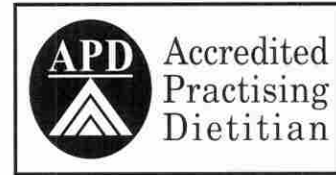


Continuing education

Thiamin, riboflavin, niacin, pantothenic acid and biotin

Continuing education and the APD program

This quiz is an ideal activity for APD members to include in your CPD log, where it relates to personal learning goals. Record the time taken, to the nearest hour, to complete the quiz and any associated research.



This quiz has been prepared by Associate Professor Samir Samman, The University of Sydney and Dr Philippa Lyons-Wall, Queensland University of Technology. Correspondence should be directed to Samir Samman email: s.samman@mmb.usyd.edu.au

Vitamins are not synthesised by the body and are required in the diet in small quantities (μg - mg per day). They have no energy value and are not used for structural purposes. Some vitamins are water-soluble while others are fat-soluble. This classification indicates whether the vitamin is likely to be absorbed as a lipid or like other water-soluble nutrients. Water-soluble vitamins were identified originally as a single factor, *water soluble B*, and distinguished from the *fat soluble A*. Further research led to the identification of nine water-soluble vitamins: thiamin (B_1), riboflavin (B_2), niacin (B_3), biotin, pantothenic acid, pyridoxine (B_6), cobalamin (B_{12}), folate and vitamin C. Two characteristics shared by most water-soluble vitamins are their function as cofactors for enzymes and their inability to be used in the form in which they are absorbed. Most vitamins must be converted or modified to the active form. For example, thiamin must be converted to thiamin pyrophosphate (TPP) to be biologically active while riboflavin and biotin require covalent attachment to specific enzymes before becoming functional (1,2). The following nutritional science quiz is the third in the series (3,4) and focuses on thiamin, riboflavin, niacin, pantothenic acid and biotin: vitamins which are unified by their involvement in energy production from macronutrients.

- Which of the following foods are good sources of thiamin?**
 - milk and dairy products, eggs, liver, yeast extracts (e.g. Vegemite)
 - whole-grain, yeast extracts (e.g. Vegemite), pork, liver and other organ meats
 - fruit and vegetables
 - protein-rich foods
- Why is niacin listed in tables of food composition as 'niacin equivalents'?**
 - niacin can be obtained preformed in the diet or from precursors in the liver
 - niacin vitamers are absorbed with different efficiencies
 - other vitamins can have activity equivalent to niacin
 - to make terminology consistent with other vitamins
- Niacin deficiency is characterised by which of the following symptoms?**
 - hypercholesterolaemia
 - dermatitis, diarrhoea and dementia
 - symptoms not clear since deficiency is rare
 - angular cheilosis and atrophy of the tongue papillae
- Which of the following is a cause of thiamin deficiency?**
 - thiaminase
 - excess intake of alcohol
 - inadequate intake of thiamin
 - all or any of the above
- 'Egg white injury' is the term given to the deficiency of which vitamin?**
 - pyridoxine
 - riboflavin
 - biotin
 - pantothenic acid
- Pantothenic acid plays a role in the release of energy from which macronutrient?**
 - protein
 - fat
 - carbohydrate
 - all of the above
- What is the primary reason for fortification with thiamin?**
 - to ensure adequate growth in children
 - for the prevention of Wernicke-Korsakoff's syndrome
 - to replenish thiamin which is destroyed during food processing
 - to prevent deficiency in the elderly
- High doses of riboflavin produce which of the following symptoms?**
 - no effect
 - flushing, headaches and nausea
 - dermatitis
 - diarrhoea
- The nutritional status of thiamin is assessed by which of the following tests?**
 - urinary N'-methylnicotinamide
 - glutathione reductase activity in red blood cells
 - transketolase activity in red blood cells
 - urinary xanthurenic acid
- Which of the following vitamins has a demonstrated drug-nutrient interaction?**
 - thiamin
 - riboflavin
 - niacin
 - all of the above

Answers

1. b

Thiamin and the other water-soluble B vitamins are widely distributed in relatively small amounts in all food groups except the fats and oils, which contain only trace amounts. Richer sources include whole-grains and foods derived from metabolically active tissues such as yeast extracts, meats and liver. Pork is notably a rich source of thiamin. Milk and dairy products are a major source of riboflavin however this vitamin is sensitive to ultraviolet light and can be easily destroyed by prolonged exposure to UV. Protein-rich foods are good sources of niacin (2).

2. a

Niacin is obtained in 2 different ways: it can be absorbed as preformed nicotinic acid or amide from the diet or synthesised in the liver from tryptophan (provitamin) via the kynurenine pathway. In the Western diet, about equal amounts are obtained from each source. One of the early enzymatic steps in the kynurenine pathway is dependant on vitamin B₆. Normally about 1/60th of the dietary tryptophan intake is converted in the liver to niacin. If the amount of tryptophan in a given food is not known, it can be estimated as 1% of its protein content. In practice this means that an average diet containing 60g protein will provide 10mg niacin from tryptophan. For a given food or dietary analysis, niacin equivalents are estimated as the amount of preformed niacin plus 1/60th of its tryptophan content. The following equations are used to determine niacin equivalents in the Australian food tables (5):

$$\text{mg niacin equivalents} = \text{mg niacin} + (\text{g protein})/6 \dots 1$$
$$\text{mg niacin equivalents} = \text{mg niacin} + (\text{mg tryptophan})/60 \dots 2$$

Equation 1 is used commonly and equation 2 is used when the tryptophan content of a food is known. If both protein and tryptophan values are known, equation 2 is used preferentially.

3. b

Niacin deficiency is characterised by the 3 Ds: dermatitis, diarrhoea and dementia. The dermatitis is photosensitive and associated with Pellagra (sour skin), inflammation and appearance of a dark band of skin below the neck, known as Casal's collar, on areas exposed to sunlight. More severe deficiency is associated with dementia possibly due to inadequate supply of tryptophan to the brain for serotonin synthesis. Historically the deficiency is associated with poor living standards and consumption of maize as the staple food. Maize is a poor source of preformed niacin and maize protein is deficient in tryptophan. Hypercholesterolaemia is not a symptom of niacin deficiency but nicotinic acid in pharmacological doses (approx 3 g/d) is used as a lipid lowering agent under some circumstances. Angular cheilosis (fissures at the corners of mouth) and atrophy of the tongue papillae are some of the minor symptoms of riboflavin deficiency (2).

4. d

Thiaminases are thiamin-degrading enzymes found in some fresh fish, shellfish, ferns and bacteria. These enzymes are heat labile and therefore less likely to be active in cooked food. Thiaminases are thought to be responsible for the death of Australian explorers Burke and Wills, who lived on inappropriately prepared indigenous food (nardoo fern) after their rations were depleted (6). Chronic high intakes of alcohol predispose to thiamin deficiency in several ways:

1. inhibition of active transport of thiamin in the gastrointestinal tract which is exacerbated by alcohol-induced gastritis or diarrhoea;
2. the diuretic effect of alcohol increases the urinary excretion of the vitamin;
3. thiamin is required for the oxidation of alcohol in the TCA cycle; and
4. alcohol reduces the hepatic conversion of thiamin to thiamin pyrophosphate (TPP), the active coenzyme form (7).

5. c

Biotin deficiency is associated with the following symptoms: dry scaly dermatitis, alopecia (hair loss), seizures, lactic acidosis and muscle pain. Biotin is a cofactor in metabolic reactions which require carboxylases. These include acetyl CoA carboxylase, the rate limiting enzyme that initiates fatty acid synthesis. Hence symptoms of scaly dermatitis and alopecia (also seen with essential fatty acid deficiency) could arise from impaired synthesis of fatty acids required for integrity of the skin epidermal layers. Deficiency has been reported following improper use of total parenteral nutrition and unusual dietary practices such as consumption of raw eggs. Raw egg white contains avidin, a glycoprotein which binds biotin irreversibly. Hence biotin deficiency is called 'egg white injury'. The avidin-biotin complex is resistant to proteolytic digestion in the gastrointestinal tract however avidin is heat labile and therefore ingestion of cooked eggs does not compromise biotin absorption (2).

6. d

Pantothenic acid undergoes metabolic transformations to become coenzyme A (CoA), a molecule which activates other molecules so that they may enter a reaction. Acetyl CoA (or 'active acetate') plays a central role in metabolism of macronutrients. For example, amino acids, fatty acids and sugars are converted to acetyl CoA for entry into the TCA cycle and oxidation to energy. Acetyl CoA is also the starting point for synthesis of lipids and ketone bodies. Other water-soluble vitamins are also involved in energy production from macronutrients. Thiamin is a coenzyme for pyruvate dehydrogenase which links glycolysis with the TCA cycle. Riboflavin is the key component for two coenzymes, flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD), essential in the electron transport chain and final oxidation of macronutrients to energy. The active forms of niacin, nicotinamide adenine dinucleotide (NAD) and

the phosphorylated form (NADP) are co-enzymes for many dehydrogenase reactions in pathways such as glycolysis, TCA cycle, electron transport chain and synthesis of lipids.

7. b

Fortification with thiamin is a public health strategy which addresses Wernicke-Korsakoff syndrome (WKS), a result of thiamin deficiency. Fortification is mandatory for bread making flour and since its introduction in Australia in 1991, the incidence of WKS has fallen significantly (8). Individuals at risk of deficiency are mainly those who consume large quantities of alcohol and inadequate diets, however fortification of alcoholic beverages is controversial. WKS is characterised by: ataxic gait (due to muscle weakness), paralysis of the external movements of the eye, loss of recent memory and confusion. Thiamin has another distinct deficiency disease known as beriberi, which was prevalent in parts of Asia where the staple diet was polished rice. It does not usually occur with WKS. Acute beriberi is characterised by cardiac failure while in chronic beriberi the peripheral nerves are affected resulting in the inability to lift up the foot and loss of sensation in the feet (2).

8. a

Riboflavin is a fluorescent yellow-green colour and while large oral doses may cause yellowish discoloration of the urine, there are no other effects. There is no evidence of toxicity after oral administration of thiamin except with very high doses (3 g/d), where reported symptoms include headache, irritability, weakness and insomnia (9,10). High doses of biotin and pantothenic acid have no reported side effects although megadoses of pantothenic acid (10 g/d) have produced mild intestinal distress and diarrhoea. Nicotinic acid (>300 mg) has resulted in flushing, headaches, nausea and a transient fall in blood pressure.

9. c

Laboratory tests are used to detect subclinical deficiency states or to confirm a clinical diagnosis. The nutritional status of thiamin is assessed by the erythrocyte transketolase (ETK) assay. This enzyme is part of the pentose phosphate pathway and is dependant on thiamin. In deficiency, the activity of ETK is low and responds to the addition of thiamin. Similarly, riboflavin status is assessed by the measurement of

glutathione reductase which is dependant on both NADPH and FAD. In deficiency, the activity is low and responds to the addition of FAD. Urinary N'-methylnicotinamide is a biochemical test of niacin status and urinary xanthurenic acid excretion following a tryptophan load test is a marker of pyridoxine status (2).

10. d

A number of drugs may influence the nutritional status of vitamins by decreasing food intake (anorectic drugs), inducing malabsorption or increasing energy expenditure, however specific drug-nutrient interactions have been reported. Alcohol inhibits the absorption of thiamin and enhances its excretion. Niacin may be antagonised by isoniazid, an antimycobacterial agent used commonly in the management of HIV and TB (10,11). Chlorpromazine, a drug used for the management of psychotic disorders, manic depressive illness and severe behavioural problems in children, may lower the status of riboflavin (10). The need for supplementation with the vitamin is determined ultimately by assessment of its nutritional status.

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