ABC of Nutrition

A STEWART TRUSWELL

VITAMINS II

Vitamin B-6

Food sources of vitamin B-6

Liver
Whole grain cereals,
meat, fish,
peanuts, bananas
walnuts, avocados,
potatoes, eggs

The term vitamin B-6 includes five closely related substances that all occur in foods and in the body: pyridoxal and pyridoxamine, their 5' phosphates, and pyridoxine, best known to doctors as the pharmaceutical form. Primary dietary deficiency is rare. An outbreak of convulsions in infants in 1954 was traced to insufficient vitamin B-6 in a milk formula because of a manufacturing error. Several drugs interfere with vitamin B-6: hydralazine, penicillamine, and possibly oestrogens. Peripheral neuropathy from high dose isoniazid is prevented with pyridoxine. There are several conditions for which pharmacological doses of 50 to 100 mg pyridoxine are probably beneficial. These include homocystinuria, hyperoxaluria, gyrate atrophy of the choroid, hypochromic sideroblastic anaemia, and radiation sickness. Some biochemical indices of vitamin B-6 state may be abnormal in women taking some oral contraceptives, and depression on the pill may respond to pyridoxine. Premenstrual tension is a very variable condition: prescribed or self medication with pyridoxine has no physiological basis and has never been subjected to a large double blind trial. A small double blind trial showed no benefit. Above 500 mg/day pyridoxine may cause severe sensory neuropathy. All seven patients in the first report of this side effect were taking pyridoxine for an inadequate indication—mostly for premenstrual oedema—and most had increased the dosage on their own. Pyridoxine should not be available over the counter at tablet size above 50 mg (which is already 25 times the nutrient requirement).

Vitamin B-12

Food sources of vitamin B-12

Liver,
kidney,
sardines,
oysters,
heart,
rabbit,
other meats,
eggs,
cheese,
milk

The red vitamin was the last to be isolated (1948). Humans eat it preformed in animal foods including fish and milk. The physiological mechanism for its absorption requires intrinsic factor from the stomach, and the complex is absorbed only at a special site in the terminal ileum. Deficiency occurs in several gastric, intestinal, and ileal diseases, including pernicious anaemia, and in vegans (pure vegetarians). Adult body stores of vitamin B-12 in the liver last longer than those for any other vitamin, but deficiency occurs more quickly in infants. Vitamin B-12 cooperates with folate in DNA synthesis so deficiency of either leads to megaloblastosis. Vitamin B-12 has a separate biochemical role, unrelated to folate, in synthesis of fatty acids in myelin. Deficiency is diagnosed by measuring the serum vitamin B-12 concentration.

Supplementation with hydroxocobalamin is desirable for adult vegans and essential for their young children. Hydroxocobalamin can improve some cases of optic neuritis, possibly by detoxifying accumulated cyanide. Apart from rare hypersensitivity reactions there are no known toxic effects from vitamin B-12. It thus makes an ideal placebo, which may still be the commonest reason for its prescription.

Folate (folacin)

Food sources of folate

Liver,
kidney, spinach,
broccoli,
Lima beans, beetroot,
bran,
peanuts,
cabbage, lettuce,
avocados, bananas,
oranges,
wholemeal bread,
eggs,
some fish

*In Britain total vegetables provide 35%,
bread and flour products 26%, fruit 6%*

In folate deficiency there is first a reduction of serum folate below 3 ng/ml and then megaloblastosis of blood cells and other cells with a rapid turnover. As well as anaemia diarrhoea is common when the deficiency results from antagonism rather than dietary lack.

Folate deficiency may occur simply from a poor diet, but it is usually seen when there is malabsorption, increased requirements because of pregnancy (see article on nutrition in pregnancy), increased cell proliferation (haemopoiesis, lymphoproliferative disorders), or antagonism from a number of drugs. Methotrexate, aminopterin, pyrimethamine, and co-trimoxazole act by inhibiting the complete reduction of folate preferentially in cancer cells or micro-organisms. Alcoholism is the commonest antagonist.

Body stores of folate are not large and deficiency can develop quickly in patients on intensive therapy. In some cases this can be ascribed to intravenous alcohol or particular amino acid mixtures. Trauma, infection, uraemia, increased haemopoiesis, dialysis, vomiting, or diarrhoea may also be partly responsible. Folate deficiency appears to be the most common vitamin deficiency among hospital patients in countries such as Britain, so supplements should be prescribed whenever patients are fed intravenously for more than a few days.

The name comes from the Latin *folia* (= leaf), but liver, legumes, nuts, and even wholemeal bread are as good dietary sources as leafy vegetables. Prolonged boiling destroys much of the vitamin in hospital cabbage. No serious toxic effects are known from moderate doses (large doses cannot be bought over the counter) except the possibility of masking vitamin B-12 deficiency so that anaemia is corrected but subacute combined degeneration gets worse. For this reason multivitamin preparations do not usually contain folic acid (Pregnavite Forte F is an exception).

Vitamin C

Food sources of vitamin C

Blackcurrants, guavas,
rosehip syrup, green peppers,
oranges,
cauliflower, broccoli,
sprouts, cabbage,
potatoes
(liver and milk)

*In Britain on average vegetables
supply 48% (21% from potatoes)
and fruits contribute 41%*

Small doses of vitamin C will cure scurvy. Lind achieved this with two oranges and a lemon in the first controlled trial on HMS *Salisbury* in 1747; 30 mg of vitamin C is more than enough to prevent scurvy.

Desirable intakes of vitamin C can be thought of at three levels.

(1) The official recommended intake for adults—30 mg/day in Britain and 60 mg/day in the USA and Canada—is for healthy people.

(2) In hospital patients this is not enough. Absorption of the vitamin may be reduced or its catabolism increased by disease. Trauma and surgery increase the need for vitamin C for collagen synthesis. Several drugs antagonise vitamin C: adrenal corticosteroids, aspirin, indomethacin, phenylbutazone, and tetracycline together with smoking. Hence it is advisable to give a supplement of up to 250 mg ascorbic acid a day to cover major surgery.

(3) The third level is the great vitamin C debate: megadoses (up to 10 g/day) proposed by Linus Pauling for superhealth—or not? The best known claim for large intakes of vitamin C is that they prevent common colds. At least 31 controlled trials have been reported and in 23 of them (including the largest and best designed ones) there was no significant preventive effect. The eight supportive trials all had qualifications—for example, they were not double blind, had tiny groups, or showed an effect only in a subgroup. At high dosage most of the vitamin does not appear to be absorbed. The law of diminishing returns applies. Large intakes of vitamin C have several disadvantages. They produce moderate increases in urinary oxalate and urate excretions, which are undesirable in stone formers, as well as dyspepsia and diarrhoea.

Nevertheless, there are two gastrointestinal actions of vitamin C which make it desirable for people to eat more than the basic recommended dietary intake of 30 mg. It enhances iron absorption from vegetable foods and it inhibits nitrosamine formation. The latter may explain the negative epidemiological associations between vitamin C intake and gastric cancer.

Vitamin C is easily destroyed by cooking (aggravated by alkaline conditions), so fresh fruit and salads should be encouraged and vegetables cooked lightly and quickly.

Vitamin D

Food sources of vitamin D

Fish liver oils
fatty fish (sardines,
herring, mackerel, tuna,
salmon, pilchards),
fortified margarine,
infant milk formulas,
eggs, liver

In Britain on average margarine supplies 44%

The natural substance cholecalciferol was originally called vitamin D₃. Vitamin D₂ is the artificially produced ergocalciferol. The natural and usual source of cholecalciferol is by the action of short wavelength ultraviolet light from the sun on a companion of cholesterol in the skin, 7-dehydrocholesterol. Cholecalciferol also occurs in a small minority of our foods. When people live in high latitudes, wear clothes, and spend nearly all the time indoors and the sky is polluted with smoke they have insufficient exposure to ultraviolet light to make the required amount of this substance, and under these conditions dietary intake becomes critical, and cholecalciferol assumes the role of a vitamin.

In rickets and osteomalacia there is reduced calcification of growing and mature bones respectively. These diseases appear to be more prevalent in the United Kingdom than in other Western countries. They tend to affect adolescents and the elderly, especially Asians in northern cities. In Britons with normal levels plasma 25-OHD₃ concentrations show annual fluctuations, with their trough in late winter and their peak after the summer holidays. It is not clear whether the lower prevalence of rickets in Canada and Sweden is because milk is fortified with vitamin D or because people receive more ultraviolet radiation of their skin over the year in those other northern countries.

The small dietary contribution of vitamin D is lost in malabsorption and chronic biliary obstruction. Long term anticonvulsants, phenobarbitone and phenytoin, increase metabolic losses. Vitamin D is indicated in these conditions. In chronic renal failure and hypoparathyroidism 1 α -hydroxylation to the active metabolite is impaired and the bone disease responds only to 1,25(OH)₂D₃ (calcitriol) or 1 α -OHD₃ (alfacalcidol), a synthetic derivative.

Irradiation of the skin may cause sunburn but does not lead to vitamin D toxicity. On the other hand, the margin of safety with oral vitamin D, between the nutrient requirements of up to 10 μ g and toxic intakes, is narrow. Overdose with vitamin D causes hypercalcaemia, with thirst, anorexia, polyuria, and the risk of metastatic calcification. Some children have developed hypercalcaemia on vitamin D intakes only five times the recommended nutrient intake. More than this should not be taken except for rickets or osteomalacia. Here 25 to 100 μ g vitamin D—for example, as ergocalciferol—is the usual therapeutic dose.

[One international unit (IU) of vitamin D=0.025 μ g of cholecalciferol—that is, to convert IU to micrograms, divide by 40.]

Vitamin E

Food sources of vitamin E

Vegetable oils, of which wheat germ oil is the richest,
margarines,
eggs, butter,
wholemeal cereals,
broccoli

The nutritional requirement for vitamin E is roughly proportional to the intake of polyunsaturated fat. Vitamin E is not easily transported across the placenta, and signs of deficiency are sometimes found in premature infants.

Patients with deficiency have a mild haemolytic anaemia, low plasma tocopherol concentration, and red cells abnormally sensitive to haemolysis in vitro by dilute hydrogen peroxide. The most severe cases of deficiency occur in patients with fat malabsorption, especially fibrocystic disease of the pancreas and abetalipoproteinaemia. As well as mild anaemia, in these conditions ataxia, loss of tendon jerks, and pigmentary retinopathy have been reported, which respond to long term vitamin E treatment.

Doses of vitamin E above the recommended 10 mg/day reduce the severity of retrolental fibroplasia in premature newborn infants who require oxygen. Many people now take vitamin E in large doses on their own initiative. In a double blind trial this showed no benefits on work performance, sexuality, or general well being. It is also clear from several trials that vitamin E does not improve athletic achievement or consistently help angina pectoris.

Vitamin K

Food sources of vitamin K

Turnip greens,
broccoli,
cabbage, lettuce,
liver
are all good sources, though there
is no systematic list

The Koagulations vitamin (Dam, 1935) comes in three chemical forms. Vitamin K₁ (phytonadione) is found mainly in vegetables. The series of K₂ vitamins (menaquinones) is produced by bacteria—for example, in the gut. Menadione (Synkavit) is synthetic, water soluble, can cause jaundice, and is obsolescent. Deficiency of vitamin K manifests itself as hypoprothrombinaemia and bleeding.

Cord blood levels of vitamin K are very low (evidently placental transfer is limited), and breast milk contains little of the vitamin unless the mother has been dosed with vitamin K. To prevent haemorrhagic diseases 1 mg of vitamin K₁ (by injection or by mouth) is given either to all infants or to those at increased risk (low birth weight or difficult delivery), depending on the hospital's policy.

Vitamin K deficiency is to be expected in obstructive jaundice and can occur in malabsorption syndromes. Vitamin K₁ must be given before surgery for these conditions. Anticoagulants of the warfarin group owe their therapeutic action to antagonism of vitamin K, and vitamin K₁ is the antidote to overdose.

Vitamins that can usually be taken for granted

Not vitamins

The following compounds sold in "health food" shops and still included in some multi-vitamin pharmaceuticals are not vitamins. They are not required in infant formulas or in fluids for total parenteral nutrition:

Bioflavonoids
Carnitine
Inositol
Orotic acid
Aminobenzoic acid (PABA)
Vitamin B15 ("pangamic acid")
Vitamin B17 (laetrile)
Vitamin P

Biotin is cofactor for several carboxylase enzymes concerned in fat synthesis and amino acid catabolism. It is widely distributed in foods, and deficiency is rare. Deficiency has occurred in people who eat large amounts of raw eggs (which contain a protein that binds biotin and prevents its absorption) and in patients receiving total parenteral nutrition with biotin omitted. They suffer scaly dermatitis, loss of hair, hypercholesterolaemia, and a characteristic combination of organic acids in the urine.

Pantothenic acid is a constituent of coenzyme A which has many functions and is widespread in the body and in foods. The name means "available everywhere." Spontaneous deficiency in man has never been proved.

Choline is part of lecithin and of sphingomyelin, the two major phospholipids in the body and it is also part of acetylcholine, the neurotransmitter. Pharmacological doses as choline or lecithin are being used to treat tardive dyskinesia and some other neurological disorders. Depression is a side effect.

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Clinical curio: does aggressive sport protect against exercise induced asthma?

Exercise induced asthma is easily provoked in susceptible subjects by various sports. I have long realised in my own case that different forms of exercise are followed by varying degrees of wheeze, which is not always limiting. For almost all sports (including soccer, tennis, running, and indoor and outdoor fitness training) except swimming I have to use a prophylactic bronchodilator to avoid wheeze. Recently, I discussed my observation that players of rugby union never require use of a prophylactic inhaler with four other people (three patients, one colleague) in this unit. Three had similar views and the other (aged 15) insisted that a small dose of his steroid inhaler was essential, although he had never played without it. All four, as well as myself, are atopic, with pronounced bronchial hyperreactivity, normal lung function at rest, and exercise induced asthma that is easily demonstrated under laboratory conditions. All four need to use a prophylactic bronchodilator before other sporting activities to avoid wheeze.

The type of activity associated with rugby union, played during the winter season, might be expected easily to provoke exercise induced asthma. Running and swimming have been compared and cause different degrees of bronchoconstriction, perhaps explained by temperature or humidity.¹ Circulating catecholamine concentrations rise during exercise in normal subjects² but do not rise to the same extent in patients with asthma.^{3,4} The aggressive nature of rugby union may be the important feature, perhaps

producing a sustained rise in catecholamine concentration that protects against exercise induced asthma. Schnall and Landau showed a protective effect of repeated short sprints in patients with exercise induced asthma, which might be related to increased production of catecholamines or to depletion of mediators.^{5,6} Those I spoke to, however, did not find that a warm up before other sports prevented exercise induced asthma.

This distinction between aggressive and non-aggressive sports in provoking different degrees of exercise induced asthma seems noteworthy and, at least to the four people I spoke to, is important.—K ANDERSON, registrar, Glasgow.

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- 4 Warren JB, Keynes RJ, Brown MJ, Jenner DA, McNicol MW. Blunted sympathoadrenal response to exercise in asthmatic subjects. *Br J Dis Chest* 1982;76:147-50.
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- 6 Godfrey S. Exercise-induced asthma. In: Clark TJH, Godfrey S, eds. *Asthma*. London: Chapman and Hall, 1983:65.