit	3.7
tomatoes	3.4
bananas	3.3
ham	3.1
apples	2.9
Chinese dishes	2.7
beer	2.4
green salad	2.3
poultry	2.1
carrots, peas	1.6
beef	1.5
fish	1.2
rice	1.1
cauliflower, brussels sprouts	1.1

Source: Flagg et al. 1994

Lipoic acid

Lipoic acid is a sulfur-containing fatty acid. It is an important constituent of co-enzymes involved in biological oxidation and reduction, and is therefore essential for protein, fat and carbohydrate metabolism. Lipoic acid is essential for the growth of some micro-organisms, but it has not been demonstrated to be essential for growth in either animals or humans. Yeast and liver are sources of lipoic acid.

Pyrroloquinolone Quinone (PQQ)

PQQ has recently been identified as a potent growth factor, important for neonatal growth and development. It also has antioxidant properties and the ability to stimulate the immune system. It does not appear to be synthesised by the gut microflora, but may be synthesised in some form by mammalian cells. PPQ is reported to be relatively ubiquitous and is found in human and bovine milk, commercial casein hydrolysates, and vegetable and yeast extracts.

Taurine

This amino acid has long been known for its role in the formation and excretion of bile salts (which are breakdown products of cholesterol). More recently it has been found to play a role in the function of the neonatal retina, and also in cognitive function, especially in the young and old. Foods which contain it in relatively greater amounts are animal derived, including shellfish and crustaceans, but one part of an animal may contain much more than another (e.g. chicken leg more than breast, see Table 16.18).

Table 16.18 Taurine content of meat and internal organs of stock and chicken (mg per 100 g edible portion)

Food	Moisture %	Taurine content
pork, foreham	71	116
tenderloin	76	122
liver	72	42
heart	79	201
kidney	87	120
beef, tenderloin	75	28
hindham	76	64
mutton foreleg	78	200
chicken, breast	72	26
leg	74	379
liver	73	156

Source: Zhao et al. 1994

VITAMIN SUPPLEMENTATION

The idea that vitamins are endowed with miraculous properties still persists, despite all that is now known about their functions. This misunderstanding, together with the belief that it is impossible to obtain all the vitamins we need from our present food supply, has prompted many Australians to supplement their diets with additional vitamins (Mackerras 1995). This trend has increased significantly in recent years. The prevalence of group or family use suggests that there is considerable prophylactic rather than therapeutic use, with the consumption of vitamin supplements as a type of 'nutritional insurance'. Since most consumers are not aware of their vitamin status nor the amount of vitamins present in their diet, they may be using vitamin supplements just to be sure. Many believe that if enough of an essential nutrient is good, then more is better. However, naturally occurring nutrients can cause adverse effects when large amounts are taken for prolonged periods, although they are vital dietary components. Vitamin supplementation for the prevention of diseases unrelated to vitamin deficiency also needs careful evaluation. From available evidence we cannot yet answer the question 'do micronutrient supplements actually improve health or decrease risk of disease where food cannot?' If a person who takes supplements does not develop a certain disease he may attribute his good luck to the supplement, but this is far from proof of their efficacy.

In Australia, with its abundant food supply, frank vitamin deficiency diseases are seldom seen and, when they do occur, can be traced to a deficiency usually induced by poverty, ignorance or indifference about food selection, adoption of bizarre eating habits or the presence of disease. Vitamin deficiency as a result of poor eating habits ('primary deficiency') is obviously best treated by correcting the diet to include food which contains the vitamin that is in low supply. Deficiencies arising from a disease condition ('secondary deficiency') should be diagnosed and evaluated by a qualified physician, who will initiate treatment on an individual basis and may prescribe supplementary vitamins during the treatment of the underlying disease. The self-treatment of secondary micronutrient deficiency may allow a disease, which requires prompt medical attention, to remain unattended. If, however, someone is seeking nutrition insurance, then they should consult a checklist like the following before taking a vitamin supplement:

1 Is there an indication of deficiency?
2 Try to correct any deficiency with an improved diet first; for example, check if less than 1200 Kcal or 4500 kJ per day have been consumed for a few months.
3 Use supplements in amounts as close to the RDI as possible.
4 Take supplements for the shortest possible time.
5 Prefer a supplement which has the full spectrum (except vitamin K) of vitamins (and ideally major and minor elements as well).

Promoters of vitamin supplements help to maintain the notion that it is difficult, if not impossible, to obtain all the vitamins we need from our current food supply alone. The large sums of money spent by supplementers suggests that advertising to this effect has been particularly successful. Vitamin supplement labelling which reflects both ingredients and RDIs, conformity with quality control standards and advertising which is accurate and honest are required to assist consumer choice. The present interest in new applications of known actions of vitamins (like antioxidants for prevention of atherosclerotic vascular disease) and newly identified actions (such as cellular differentiation and immunomodulation by vitamin D; folacin in the prevention of neural tube defects in fetal life) encourage a revision of the RDIs for vitamins, their use in novel or designer foods (functional foods), and more targeted supplementation for particular physiological or pathophysiological purposes. Perhaps some of these

strategies will ultimately be scientifically defensible on the basis of clinical trials and surveillance of groups of individuals engaged in such usage, with risk-benefit analysis. But it is worth remembering that the margin of safety will be greater if the background diet to such increased essential micronutrient usage is itself nutrient dense, of wide variety, and derived from recognisable basic food commodities (fruits, vegetables, meat, fish, eggs, milk) (Kant et al. 1993). This is particularly so because of the many biologically active compounds in food where usefulness is yet to be adequately evaluated. The toxicity arising from the consumption of large amounts of certain vitamins (symptoms of which are well documented in Tables 16.1 to 16.14) can be as hazardous as a deficiency. Vitamins, when consumed in amounts far exceeding those found in food, assume the properties of medications or drugs, and as such need careful monitoring. In addition, the consumption of excessive amounts of one vitamin could well cause a deficiency of another micronutrient. For example, in susceptible individuals, iron storage disease may also occur with excessive vitamin C intake. Pyridoxine (vitamin B-6) in excess can cause a neuropathy of the sensory nerves to the limbs. Evidence of the potential danger associated with megadoses (amounts of vitamins at least 10 times the RDI) of vitamins is growing and there is no scientifically sound evidence to support the unrestricted use of megadoses of vitamins for healthy individuals. Acceptable and possible uses of megavitamin therapy are shown in Tables 16.19 and 16.20.

Table 16.19 Acceptable uses of megavitamin therapy

Disorder	Vitamin
Inherited metabolic disorders	
Leigh's necrotising encephalopathy; lactic acidosis;	
'maple syrup' urine disease	thiamin
Hartnup disease	niacinamide
inherited vitamin B-6 dependency	vitamin B-6
multiple carboxylase deficiency	biotin
Leiner's disease	biotin
Drug induced increased requirement	
methotrexate and pyrimethamine	folacin
isoniazid, cycloserine, penicillamine hydralazine, L-dopa	vitamin B-6
anticoagulant (warfarin) overdose	vitamin K
hyperlipidaemia	nicotinic acid
Wernicke's encephalopathy and beri-beri heart disease	thiamin
disfiguring acne	vitamin A analogues
malabsorption syndromes	vitamins A, D, E, K, folacin, B-12
urinary tract infection (some only)	vitamin C

Source: Wahlqvist 1987

Table 16.20 Possible uses of megavitamin therapy

Disorder	Vitamin
prevention of congenital neural tube defects	B-group vitamin folacin
prevention of cleft lip and palate	B-group vitamins folacin
treatment of cervical dysplasia	folacin
reduction in risk of certain tumours (lung, prostate)	vitamin A analogues, carotenoids
diminution of symptoms of the common cold	vitamin C
reduction in symptoms of premenstrual tension, menopause, first trimester pregnancy morning sickness, oral contraceptive pill	vitamin B-6
symptoms of osteoarthritis and rheumatoid arthritis	pantothenic acid
treatment of toxic amblyopia	vitamin B-12
prevention of retrolental fibroplasia	vitamin E
prevention of postoperative thromboembolism	vitamin E
prevention of coronary heart disease	vitamin E

Source: Wahlqvist 1987

SUMMARY

- Vitamins are organic compounds essential for normal growth and metabolic processes.
- They cannot be synthesised by humans in adequate amounts and, therefore, must be obtained from food.
- Vitamins A, D, E and K are fat soluble and are present in animal and plant fats and oils. They can be stored in body tissues, and if excessive amounts are consumed, toxicity can occur.
- The water soluble vitamins, vitamin C and vitamins of the B complex, are normally excreted in the urine if excessive amounts are consumed.
- A single vitamin deficiency seldom occurs in isolation; more often a multi-vitamin deficiency occurs.
- Vitamin supplementation is not necessary for individuals who consume a wide variety of foods, and who are physically active enough to consume, commensurately, enough energy.
- A growing number of compounds that fit the definition of vitamins are being identified. Some of these are derived from plants ('phytochemicals'); some may not be essential in all circumstances (i.e. they are 'conditionally essential') and their functions may be partly assumed by other compounds; and some may be inadequately formed in humans.

REFERENCES

Enstrom, J.E., Kanim, L.E. & Klein, M.A. Vitamin C intake and mortality among a sample of the United States population. *Epidemiology* 1992; 3:194–202.

Flagg, E.W., Coates, R.J., Eley, W., Jones, D.P., Gunter, E.W., Byers, T.E., Block, G.S. & Greenberg, R.S. Dietary glutathione intake in humans and the relationship between intake and plasma total glutathione level. *Nutr Cancer* 1994; 21(1):33–46.

Hertog, G.L., Kromhout, D., Aravanis, C., Blackburn, H., Buzina, R., Fidanza, F. & Giampaoli, S. et al. Flavonoid intake and long term risk of coronary heart disease and cancer in the seven countries study. *Arch Intern Med* 1995; 155:381–86.

Kant, A., Schatzkin, A., Harris, T.B., Ziegler, R. & Block, G. Dietary diversity and subsequent mortality in the First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study. *Am J Clin Nutr* 1993; 57:434–40.

Knekt, P. Vitamin E and cancer prevention. In: *Natural Antioxidants in Human Health and Disease*. B. Frei (ed.). Academic Press, San Diego, 1994; 199–238.

Machlin, L.J. *Handbook of Vitamins: Nutritional, Biochemical and Clinical Aspects*. Marcel Dekker Inc., New York, 1984.

Mackerras, D. Antioxidants and health—fruits and vegetables or supplements? *Food Australia* 1995 (November Supplement):S1–S24.

Shils, M.E., Olson, J.A., Shike, M. & Ross, A.C. (eds). *Modern Nutrition in Health and Disease*. 9th edn. Lippincott, Williams & Wilkins, Maryland and Pennsylvania, 1998.

Snodderly, D.M. Evidence for protection against age-related macular degeneration by carotenoids and antioxidant vitamins. *Am J Clin Nutr* 1995; 62(6 Suppl):1448S–61S.

Solomons, N. & Bulux, J. Plant sources of provitamin A and human nutriture. *Nutrition Reviews* 1993; 51(7):199–204.

Wahlqvist, M.L. Vitamin use in clinical medicine. *Med J Aust* 1987; 146(1):30–7.

Wahlqvist, M.L. & Briggs, D.R. *Food Questions and Answers: Sort the Facts from the Fads to Help You Choose a Healthy Diet*. Penguin Books, Melbourne, 1991; 134.

Wahlqvist, M., Huang, S. & Worsley, A. *Use and Abuse of Vitamins: Food Versus Pills*. 2nd edn. Sun Books, Melbourne, 1987.

Wahlqvist, M.L., Wattanapenpaiboon, N., Kouris-Blazos, A., Mohandoss, P. & Savige, G.S. Dietary reference values for phytochemicals. *Proc Nutr Soc Aust* 1998; 22:34–40.

Wilcox, G., Wahlqvist, M.L., Burger, H.G. & Medley, G. Oestrogenic effects of plant foods in postmenopausal women. *BMJ* 1990; 301:905–6.

Zhao, X., Jia, J., Zhang, Q., Lin, Y. & Xu, Z. Taurine contents of Chinese foods. *Acta Nutrimenta Sinica* 1994; 16(3):321–23.

FOOD AND NUTRITION

Australasia, Asia and the Pacific

Second Edition

Edited by
Mark L. Wahlqvist

Contributors
Madeleine Ball
David R. Briggs
Patricia A. Crotty
Gwyn P. Jones
Antigone Kouris-Blazos
Louise B. Lennard
Richard S.D. Read
Iain Robertson
Ingrid H.E. Rutishauser
Mark L. Wahlqvist
Naiyana Wattanapenpaiboon

Thanks to Antigone Kouris-Blazos for her editorial and technical assistance.

ALLEN&UNWIN

First published in 1997
Second edition published in 2002 by
Allen & Unwin Pty Ltd
83 Alexander Street, Crows Nest, NSW 1590 Australia
Phone: (61 2) 8425 0100
Fax: (61 2) 9906 2218
E-mail: info@allenandunwin.com
Web: www.allenandunwin.com

National Library of Australia
Cataloguing-in-Publication entry:

Food and nutrition: Australasia, Asia and the Pacific.

2nd ed.
Includes index.
ISBN 1 86508 692 4

1. Food. 2. Food analysis. 3. Food—Australian.
4. Food—New Zealand. 5. Nutrition.
6. Nutrition—Requirements. 7. Nutrition
Australia. 8. Nutrition—New Zealand.
I. Wahlqvist, Mark L.

641.3

Set in 10/12 Bembo by Asset Typesetting Pty Ltd
Index compiled by Russell Brooks
Printed by South Wind Productions, Singapore

10 9 8 7 6 5 4 3 2

Contents