Micronutrient deficiencies, vitamin pills and nutritional supplements

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Abstract

In the 21st century, it is hard to reconcile the concepts of the Western diet and overconsumption with the risk of micronutrient deficiencies. However, deficiencies can arise from poor dietary intake, alone or combined with physiological or metabolic injury. Micronutrients are essential to fulfil a broad range of biochemical and physiological functions, and are tightly regulated by homeostatic processes. Diagnosis of deficiency is complex and requires the use of separate investigations (dietary, functional, biochemical). While the role of micronutrients in the prevention or treatment of diseases (including cancer, type 2 diabetes) is of interest, a key driver for the vitamins and supplement market is their advertised potential to optimize health and performance in healthy individuals. The evidence so far indicates that multivitamins supplements offer no health protection, increase all-cause mortality, and risk of cancers in some subgroups. A nutritionally balanced diet is a safer way to achieve sufficiency.

Keywords Antioxidant; deficiency; evidence; micronutrients; recommendations; supplementation

Micronutrients — intake, metabolism and storage

There are 15 vitamins (11 water-soluble, and 4 lipid soluble) and 20 minerals (7 macroelements, 7 trace elements) essential for sustaining human life (Table 1). All vitamins and minerals can be obtained from a balanced diet that includes the main food groups. That diseases can arise from dietary deficiency has been well understood since the identification, in the 18th century, that supplementing the diet with citrus fruit could cure scurvy.

The physiological functions of micronutrients include acting as:

- co-enzymes in key metabolic reactions
- antioxidants in the control of damage caused by reactive oxygen species
- modulators of gene transcription
- components of and co-factors for enzymes and
- structural components of tissues.[1]

The human body is highly adaptable with efficient homeostatic mechanisms, often under hormonal control, that balance the absorption, transport, storage, utilization and excretion of micronutrients. These mechanisms enable maintenance of appropriate circulating and stored reserves for use in tissue function. Such controls allow the body to function normally across a wide range of nutrient intakes, so that it can take some time before an overt deficiency disease materializes (Figure 1).[2]

For example the metabolic pool of calcium in the extracellular fluid (ECF) is very small compared with the large skeletal reserves, mobilization of which compensates for an inadequate intake of calcium. Conversely, there are no specific reserves for minerals such as zinc and the water-soluble vitamins, and the body is largely dependent on a regular supply in the diet. Interestingly, there is no physiological mechanism for iron excretion and iron balance is maintained through the regulation of its absorption from the diet. If iron is not required, it is stored in duodenal mucosal cells as ferritin and excreted in the faeces when mucosal cells are exfoliated.

The bioavailability of a nutrient can be defined as the proportion of that nutrient ingested from a particular food that can be absorbed and made available to the body for normal metabolic functions. This is the result of the interaction between the nutrient, other components of the diet (the food matrix) and the physiological status of the individual. For example, ascorbic acid (vitamin C) will increase non-haem iron absorption, as will the presence of haem iron in the duodenum and the iron deficient status of the individual. Conversely phytates, iron-binding phenolic compounds and replete iron stores will decrease absorption. Several vitamins and minerals, such as calcium, iron, zinc and a number of the B vitamins display such interactions.

Phytochemicals

Foods, especially plant foods, contain phytochemicals (including polyphenols, sterols), which are not recognized as nutrients but may have properties (e.g. antioxidant, anti-inflammatory or cholesterol-lowering) that are health-promoting. These properties have fuelled the expansion of the nutritional supplement market, despite the European Food Safety Authority (EFSA) regulating the health claim market in Europe and requiring substantial evidence to justify claims.[3]

The UK's Department of Health report on dietary reference values found no convincing evidence that it is necessary to include such compounds in a normal human diet and thus gave no further consideration to these or other unnecessary substances, including ornithine, orotic acid, lecithin, 'vitamin B_{15}' (pangamic acid), 'vitamin B_{17}' (laetrile), bioflavonoids (e.g. rutin, hesperidin, quercitin) or ubiquinones (co-enzyme Q).[4]

Too much, too little — the U-shape relationship between micronutrients and health

A U-shape describes the dose-response relationship of micronutrients, with insufficient intake increasing the risk of deficiency, and excessive intake (acute and chronic exposure) increasing the risk of toxicity and associated diseases.

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Summary of micronutrient physiological functions and deficiency diseases

Minerals	Physiological functions	Known deficiency diseases[a]	Possible benefits of high status[23,24]
A — Retinol, beta-carotene	Visual pigments, gene expression, cell differentiation, antioxidant	Night blindness, xerophthalmia, keratinization of the skin	
D — Calciferol	Calcium homeostasis, cell maturation in small intestine, insulin secretion	Rickets (poor mineralization of bone), osteomalacia (demineralization of bone)	↓ Some cancers, diabetes, metabolic syndrome, multiple sclerosis
E — Tocopherols	Antioxidant, particularly in cell membranes	Rare — serious neurological dysfunction	↓ Atherosclerosis and ischaemic heart disease
K — Phylloquinone, menaquinones	Co-enzyme for enzymes of blood clotting and bone matrix	Impaired blood clotting, haemorrhagic disease	
C — Ascorbic acid	Antioxidant, promotes iron absorption, collagen synthesis, production of noradrenaline, inhibits production of nitrosamines in stomach	Scurvy (impaired wound healing, loss of dental cement, subcutaneous haemorrhage)	↓ All-cause mortality
B_1 — Thiamine	Co-enzyme in pyruvate and 2-keto-glutarate dehydrogenase and transketolase, Poorly defined role in nerve conduction	Beriberi (peripheral nerve damage), Wernicke—Korsakoff syndrome (central nerve damage)	
B_2 — Riboflavin	Co-enzyme in oxidation and reduction reactions, prosthetic group of flavoproteins	Lesions of corner of mouth, lips and tongue; seborrhoeic dermatitis	
Niacin — Nicotinic acid, nicotinamide	Co-enzyme in oxidation and reduction reactions, functional part of NAD and NADP	Pellagra (photosensitive dermatitis, depressive psychosis)	
B_6 — Pyridoxine, pyridoxal, pyridoxamine	Co-enzyme in transamination and decarboxylation of amino acids and glycogen phosphorylase, steroid hormone production	Disorders of amino acid metabolism, convulsions	
B_9 — Folic acid	Co-enzyme in transfer of one carbon fragments	Megaloblastic anaemia, neural tube defects in babies	↓ Some cancers, especially colorectal cancer
B_{12} — Cobalamin	Co-enzyme in transfer of one carbon fragments and metabolism of folic acid	Pernicious anaemia (megaloblastic anaemia with degeneration of the spinal cord)	
Pantothenic acid	Functional part of co-enzyme A and acyl carrier protein	Neuromotor disorders, mental depression, GI complaints and increased insulin sensitivity	
Biotin	Co-enzyme in carboxylation reactions in gluconeogenesis and fatty acid synthesis	Impaired fat and carbohydrate metabolism, dermatitis	
Minerals	**Physiological functions**	**Known deficiency diseases[a]**	**Possible benefits of high status[23,24]**
Calcium	Skeletal growth and development, vascular and muscle contraction, nerve transmission, insulin release	Failure to attain peak bone mass, osteoporosis in later life	↓ Hypertension and colon cancer
Chloride	Hydrochloric acid in the stomach, chloride shift in erythrocyte plasma membrane, regulation of osmotic and electrolyte balances	Not diet related— only due to clinical conditions (e.g. major trauma)	
Chromium	Insulin action, carbohydrate, lipid and nucleic acid metabolism	Severe deficiency can cause insulin resistance	
Copper	Immune, nervous and cardiovascular systems, bone health, iron metabolism, haemoglobin synthesis, regulation of mitochondria, other gene expression.	Unlikely due to remarkable homeostatic mechanisms	↓ (Speculation) cardiovascular disease and osteoporosis
Fluoride	Fluorapatite in teeth and bones	Increased risk of dental caries	
Iodine	Thyroid hormones growth and mental development, possibly antibiotic and anti-cancer	Goitre, hypothyroidism, cretinism (collectively termed iodine deficiency disorders)	↑ Infection control and cancer prevention

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