

Introduction



Vitamins are essential organic nutrients required in very small amounts for normal metabolism, growth and physical well-being. Most vitamins are not made in the body, or only in insufficient amounts, and are mainly obtained through food. When their intake is inadequate, vitamin deficiency disorders are the consequence. Vitamins are present in food in minute quantities compared to the macronutrients protein, carbohydrates and fat. The average adult in industrialised countries eats about 600g of food per day on a dry-weight basis, of which less than 1 gram consists of vitamins.

No single food contains all of the vitamins and, therefore, a balanced and varied diet is necessary for an adequate intake. Each of the **13 vitamins** known today has specific functions in the body, which makes every one of them unique and irreplaceable. **Vitamins are essential for life!**

Of the 13 vitamins, 4 are fat-soluble, namely vitamins A, D, E and K. The other vitamins are water-soluble: vitamin C and the B-complex, consisting of vitamins B₁, B₂, B₆, B₁₂, folic acid, biotin, pantothenic acid and niacin.

The history of vitamins can be divided into five periods.

Table 1: The History of Vitamins

Vitamin	Discovery	Isolation	Structure	Synthesis
Vitamin A	1909	1931	1931	1947
Provitamin A (Beta-carotene)		1831	1930	1950
Vitamin D	1918	1932	1936	1959
Vitamin E	1922	1936	1938	1938
Vitamin K	1929	1939	1939	1939
Vitamin B ₁	1897	1926	1936	1936
Vitamin B ₂	1920	1933	1935	1935
Niacin	1936	1935	1937	1894
Vitamin B ₆	1934	1938	1938	1939
Vitamin B ₁₂	1926	1948	1956	1972
Folic Acid	1941	1941	1946	1946
Pantothenic Acid	1931	1938	1940	1940
Biotin	1931	1935	1942	1943
Vitamin C	1912	1928	1933	1933

1. The **empirical healing** of diseases, now associated with vitamin deficiency, through consumption of particular foods. An example is the use of liver to treat night blindness (vitamin A deficiency) by the Egyptians (Papyrus Ebers 1550-1570 BC), Assyrians, Chinese, Japanese, Greeks, Romans, Persians and Arabs.
2. The second phase was characterised by the ability to **induce a deficiency disease** in animals, which started with the classical studies of Lunin and Eijkman around 1890. The ability to produce deficiency diseases, such as beriberi in animals, led to Hopkins' concept that small amounts of "accessory growth factors" are necessary for growth and life, and the coining of the term "vitamine" in 1912 by the Polish-American scientist, Funk.
3. The third phase consisted in seven decades of exciting research involving the **discovery, isolation, structure elucidation and synthesis** of all the vitamins, and culminating in the synthesis of vitamin B₁₂ in 1972. Most scientists think that the discovery of any new vitamin is quite unlikely, although efforts are still continuing in that quest. Many of the researchers involved in this golden age of the vitamins received a Nobel prize in recognition of their great achievements (Table 2).
4. During the era of discovery, a fourth period began which was concerned with the **biochemical functions, establishment of dietary requirements and commercial production**. In the early 1930s it was realised that riboflavin (vitamin B₂) was part of the "yellow enzyme", which in time led to the elucidation of the role of the B-vitamins as coenzymes. The subsequent identification of most of the B-vitamins as coenzymes remained a central theme, defining their function for many decades. The first commercial synthesis of vitamin C by Reichstein in 1933 was the start of a successful industrial effort that led to the availability of relatively inexpensive vitamins for research and use in animal feedstuffs, for the fortification of food products, and for supplements.
5. The accumulation of reports of **health benefits beyond preventing deficiencies** and exciting **new biochemical functions** of vitamins ushered in a fifth period, starting with the report in 1955 of the cholesterol-lowering effect of niacin (1). This is now a well accepted effect of the vitamin, which has nothing at all to do with its classical coenzyme role, and is a clear health effect beyond preventing the deficiency disease pellagra.

Finally, work on the biochemical function of vitamins in the last three decades has considerably expanded our concept of how vitamins function in the body and has helped provide a chemical basis for the in vivo observation of their health effects (Table 3).

Table 2: Vitamin-Related Nobel Prize Winners

Year	Name	Field	Comments
1928	Adolf Windaus	Chemistry	for his research into the constitution of the steroids and their connection with vitamins
1929	Christiaan Eijkman	Medicine & Physiology	for his discovery of the antineuritic vitamins
	Sir Frederick G. Hopkins	Medicine & Physiology	for his discovery of the growth stimulating vitamin
1934	George R. Minot William P. Murphy George H. Whipple	Medicine & Physiology	for their discoveries concerning liver therapy of anaemias
1937	Sir Walter N. Haworth	Chemistry	for his research into the constitution of carbohydrates and vitamin C
	Paul Karrer	Chemistry	for his research into the constitution of carotenoids, flavins and vitamins A and B ₂
	Albert Szent-Györgyi	Medicine & Physiology	for his discoveries in connection with the biological combustion processes, with particular reference to vitamin C and the catalysis of fumaric acid
1938	Richard Kuhn	Chemistry	for his work on carotenoids and vitamins
1943	Carl Peter Henrik Dam	Medicine & Physiology	for his discovery of vitamin K
	Edward A. Doisy	Medicine & Physiology	for his discovery of the chemical nature of vitamin K
1953	Fritz A. Lipmann	Medicine & Physiology	for his discovery of Coenzyme A and its importance for intermediary metabolism
1955	Axel H.T. Theorell	Medicine & Physiology	for his discoveries concerning the nature and mode of action of oxidation enzymes
1964	Konrad E. Bloch	Medicine & Physiology	for his discoveries concerning the mechanism and regulation of cholesterol and fatty acid metabolism
	Feodor Lynen	Medicine & Physiology	as above
	Dorothy C. Hodgkin	Chemistry	for her structural determination of vitamin B ₁₂
1967	Ragnar A. Granit	Medicine & Physiology	for his research, which illuminated the electrical properties of vision by studying wavelength discrimination in the eye
	Halden K. Hartline	Medicine & Physiology	for his research on the mechanisms of sight
	George Wald	Medicine & Physiology	for his research on the chemical processes that allow pigments in the retina of the eye to convert light into vision

Table 3: Biochemical Function of Vitamins

Vitamin	Classical Role	More Recent Role
Vitamin C	Hydroxylation Reaction	In Vivo Antioxidant
Beta-carotene	Provitamin A	Antioxidant, Immune Function
Vitamin K	Clotting Factors	Calcium Metabolism
Vitamin D	Calcium Absorption, Mineralisation of Bone	Differentiation and Growth, Immune Function
Vitamin B ₆	Coenzyme	Steroid Regulation
Niacin	Coenzyme	Lipid Lowering
Folic Acid	Production and Maintenance of New Cells	Protection Against Neural Tube Birth Defects
Folic Acid, B ₆ and B ₁₂	Energy Metabolism	May Lower Risk of Heart Disease and Stroke*
Antioxidant vitamins		Protection against Cancer and Heart Disease*

*Research ongoing

Dietary Reference Intakes

From 1941 until 1989, RDAs (Recommended Dietary Allowances) were established and used to evaluate and plan menus to meet the nutrient requirements of certain groups. They were also used in other applications such as interpreting food consumption records of populations, establishing standards for food assistance programs, establishing guidelines for nutrition labelling, etc.

The primary goal of RDAs was to prevent diseases caused by nutrient deficiencies.

In the early 1990s, the Food and Nutrition Board (FNB), the Institute of Medicine, the National Academy of Sciences (USA), with the involvement of Health Canada, undertook the task of revising the RDAs, and a new family of nutrient reference values was born – the Dietary Reference Intakes (DRIs).

The primary goal of having these new dietary reference values was not only to prevent nutrient deficiencies, but also to reduce the risk of chronic diseases such as osteoporosis, cancer, and cardiovascular disease.

The first report, Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D and Fluoride, was published in 1997. Since then, three additional vitamin related reports have been released, addressing folate and other B vitamins, dietary antioxidants (vitamins C, E, selenium and the carotenoids), and the micronutrients (vitamins A, K, and trace elements such as iron, iodine, etc). The DRIs are a comprehensive scientific source primarily for nutrition scientists (see References). They are used by health authorities in many countries as a basis for decisions regarding nutritional information on micronutrients.

There are four types of DRI reference values: the Estimated Average Requirement (EAR), the Recommended Dietary Allowance (RDA), the Adequate Intake (AI) and the Tolerable Upper Intake Level (UL).

- **Estimated Average Requirement (EAR)** – the amount of a nutrient that is estimated to meet the requirement of half of all healthy individuals in a given age and gender group. This value is based on a thorough review of the scientific literature.

- **Recommended Dietary Allowance (RDA)** – the average daily dietary intake of a nutrient that is sufficient to meet the requirement of nearly all (97-98%) healthy persons. This is the number to be used as a goal for individuals. It is calculated from the EAR.

- **Adequate Intake (AI)** – only established when an EAR (and thus an RDA) cannot be determined because the data are not clear-cut enough; a nutrient has either an RDA or an AI. The AI is based on experimental data or determined by estimating the amount of a nutrient eaten by a group of healthy people and assuming that the amount they consume is adequate to promote health.

- **Tolerable Upper Intake Level (UL)** – the highest continuing daily intake of a nutrient that is likely to pose no risks of adverse health effects for almost all individuals. As intake increases above the UL, the risk of adverse effects increases. Consistently consuming a nutrient at the upper level should not cause adverse effects. Intake levels at the UL can be interpreted as a ‘warning flag’, not as reason for alarm.

Certain groups at risk of vitamin deficiencies

With the advent of vitamin fortification in the manufacturing of flour, cereals and other foods, specific vitamin deficiency diseases such as scurvy, beriberi, rickets and pellagra have become rare in most industrialised countries. However, in many African, Asian and Latin American countries, chronic, diet-related diseases continue to be a major health problem. In these countries there is a need to eliminate frank vitamin A, C and B-complex deficiencies, as well as other micronutrient deficiencies (iodine, iron, selenium, zinc and calcium).

However, even in highly industrialised countries, numerous large government nutrition surveys of the population indicate that marginal vitamin deficiencies with unspecific symptoms, like fatigue and frequent headaches, are probably not rare. They are difficult for the individual to detect and are largely ignored. Marginal vitamin deficiency is a “state of gradual vitamin depletion in which there is evidence of personal lack of well-being associated with impairment of certain biochemical reactions”. Studies have found that many people have nutritional deficiencies which do not show up in a routine physical examination. It has

also been suggested that marginal deficiencies are linked to behavioural and physiological changes. Extensive surveys have revealed that more than 60% of the elderly have deficient dietary intake of vitamin D, E and folate. Other vitamins – critical not just for the elderly – include thiamin (B₁), panthothenic acid, and biotin.

Many individuals have health problems, habits, or living situations in which chronic or periodic intake of vitamins should exceed the ordinary requirement. High-risk-groups include:

- the elderly
- adolescents
- young or pregnant and lactating women
- alcoholics
- cigarette smokers
- vegetarians
- people fasting or on dietary intervention
- laxative abusers
- users of contraceptives and analgesics and other medications for chronic disease
- people with specific disorders of the gastrointestinal tract.

However, marginal deficiencies are not only limited to those groups listed. The gradual change in the way we live has influenced our diets and has altered our habitual intake of vitamins and minerals. Hectic lifestyles, reduced physical activity and an increase in fast and convenience food have all played a significant role. As a result, a significant proportion of the population fails to reach recommended intake levels.

Antioxidant Vitamins

Vitamin C, vitamin E and carotenoids, such as beta-carotene, are micronutrients with antioxidant properties. Antioxidants are substances that prevent oxidation or chemical reactions involving oxygen.

As the atmosphere changed from being anaerobic to aerobic, oxygen became available in energy production for living organisms, but it also carried a price. When energy is produced, unstable oxygen species known as free radicals are formed. Free radicals are also produced at other sites in the metabolism (e.g., by activated phagocytes as part of the immune defence), and through exogenous sources such as exposure to cigarette smoke, environmental pollutants and ultraviolet light. Free radicals are atoms or molecules that have an unpaired electron which makes them very reactive. They have the potential to damage DNA, proteins, carbohydrates, lipids and cell membranes. In addition to free radicals, there is another highly reactive compound that is a potent generator of free radicals: it is called singlet oxygen. This molecule is unique in that it contains a pair of electrons but exists in an unstable configuration and is very reactive.

The body has an elaborate antioxidant defence system that works to neutralise free radicals and other highly reactive species. The major biological antioxidants are enzymes (superoxide dismutase, catalase and glutathione peroxidase) as well as non-enzymatic scavengers (such as uric acid, CoQ10, glutathione, thiols in proteins) and the antioxidant vitamins (beta-carotene, vitamin C and E).

Each of the antioxidant nutrients has specific characteristics, and they often work synergistically to

strengthen the overall antioxidant capability of the body.

Vitamin E is the principal fat-soluble antioxidant in the body and is responsible for protecting the polyunsaturated fatty acids in cell membranes from oxidation by free radicals. Vitamin E exhibits a sparing effect on beta-carotene by protecting the conjugated double bonds from being oxidised. Exposure to increased oxygen levels, such as reperfusion, results in free radical-mediated tissue damage. However, due to the capability of vitamin E to work at higher oxygen pressures, free radicals are scavenged and tissue injury is minimised.

Beta-carotene also has antioxidant properties and is one of the most powerful quenchers of singlet oxygen. It can dissipate the energy of singlet oxygen, thus preventing this active molecule from generating free radicals.

Vitamin C, a water-soluble antioxidant, interacts with free radicals in the aqueous compartment of cells. Additionally, vitamin C is considered the most important antioxidant in extra-cellular fluids. Vitamin C has the ability to regenerate vitamin E after it has neutralised free radicals and terminated chain reactions.

The balance of free radical production and the level of antioxidant defences have important disease and health implications. If there are too many free radicals produced, and too few antioxidants, to a condition of "oxidative stress" develops which can lead to chronic injury.

It has therefore been suggested that oxidative stress might play a role in the development of a number of diseases:

- cancer
- atherosclerosis
- cardiovascular diseases
- cataracts
- age-related macular degeneration
- Alzheimer's disease
- immune dysfunction
- rheumatoid arthritis

Oxidative stress also plays a role in the aging process.

The scientific literature contains many research articles on the potential roles of the antioxidant nutrients in disease prevention. Many studies are just beginning while others continue to show the positive effects of the antioxidant nutrients. It therefore seems prudent to ensure an adequate intake of beta-carotene, vitamin C and vitamin E in the diet or through supplementation.

Vitamins continue to fascinate, and have become the focus of renewed

attention on the part of researchers, health/nutrition professionals, and government policymakers, as well as the general public.

References

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