Organic substances

A balanced human diet needs to contain a large number of different components. These include *proteins, carbohydrates, fats, minerals* (including water), and *vitamins.* These substances can occur in widely varying amounts and proportions, depending on the type of diet. As several components of the diet are *essential for life,* they have to be regularly ingested with food. Recommended daily minimums for nutrients have been published by the World Health Organization (WHO) and a number of national expert committees.

A. Energy requirement ●

The amount of energy required by a human is expressed in kJ d^{-1} (kilojoule per day). An older unit is the kilocalorie (kcal; 1 kcal = 4.187 kJ). The figures given are recommended values for adults with a normal body weight. However, actual requirements are based on age, sex, body weight, and in particular on physical activity. In those involved in competitive sports, for example, requirements can increase from 12 000 to 17 000 kJ d^{-1}.

It is recommended that about half of the energy intake should be in the form of carbohydrates, a third at most in the form of fat, and the rest as protein. The fact that *alcoholic beverages* can make a major contribution to daily energy intake is often overlooked. Ethanol has a caloric value of about 30 kJ g^{-1} (see p. 320).

B. Nutrients ●

Proteins provide the body with amino acids, which are used for endogenous protein biosynthesis. Excess amino acids are broken down to provide energy (see p. 174). Most amino acids are *glucogenic*—i. e., they can be converted into glucose (see p. 180).

Proteins are essential components of the diet, as they provide **essential amino acids** that the human body is not capable of producing on its own (see the table). Some amino acids, including cysteine and histidine, are not absolutely essential, but promote growth in children. Some amino acids are able to substitute for each other in the diet. For example, humans can form tyrosine, which is actually essential, by hydroxylation from phenylalanine, and cysteine from methionine.

The *minimum daily requirement* of protein is 37 g for men and 29 g for women, but the recommended amounts are about twice these values. Requirements in pregnant and breastfeeding women are even higher. Not only the quantity, but also the quality of protein is important. Proteins that lack several essential amino acids or only contain small quantities of them are considered to be of low value, and larger quantities of them are therefore needed. For example, pulses only contain small amounts of methionine, while wheat and corn proteins are poor in lysine. In contrast to vegetable proteins, most animal proteins are high-value (with exceptions such as collagen and gelatin).

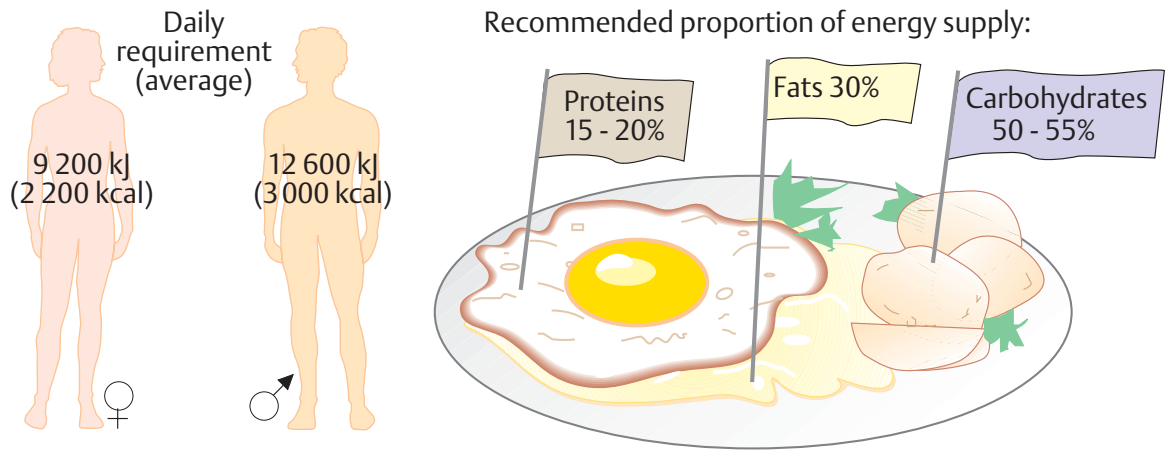
Carbohydrates serve as a general and easily available energy source. In the diet, they are present as *monosaccharides* in honey and fruit, or as *disaccharides* in milk and in all foods sweetened with sugar (sucrose). Metabolically usable *polysaccharides* are found in vegetable products (starch) and animal products (glycogen). Carbohydrates represent a substantial proportion of the body's energy supply, but they are not essential.

Fats are primarily important energy suppliers in the diet. Per gram, they provide more than twice as much energy as proteins and carbohydrates. Fats are essential as suppliers of *fat-soluble vitamins* (see p. 364) and as sources of *polyunsaturated fatty acids,* which are needed to biosynthesize eicosanoids (see pp. 48, 390).

Mineral substances and trace elements, a very heterogeneous group of essential nutrients, are discussed in more detail on p. 362. They are usually divided into macrominerals and microminerals.

Vitamins are also indispensable components of the diet. The animal body requires them in very small quantities in order to synthesize coenzymes and signaling substances (see pp. 364–369).

A. Energy requirement



B. Nutrients

	Quantity in body (kg)	Energy content kJ · g^{-1} (kcal · g^{-1})	Daily requirement (g) a	b	c	General function in metabolism	Essential constituents
Proteins	10	17 (4.1)	♂ 37 ♀ 29	55 45	92 75	Supplier of amino acids Energy source Daily requirement in mg per kg body weight	Essential amino acids:: Val (14) Leu (16) Ile (12) Lys (12) Phe (16) Trp (3) Met (10) Thr (8) Cys and His stimulate growth
Carbohydrates	1	17 (4.1)	0	390	240-310	General source of energy (glucose) Energy reserve (glycogen) Roughage (cellulose) Supporting substances (bones, cartilage, mucus)	Non-essential nutritional constituent
Fats	10-15	39 (9.3)	10	80	130	General energy source Most important energy reserve Solvent for vitamins Supplier of essential fatty acids	Poly-unsaturated fatty acids: Linoleic acid Linolenic acid Arachidonic acid (together 10 g/day)
Water	35-40	0	2 400	–	–	Solvent Cellular building block Dielectric Reaction partner Temperature regulator	
Minerals	3	0				Building blocks Electrolytes Cofactors of enzymes	Macrominerals Microminerals (trace elements)
Vitamins	–	–				Often precursors of coenzymes	Lipid-soluble vitamins Water-soluble vitamins

a: Minimum daily requirement b: Recommended daily intake c: Actual daily intake in industrialized nations

Minerals and trace elements

A. Minerals ◑

Water is the most important essential inorganic nutrient in the diet. In adults, the body has a daily requirement of 2–3 L of water, which is supplied from drinks, water contained in solid foods, and from the *oxidation water* produced in the respiratory chain (see p. 140). The special role of water for living processes is discussed in more detail elsewhere (see p. 26).

The elements essential for life can be divided into **macroelements** (daily requirement > 100 mg) and **microelements** (daily requirement < 100 mg). The macroelements include the **electrolytes** sodium (Na), potassium (K), calcium (Ca), and magnesium (Mg), and the nonmetals chlorine (Cl), phosphorus (P), sulfur (S), and iodine (I).

The essential microelements are only required in trace amounts (see also p. 2). This group includes iron (Fe), zinc (Zn), manganese (Mn), copper (Cu), cobalt (Co), chromium (Cr), selenium (Se), and molybdenum (Mo). Fluorine (F) is not essential for life, but does promote healthy bones and teeth. It is still a matter of controversy whether vanadium, nickel, tin, boron, and silicon also belong to the essential trace elements.

The second column in the table lists the average **amounts** of mineral substances in the body of an adult weighing 65 kg. The **daily requirements** listed in the fourth column also apply to an adult, and are *average values.* Children, pregnant and breast-feeding women, and those who are ill generally have higher mineral requirements relative to body weight than men.

As the human body is able to store many minerals, deviations from the daily ration are balanced out over a given period of time. Minerals stored in the body include water, which is distributed throughout the whole body; calcium, stored in the form of apatite in the bones (see p. 340); iodine, stored as thyroglobulin in the thyroid; and iron, stored in the form of ferritin and hemosiderin in the bone marrow, spleen, and liver (see p. 286). The storage site for many trace elements is the liver. In many cases, the metabolism of minerals is regulated by *hormones*—for example, the uptake and excretion of H_2O, Na^+, Ca^{2+}, and phosphate (see p. 328), and storage of Fe^{2+} and I^-.

Resorption of the required mineral substances from food usually depends on the body's requirements, and in several cases also on the composition of the diet. One example of dietary influence is calcium (see p. 342). Its resorption as Ca^{2+} is promoted by lactate and citrate, but phosphate, oxalic acid, and phytol inhibit calcium uptake from food due to complex formation and the production of insoluble salts.

Mineral deficiencies are not uncommon and can have quite a variety of causes—e. g., an unbalanced diet, resorption disturbances, and diseases. *Calcium deficiency* can lead to rickets, osteoporosis, and other disturbances. *Chloride deficiency* is observed as a result of severe Cl^- losses due to vomiting. Due to the low content of iodine in food in many regions of central Europe, *iodine deficiency* is widespread there and can lead to goiter. *Magnesium deficiency* can be caused by digestive disorders or an unbalanced diet—e. g., in alcoholism. Trace element deficiencies often result in a disturbed blood picture—i. e., forms of anemia.

The last column in the table lists some of the functions of minerals. It should be noted that almost all of the **macroelements** in the body function either as *nutrients* or *electrolytes.* Iodine (as a result of its incorporation into iodothyronines) and calcium act as *signaling substances.* Most **trace elements** are *cofactors for proteins,* especially for enzymes. Particularly important in quantitative terms are the *iron proteins* hemoglobin, myoglobin, and the cytochromes (see p. 286), as well as more than 300 different *zinc proteins.*

A. Minerals

Mineral	Content * (g)	Major source	Daily requirement (g)	Functions/Occurrence
Water	35 000-40 000	Drinks Water in solid foods From metabolism 300g	1200 900	Solvent, cellular building block, dielectric, coolant, medium for transport, reaction partner
Macroelements (daily requirement >100 mg)				
Na	100	Table salt	1.1-3.3	Osmoregulation, membrane potential, mineral metabolism
K	150	Vegetables, fruit, cereals	1.9-5.6	Membrane potential, mineral metabolism
Ca	1 300	Milk, milk products	0.8	Bone formation, blood clotting, signal molecule
Mg	20	Green vegetables	0.35	Bone formation, cofactor for enzymes
Cl	100	Table salt	1.7-5.1	Mineral metabolism
P	650	Meat, milk, cereals, vegetables	0.8	Bone formation, energy metabolism, nucleic acid metabolism
S	200	*S*-containing amino acids (Cys and Met)	0.2	Lipid and carbohydrate metabolism, conjugate formation
Microelements (trace elements)			(mg	
Fe	4-5	Meat, liver, eggs, vegetables, potatoes, cereals	10	Hemoglobin, myoglobin, cytochromes, Fe/S clusters
Zn	2-3	Meat, liver, cereals	15	Zinc enzymes
Mn	0.02	Found in many foodstuffs	2-5	Enzymes
Cu	0.1-0.2	Meat, vegetables, fruit, fish	2-3	Oxidases
Co	<0.01	Meat	Traces	Vitamin B_{12}
Cr	<0.01		0.05-0.2	Not clear
Mo	0.02	Cereals, nuts, legumes	0.15-0.5	Redox enzymes
Se		Vegetables, meat	0.05-0.2	Selenium enzymes
I	0.03	Seafood, iodized salt, drinking water	0.15	Thyroxin
Requirement not known				Metals Non-metals
F		Drinking water (fluoridated), tea, milk	0.0015-0.004	Bones, dental enamel

* Content in the body of a 65 kg adult

Lipid-soluble vitamins

Vitamins are essential organic compounds that the animal organism is not capable of forming itself, although it requires them in small amounts for metabolism. Most vitamins are **precursors of coenzymes**; in some cases, they are also precursors of **hormones** or act as **antioxidants**. Vitamin requirements vary from species to species and are influenced by age, sex, and physiological conditions such as pregnancy, breast-feeding, physical exercise, and nutrition.

A. Vitamin supply ●

A healthy diet usually covers average daily vitamin requirements. By contrast, malnutrition, malnourishment (e.g., an unbalanced diet in older people, malnourishment in alcoholics, ready meals), or resorption disturbances lead to an inadequate supply of vitamins from which **hypovitaminosis,** or in extreme cases avitaminosis, can result. Medical treatments that kill the intestinal flora—e.g., antibiotics—can also lead to vitamin deficiencies (K, B_{12}, H) due to the absence of bacterial vitamin synthesis.

Since only a few vitamins can be stored (A, D, E, B_{12}), a lack of vitamins quickly leads to **deficiency diseases.** These often affect the skin, blood cells, and nervous system. The causes of vitamin deficiencies can be treated by improving nutrition and by administering vitamins in tablet form. An overdose of vitamins only leads to **hypervitaminoses**, with toxic symptoms, in the case of vitamins A and D. Normally, excess vitamins are rapidly excreted with the urine.

B. Lipid-soluble vitamins ◑

Vitamins are classified as either lipid-soluble or water-soluble. The lipid-soluble vitamins include vitamins A, D, E, and K, all of which belong to the isoprenoids (see p. 52).

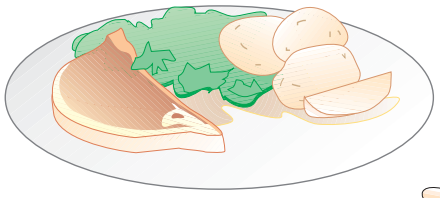
Vitamin A (retinol) is the parent substance of the *retinoids,* which include *retinal* and *retinoic acid.* The retinoids also can be synthesized by cleavage from the provitamin β-carotene. Retinoids are found in meat-containing diets, whereas β-carotene occurs in fruits and vegetables (particularly carrots). **Retinal** is involved in visual processes as the pigment of the chromoprotein *rhodopsin* (see p. 358). **Retinoic acid**, like the steroid hormones, influences the transcription of genes in the cell nucleus. It acts as a differentiation factor in growth and development processes. Vitamin A deficiency can result in *night blindness, visual impairment,* and *growth disturbances.*

Vitamin D (calciol, cholecalciferol) is the precursor of the hormone *calcitriol* (1α,25-dihydroxycholecalciferol; see p. 320). Together with two other hormones (parathyrin and calcitonin), calcitriol regulates the calcium metabolism (see p. 342). Calciol can be synthesized in the skin from 7-dehydrocholesterol, an endogenous steroid, by a photochemical reaction. Vitamin D deficiencies only occur when the skin receives insuf cient exposure to ultraviolet light and vitamin D is lacking in the diet. Deficiency is observed in the form of *rickets* in children and *osteomalacia* in adults. In both cases, bone mineralization is disturbed.

Vitamin E (tocopherol) and related compounds only occur in plants (e.g., wheat germ). They contain what is known as a *chroman ring.* In the lipid phase, vitamin E is mainly located in biological membranes, where as an *antioxidant* it protects unsaturated lipids against ROS (see p. 284) and other radicals.

Vitamin K (phylloquinone) and similar substances with modified side chains are involved in carboxylating glutamate residues of coagulation factors in the liver (see p. 290). The form that acts as a cofactor for carboxylase is derived from the vitamin by enzymatic reduction. Vitamin K antagonists (e.g., coumarin derivatives) inhibit this reduction and consequently carboxylation as well. This fact is used to inhibit blood coagulation in *prophylactic treatment against thrombosis*. Vitamin K deficiency occurs only rarely, as the vitamin is formed by bacteria of the intestinal flora.

A. Vitamin supply



Healthy nutrition

Vitamin requirement satisfied

Vitamin poisoning

Vitamin A and D

Poor nutrition
Malnutrition
Antibiotics
Disturbed resorption

Vitamin intake

Hypervitaminosis

Excess vitamins

Overdose

Diseases

Hypovitaminosis

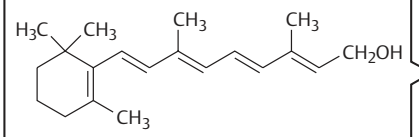
Urine

B. Lipid-soluble vitamins

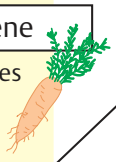
* Adult daily requirement

Provitamin	Functional form	Important for
β-Carotene	Retinal	Sight
Retinol	Retinol	Sugar transport
	Retinoic acid	Development Differentiation
Cholesterol	Calciol	Calcium metabolism
Tocopherols	Tocopherols	Anti-oxidant
Phylloquinones	Phyllohydroquinones	Blood clotting (carboxylation of plasma proteins)

A



Vegetables
Fruit



Visual pigments

1

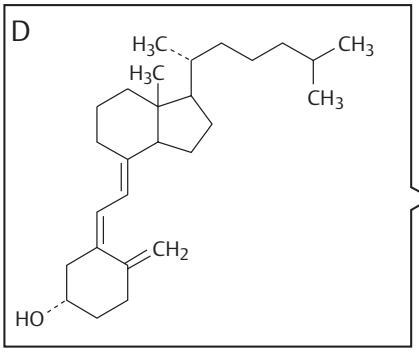
Milk
Liver
Egg yolk

Coenzyme

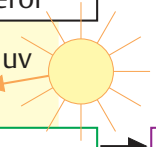
Retinoic acid

Signal molecule

D

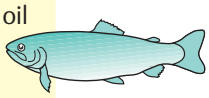


uv



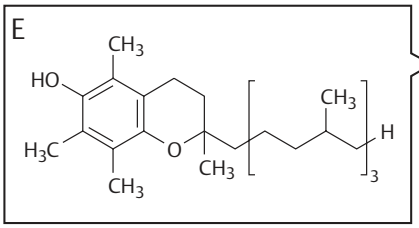
0.01

Cod liver oil
Milk
Egg yolk



Hormone

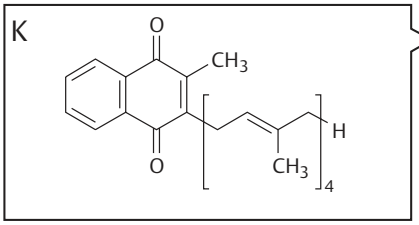
E



10

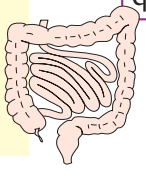
Cereals
Liver
Eggs
Seed oil

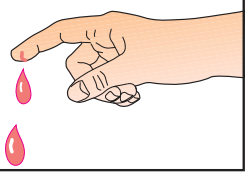
K



0.08

Intestinal bacteria
Vegetables
Liver





Water-soluble vitamins I

The B group of vitamins covers water-soluble vitamins, all of which serve as precursors for coenzymes. Their numbering sequence is not continuous, as many substances that were originally regarded as vitamins were not later confirmed as having vitamin characteristics.

A. Water-soluble vitamins I ◑

Vitamin B_1 (thiamine) contains two heterocyclic rings—a *pyrimidine ring* (a six-membered aromatic ring with two Ns) and a *thiazole ring* (a five-membered aromatic ring with N and S), which are joined by a methylene group. The active form of vitamin B_1 is **thiamine diphosphate** (TPP), which contributes as a coenzyme to the transfer of hydroxyalkyl residues (active aldehyde groups). The most important reactions of this type are oxidative decarboxylation of 2-oxoacids (see p. 134) and the transketolase reaction in the pentose phosphate pathway (see p. 152). Thiamine was the first vitamin to be discovered, around 100 years ago. Vitamin B_1 deficiency leads to *beriberi,* a disease with symptoms that include neurological disturbances, cardiac insuf ciency, and muscular atrophy.

Vitamin B_2 is a complex of several vitamins: riboflavin, folate, nicotinate, and pantothenic acid.

Riboflavin (from the Latin *flavus,* yellow) serves in the metabolism as a component of the redox coenzymes flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD; see p. 104). As prosthetic groups, **FMN** and **FAD** are cofactors for various oxidoreductases (see p. 32). No specific disease due to a deficiency of this vitamin is known.

Folate, the anion of folic acid, is made up of three different components—a *pteridine derivative, 4-aminobenzoate,* and one or more *glutamate* residues. After reduction to tetrahydrofolate (**THF**), folate serves as a coenzyme in the C_1 metabolism (see p. 418). Folate deficiency is relatively common, and leads to disturbances in nucleotide biosynthesis and thus cell proliferation. As the precursors for blood cells divide particularly rapidly, disturbances of the blood picture can occur, with increased amounts of abnormal precursors for megalocytes (*megaloblastic anemia*). Later, general damage ensues as phospholipid synthesis and the amino acid metabolism are affected.

In contrast to animals, microorganisms are able to synthesize folate from their own components. The growth of microorganisms can therefore be inhibited by *sulfonamides,* which competitively inhibit the incorporation of 4-aminobenzoate into folate (see p. 254). Since folate is not synthesized in the animal organism, sulfonamides have no effect on animal metabolism.

Nicotinate and **nicotinamide,** together referred to as "niacin," are required for biosynthesis of the coenzymes nicotinamide adenine dinucleotide (**NAD^+**) and nicotinamide adenine dinucleotide phosphate (**$NADP^+$**). These both serve in energy and nutrient metabolism as carriers of *hydride ions* (see pp. 32, 104). The animal organism is able to convert *tryptophan* into nicotinate, but only with a poor yield. Vitamin deficiency therefore only occurs when nicotinate, nicotinamide, and tryptophan are all simultaneously are lacking in the diet. It manifests in the form of skin damage (*pellagra*), digestive disturbances, and depression.

Pantothenic acid is an acid amide consisting of β-alanine and 2,4-dihydroxy-3,3′-dimethylbutyrate (pantoic acid). It is a precursor of *coenzyme A,* which is required for activation of acyl residues in the lipid metabolism (see pp. 12, 106). *Acyl carrier protein* (ACP; see p. 168) also contains pantothenic acid as part of its prosthetic group. Due to the widespread availability of pantothenic acid in food (Greek *pantothen* = "from everywhere"), deficiency diseases are rare.

Further information

The requirement for vitamins in humans and other animals is the result of mutations in the enzymes involved in biosynthetic coenzymes. As intermediates of coenzyme biosynthesis are available in suf cient amounts in the diet of heterotrophic animals (see p. 112), the lack of endogenous synthesis did not have unfavorable effects for them. Microorganisms and plants whose nutrition is mainly autotrophic have to produce all of these compounds themselves in order to survive.

A. Water-soluble vitamins I

* Adult daily requirement

Vitamin	Active form: coenzyme	Function in metabolism
B_1		
Thiamine	TPP Thiamine diphosphate	Transfer of hydroxy-alkyl residues
1.5 mg *		
Grain Yeast products Pork		
B_2		
Riboflavin	FMN FAD	Hydrogen transfer
1.8 mg*		
Milk Eggs		
4-Aminobenzoate residue Pteridine derivative Glu		
Folate	THF Tetrahydro-folate	C_1-metabolism
0.2 mg*		
Fresh green vegetables Liver		
Nicotinate Nicotinamide		
Nicotinate Nicotinamide	NADP NAD	Hydride transfer
20 mg*		
(or 1.2 g tryptophan)		
Meat, yeast products Fruit and vegetables		
Pantoinate β-Alanine		
Pantothenate	CoA	Activation of carboxy-lic acids
7 mg*		
Widely distributed		

Water-soluble vitamins II

A. Water-soluble vitamins II ◑

Vitamin B_6 consists of three substituted pyridines—**pyridoxal**, **pyridoxol**, and **pyridoxamine.** The illustration shows the structure of pyridoxal, which carries an aldehyde group (–CHO) at C-4. Pyridoxol is the corresponding alcohol ($–CH_2OH$), and pyridoxamine the amine ($–CH_2NH_2$).

The active form of vitamin B_6, **pyridoxal phosphate,** is the most important coenzyme in the amino acid metabolism (see p. 106). Almost all conversion reactions involving amino acids require pyridoxal phosphate, including transaminations, decarboxylations, dehydrogenations, etc. *Glycogen phosphorylase,* the enzyme for glycogen degradation, also contains pyridoxal phosphate as a cofactor. Vitamin B_6 deficiency is rare.

Vitamin B_{12} (cobalamine) is one of the most complex low-molecular-weight substances occurring in nature. The core of the molecule consists of a tetrapyrrol system (*corrin*), with cobalt as the central atom (see p. 108). The vitamin is exclusively synthesized by microorganisms. It is abundant in liver, meat, eggs, and milk, but not in plant products. As the intestinal flora synthesize vitamin $B_{12,}$ strict vegetarians usually also have an adequate supply of the vitamin.

Cobalamine can only be resorbed in the small intestine when the gastric mucosa secretes what is known as *intrinsic factor*—a glycoprotein that binds cobalamine (the *extrinsic factor*) and thereby protects it from degradation. In the blood, the vitamin is bound to a special protein known as *transcobalamin.* The liver is able to store vitamin B_{12} in amounts suf cient to last for several months. Vitamin B_{12} deficiency is usually due to an absence of intrinsic factor and the resulting resorption disturbance. This leads to a disturbance in blood formation known as *pernicious anemia.*

In animal metabolism, derivatives of cobalamine are mainly involved in rearrangement reactions. For example, they act as coenzymes in the conversion of methylmalonyl-CoA to succinyl-CoA (see p. 166), and in the formation of methionine from homocysteine (see p. 418). In prokaryotes, cobalamine derivatives also play a part in the reduction of ribonucleotides.

Vitamin C is L-**ascorbic acid** (chemically: 2-oxogulonolactone). The two hydroxyl groups have acidic properties. By releasing a proton, ascorbic acid therefore turns into its anion, **ascorbate**. Humans, apes, and guinea pigs require vitamin C because they lack the enzyme L-*gulonolactone oxidase (1.1.3.8),* which catalyzes the final step in the conversion of glucose into ascorbate.

Vitamin C is particularly abundant in fresh fruit and vegetables. Many soft drinks and foodstuffs also have synthetic ascorbic acid added to them as an antioxidant and flavor enhancer. Boiling slowly destroys vitamin C. In the body, ascorbic acid serves as a reducing agent in variations reactions (usually hydroxylations). Among the processes involved are *collagen synthesis, tyrosine degradation, catecholamine synthesis,* and *bile acid biosynthesis.* The daily requirement for ascorbic acid is about 60 mg, a comparatively large amount for a vitamin. Even higher doses of the vitamin have a protective effect against infections. However, the biochemical basis for this effect has not yet been explained. Vitamin C deficiency only occurs rarely nowadays; it becomes evident after a few months in the form of *scurvy,* with connective-tissue damage, bleeding, and tooth loss.

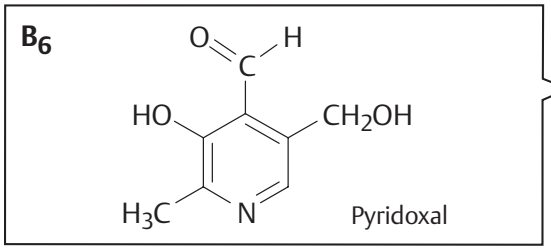
Vitamin H (**biotin)** is present in liver, egg yolk, and other foods; it is also synthesized by the intestinal flora. In the body, biotin is covalently attached via a lysine side chain to enzymes that catalyze carboxylation reactions. Biotin-dependent carboxylases include *pyruvate carboxylase* (see p. 154) and *acetyl-CoA carboxylase* (see p. 162). CO_2 binds, using up ATP, to one of the two N atoms of biotin, from which it is transferred to the acceptor (see p. 108).

Biotin binds with high af nity ($K_d = 10^{-15}$ M) and specificity to *avidin*, a protein found in egg white. Since boiling denatures avidin, biotin deficiency only occurs when egg whites are eaten raw.

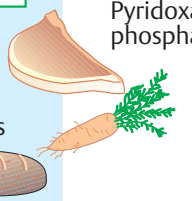
A. Water-soluble vitamins II

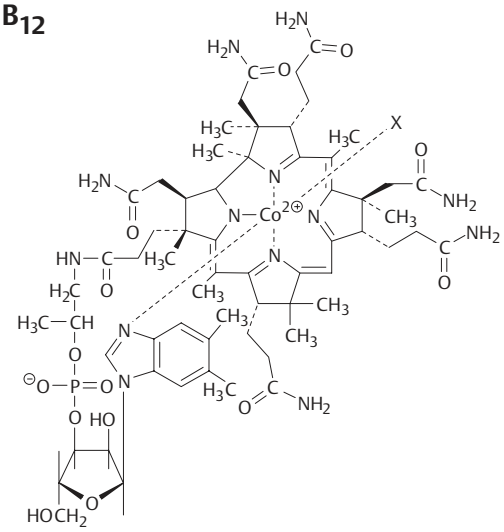
* Adult daily requirement

Vitamin	Active form: coenzyme	Function in metabolism
B_6	Pyridoxal Pyridoxol Pyridoxamine	PLP Pyridoxal phosphate	Activation of amino acids
B_{12}	Cobalamine	5-Deoxy-adenosyl cobalamine	Isomerization e.g.
C	Ascorbic acid	Ascorbate	Stabilization of enzyme systems, coenzyme, antioxidant
H	Biotin	B Biotin	Transfer of carboxyl groups

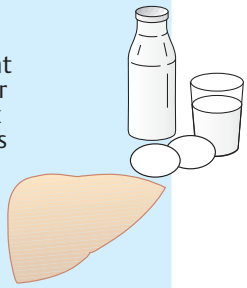


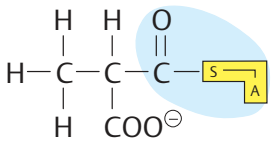
2 mg*
Meat
Vegetables
Grain products



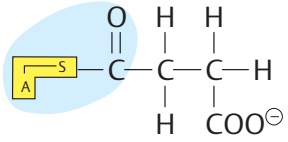


0.002 mg*
Meat
Liver
Milk
Eggs

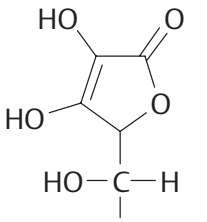




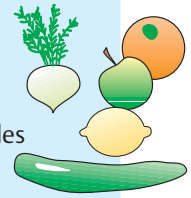
Methylmalonyl CoA

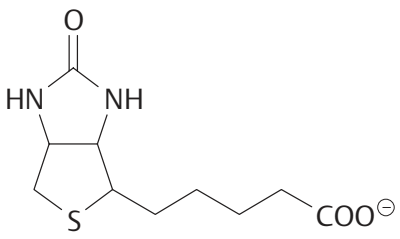


Succinyl CoA



60 mg*
Fruit
Vegetables





0.1 mg*
Yeast products
Legumes
Nuts