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18/MHS05/005

PHYSIOLOGY

Bch 204

Question: Vitamins and Coenzymes.

**VITAMINS**

A **vitamin** is an [organic molecule](https://en.m.wikipedia.org/wiki/Organic_molecule) (or related set of molecules) that is an [essential micronutrient](https://en.m.wikipedia.org/wiki/Nutrient#Essential_nutrients) which an [organism](https://en.m.wikipedia.org/wiki/Organism) needs in small quantities for the proper functioning of its [metabolism](https://en.m.wikipedia.org/wiki/Metabolism). Essential nutrients cannot be [synthesized](https://en.m.wikipedia.org/wiki/Biosynthesis) in the organism, either at all or not in sufficient quantities, and therefore must be obtained through the [diet](https://en.m.wikipedia.org/wiki/Diet_%28nutrition%29). [Vitamin C](https://en.m.wikipedia.org/wiki/Vitamin_C) can be synthesized by some species but not by others; it is not a vitamin in the first instance but is in the second. The term vitamin does not include the three other groups of essential nutrients: [minerals](https://en.m.wikipedia.org/wiki/Mineral_%28nutrient%29), [essential fatty acids](https://en.m.wikipedia.org/wiki/Essential_fatty_acid), and [essential amino acids](https://en.m.wikipedia.org/wiki/Essential_amino_acid). Most vitamins are not single molecules, but groups of related molecules called [vitamins](https://en.m.wikipedia.org/wiki/Vitamers). For example, [vitamin E](https://en.m.wikipedia.org/wiki/Vitamin_E) consists of four [tocopherols](https://en.m.wikipedia.org/wiki/Tocopherol) and four [tocotrienols](https://en.m.wikipedia.org/wiki/Tocotrienol%22%20%5Co%20%22Tocotrienol). The thirteen vitamins required by human metabolismare [vitamin A](https://en.m.wikipedia.org/wiki/Vitamin_A) (as all-*trans*-[retinol](https://en.m.wikipedia.org/wiki/Retinol), all-*trans*-retinyl-esters, as well as all-*trans*-[beta-carotene](https://en.m.wikipedia.org/wiki/Beta-carotene) and other provitamin A carotenoids), vitamin B1 ([thiamine](https://en.m.wikipedia.org/wiki/Thiamine)), vitamin B2 ([riboflavin](https://en.m.wikipedia.org/wiki/Riboflavin)), vitamin B3 ([niacin](https://en.m.wikipedia.org/wiki/Niacin)), vitamin B5 ([pantothenic acid](https://en.m.wikipedia.org/wiki/Pantothenic_acid%22%20%5Co%20%22Pantothenic%20acid)), vitamin B6 ([pyridoxine](https://en.m.wikipedia.org/wiki/Pyridoxine)), vitamin B7 ([biotin](https://en.m.wikipedia.org/wiki/Biotin)), vitamin B9 ([folic acid](https://en.m.wikipedia.org/wiki/Folic_acid) or [folate](https://en.m.wikipedia.org/wiki/Folate)), vitamin B12 ([cobalamins](https://en.m.wikipedia.org/wiki/Cobalamin%22%20%5Co%20%22Cobalamin)), vitamin C ([ascorbic acid](https://en.m.wikipedia.org/wiki/Ascorbic_acid)), [vitamin D](https://en.m.wikipedia.org/wiki/Vitamin_D) ([calciferols](https://en.m.wikipedia.org/wiki/Vitamin_D%22%20%5Co%20%22Vitamin%20D)), [vitamin E](https://en.m.wikipedia.org/wiki/Vitamin_E) ([tocopherols](https://en.m.wikipedia.org/wiki/Tocopherol%22%20%5Co%20%22Tocopherol) and [tocotrienols](https://en.m.wikipedia.org/wiki/Tocotrienol%22%20%5Co%20%22Tocotrienol)), and [vitamin K](https://en.m.wikipedia.org/wiki/Vitamin_K) ([quinones](https://en.m.wikipedia.org/wiki/Quinone%22%20%5Co%20%22Quinone)).

Vitamins have diverse biochemical functions. Vitamin A acts as a regulator of cell and tissue growth and differentiation. Vitamin D provides a hormone-like function, regulating mineral metabolism for bones and other organs. The [B complex](https://en.m.wikipedia.org/wiki/B_complex) vitamins function as enzyme [cofactors](https://en.m.wikipedia.org/wiki/Cofactor_%28biochemistry%29) (coenzymes) or the [precursors](https://en.m.wikipedia.org/wiki/Precursor_%28chemistry%29) for them. Vitamins C and E function as [antioxidants](https://en.m.wikipedia.org/wiki/Antioxidant%22%20%5Co%20%22Antioxidant).Both deficient and excess intake of a vitamin can potentially cause clinically significant illness, although excess intake of water-soluble vitamins is less likely to do so.

## List

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| --- | --- | --- | --- | --- | --- | --- |
| **Vitamin genericdescriptor name** | [**Vitamer**](https://en.m.wikipedia.org/wiki/Vitamer)**chemical name(s) (list not complete)** | [**Solubility**](https://en.m.wikipedia.org/wiki/Solubility) | **US**[**Recommended dietary allowances**](https://en.m.wikipedia.org/wiki/Reference_Daily_Intake)**(male/female, age 19–70)**[[8]](https://en.m.wikipedia.org/wiki/Vitamin#cite_note-DRITable-8) | **Deficiency disease** | **Overdose syndrome/symptoms** | **Food sources** |
| [**Vitamin A**](https://en.m.wikipedia.org/wiki/Vitamin_A) | all-*trans*-[Retinol](https://en.m.wikipedia.org/wiki/Retinol), [Retinal](https://en.m.wikipedia.org/wiki/Retinal), andalternative provitamin A-functioning [Carotenoids](https://en.m.wikipedia.org/wiki/Carotenoid%22%20%5Co%20%22Carotenoid)including all-*trans*-[beta-carotene](https://en.m.wikipedia.org/wiki/Beta-carotene) | Fat | 900 µg/700 µg | [Night blindness](https://en.m.wikipedia.org/wiki/Night_blindness), [hyperkeratosis](https://en.m.wikipedia.org/wiki/Hyperkeratosis), and [keratomalacia](https://en.m.wikipedia.org/wiki/Keratomalacia%22%20%5Co%20%22Keratomalacia)[[9]](https://en.m.wikipedia.org/wiki/Vitamin#cite_note-GOVa-9) | [Hypervitaminosis A](https://en.m.wikipedia.org/wiki/Hypervitaminosis_A) | from animal origin as Vitamin A / all-*trans*-Retinol: Fish in general, liver and dairy products;from plant origin as provitamin A / all-*trans*-beta-carotene: orange, ripe yellow fruits, leafy vegetables, carrots, pumpkin, squash, spinach; |
| [**Vitamin B1**](https://en.m.wikipedia.org/wiki/Thiamine) | [Thiamine](https://en.m.wikipedia.org/wiki/Thiamine) | Water | 1.2 mg/1.1 mg | [Beriberi](https://en.m.wikipedia.org/wiki/Beriberi), [Wernicke-Korsakoff syndrome](https://en.m.wikipedia.org/wiki/Wernicke%E2%80%93Korsakoff_syndrome%22%20%5Co%20%22Wernicke%E2%80%93Korsakoff%20syndrome) | Drowsiness and muscle relaxation[[10]](https://en.m.wikipedia.org/wiki/Vitamin#cite_note-10) | Pork, wholemeal grains, brown rice, vegetables, potatoes, liver, eggs |
| [**Vitamin B2**](https://en.m.wikipedia.org/wiki/Riboflavin) | [Riboflavin](https://en.m.wikipedia.org/wiki/Riboflavin) | Water | 1.3 mg/1.1 mg | [Ariboflavinosis](https://en.m.wikipedia.org/wiki/Ariboflavinosis), [glossitis](https://en.m.wikipedia.org/wiki/Glossitis%22%20%5Co%20%22Glossitis), [angular stomatitis](https://en.m.wikipedia.org/wiki/Angular_stomatitis) |  | Dairy products, bananas, green beans, asparagus |
| [**Vitamin B3**](https://en.m.wikipedia.org/wiki/Niacin) | [Niacin](https://en.m.wikipedia.org/wiki/Niacin), [Niacin amide](https://en.m.wikipedia.org/wiki/Niacinamide), [Nicotinamide riboside](https://en.m.wikipedia.org/wiki/Nicotinamide_riboside%22%20%5Co%20%22Nicotinamide%20riboside) | Water | 16 mg/14 mg | [Pellagra](https://en.m.wikipedia.org/wiki/Pellagra) | [Liver](https://en.m.wikipedia.org/wiki/Liver) damage (doses > 2g/day)[[11]](https://en.m.wikipedia.org/wiki/Vitamin#cite_note-11) and [other problems](https://en.m.wikipedia.org/wiki/Niacin#Toxicity) | Meat, fish, eggs, many vegetables, mushrooms, tree nuts |
| [**Vitamin B5**](https://en.m.wikipedia.org/wiki/Pantothenic_acid) | [Pantothenic acid](https://en.m.wikipedia.org/wiki/Pantothenic_acid) | Water | 5 mg/5 mg | [Paraesthesia](https://en.m.wikipedia.org/wiki/Paresthesia) | Diarrhoea; possibly nausea and heartburn.[[12]](https://en.m.wikipedia.org/wiki/Vitamin#cite_note-12) | Meat, broccoli, avocados |
| [**Vitamin B6**](https://en.m.wikipedia.org/wiki/Vitamin_B6) | [Pyridoxine](https://en.m.wikipedia.org/wiki/Pyridoxine), [Pyroxamine](https://en.m.wikipedia.org/wiki/Pyridoxamine%22%20%5Co%20%22Pyridoxamine), [Pyridoxal](https://en.m.wikipedia.org/wiki/Pyridoxal%22%20%5Co%20%22Pyridoxal) | Water | 1.3–1.7 mg/1.2–1.5 mg | [Anaemia](https://en.m.wikipedia.org/wiki/Anemia),[[13]](https://en.m.wikipedia.org/wiki/Vitamin#cite_note-GOVb6-13) [Peripheral neuropathy](https://en.m.wikipedia.org/wiki/Peripheral_neuropathy) | Impairment of [proprioception](https://en.m.wikipedia.org/wiki/Proprioception%22%20%5Co%20%22Proprioception), nerve damage (doses > 100 mg/day) | Meat, vegetables, tree nuts, bananas |
| [**Vitamin B7**](https://en.m.wikipedia.org/wiki/Biotin) | [Biotin](https://en.m.wikipedia.org/wiki/Biotin) | Water | AI: 30 µg/30 µg | [Dermatitis](https://en.m.wikipedia.org/wiki/Dermatitis), [enteritis](https://en.m.wikipedia.org/wiki/Enteritis) |  | Raw egg yolk, liver, peanuts, leafy green vegetables |
| [**Vitamin B9**](https://en.m.wikipedia.org/wiki/Folate) | [Folates](https://en.m.wikipedia.org/wiki/Folate), [Folic acid](https://en.m.wikipedia.org/wiki/Folic_acid) | Water | 400 µg/400 µg | [Megaloblastic anaemia](https://en.m.wikipedia.org/wiki/Megaloblastic_anemia) and deficiency during pregnancy is associated with [birth defects](https://en.m.wikipedia.org/wiki/Birth_defects), such as [neural tube](https://en.m.wikipedia.org/wiki/Neural_tube) defects | May mask symptoms of vitamin B12 deficiency; [other effects](https://en.m.wikipedia.org/wiki/Folate#Toxicity). | Leafy vegetables, pasta, bread, cereal, liver |
| [**Vitamin B12**](https://en.m.wikipedia.org/wiki/Vitamin_B12) | [Cyanocobalamin](https://en.m.wikipedia.org/wiki/Cyanocobalamin), [Hydroxocobalamin](https://en.m.wikipedia.org/wiki/Hydroxocobalamin), [Methylcobalamin](https://en.m.wikipedia.org/wiki/Methylcobalamin), [Adenosylcobalamin](https://en.m.wikipedia.org/wiki/Adenosylcobalamin) | Water | 2.4 µg/2.4 µg | [Vitamin B12 deficiency anaemia](https://en.m.wikipedia.org/wiki/Vitamin_B12_deficiency_anemia) | None proven | Meat, poultry, fish, eggs, milk |
| [**Vitamin C**](https://en.m.wikipedia.org/wiki/Vitamin_C) | [Ascorbic acid](https://en.m.wikipedia.org/wiki/Ascorbic_acid) | Water | 90 mg/75 mg | [Scurvy](https://en.m.wikipedia.org/wiki/Scurvy) | None known | Many fruits and vegetables, liver |
| [**Vitamin D**](https://en.m.wikipedia.org/wiki/Vitamin_D) | [Cholecalciferol](https://en.m.wikipedia.org/wiki/Cholecalciferol) (D3), [Ergocalciferol](https://en.m.wikipedia.org/wiki/Ergocalciferol%22%20%5Co%20%22Ergocalciferol) (D2)6 | Fat | 15 µg/15 µg | [Rickets](https://en.m.wikipedia.org/wiki/Rickets) and [osteomalacia](https://en.m.wikipedia.org/wiki/Osteomalacia%22%20%5Co%20%22Osteomalacia) | [Hypervitaminosis D](https://en.m.wikipedia.org/wiki/Hypervitaminosis_D) | Lichen, eggs, liver, certain fish species such as [sardines](https://en.m.wikipedia.org/wiki/Sardine), certain mushroom species such as [shiitake](https://en.m.wikipedia.org/wiki/Shiitake) |
| [**Vitamin E**](https://en.m.wikipedia.org/wiki/Vitamin_E) | [Tocopherols](https://en.m.wikipedia.org/wiki/Tocopherol), [Tocotrienols](https://en.m.wikipedia.org/wiki/Tocotrienol%22%20%5Co%20%22Tocotrienol) | Fat | 15 mg/15 mg | Deficiency is very rare; mild [haemolyticanaemia](https://en.m.wikipedia.org/wiki/Hemolytic_anemia%22%20%5Co%20%22Hemolytic%20anemia) in new-born infants[[15]](https://en.m.wikipedia.org/wiki/Vitamin#cite_note-Merck-15) | Possible increased incidence of congestive heart failure.[[16]](https://en.m.wikipedia.org/wiki/Vitamin#cite_note-16)[[17]](https://en.m.wikipedia.org/wiki/Vitamin#cite_note-Higdon-17) | Many fruits and vegetables, nuts and seeds, and seed oils |
| [**Vitamin K**](https://en.m.wikipedia.org/wiki/Vitamin_K) | [Phyllo Quinone](https://en.m.wikipedia.org/wiki/Phylloquinone), [Menaquinones](https://en.m.wikipedia.org/wiki/Menaquinone%22%20%5Co%20%22Menaquinone) | Fat | AI: 110 µg/120 µg | [Bleeding diathesis](https://en.m.wikipedia.org/wiki/Bleeding_diathesis) | Decreased anticoagulation effect of [warfarin](https://en.m.wikipedia.org/wiki/Warfarin%22%20%5Co%20%22Warfarin).[[18]](https://en.m.wikipedia.org/wiki/Vitamin#cite_note-18) | Leafy green vegetables such as spinach; egg yolks; liver |

**CLASSIFICATION**

Vitamins are classified as either [water](https://en.m.wikipedia.org/wiki/Water)-soluble or [fat-soluble](https://en.m.wikipedia.org/wiki/Lipophilicity). In humans there are 13 vitamins: 4 fat-soluble (A, D, E, and K) and 9 water-soluble (8 B vitamins and vitamin C). Water-soluble vitamins dissolve easily in water and, in general, are readily excreted from the body, to the degree that urinary output is a strong predictor of vitamin consumption. Because they are not as readily stored, more consistent intake is important. Fat-soluble vitamins are absorbed through the [intestinal tract](https://en.m.wikipedia.org/wiki/Intestinal_tract) with the help of [lipids](https://en.m.wikipedia.org/wiki/Lipid) (fats). Vitamins A and D can accumulate in the body, which can result in dangerous [hypervitaminosis](https://en.m.wikipedia.org/wiki/Hypervitaminosis). Fat-soluble vitamin deficiency due to malabsorption is of particular significance in [cystic fibrosis](https://en.m.wikipedia.org/wiki/Cystic_fibrosis).

**ANTI VITAMINS**

Anti-vitamins are chemical compounds that inhibit the absorption or actions of vitamins. For example, [avidin](https://en.m.wikipedia.org/wiki/Avidin) is a protein in raw egg whites that inhibits the absorption of [biotin](https://en.m.wikipedia.org/wiki/Biotin); it is deactivated by cooking. Pyrithiamine, a synthetic compound, has a molecular structure similar to thiamine, [vitamin B1](https://en.m.wikipedia.org/wiki/Vitamin_B1), and inhibits the [enzymes](https://en.m.wikipedia.org/wiki/Enzyme) that use thiamine.

**COENZYME**

**Coenzyme A** (**CoA**, **SHCoA**, **CoASH**) is a [coenzyme](https://en.m.wikipedia.org/wiki/Coenzyme), notable for its role in the [synthesis](https://en.m.wikipedia.org/wiki/Fatty_acid_metabolism#Synthesis) and [oxidation](https://en.m.wikipedia.org/wiki/Fatty_acid_metabolism#.CE.B2-Oxidation) of [fatty acids](https://en.m.wikipedia.org/wiki/Fatty_acid), and the oxidation of [pyruvate](https://en.m.wikipedia.org/wiki/Pyruvic_acid%22%20%5Co%20%22Pyruvic%20acid) in the [citric acid cycle](https://en.m.wikipedia.org/wiki/Citric_acid_cycle). All [genomes](https://en.m.wikipedia.org/wiki/Genome) sequenced to date encode enzymes that use coenzyme A as a substrate, and around 4% of cellular enzymes use it (or a [thioester](https://en.m.wikipedia.org/wiki/Thioester%22%20%5Co%20%22Thioester)) as a substrate. In humans, CoA biosynthesis requires [cysteine](https://en.m.wikipedia.org/wiki/Cysteine%22%20%5Co%20%22Cysteine), [pantothenate](https://en.m.wikipedia.org/wiki/Pantothenic_acid%22%20%5Co%20%22Pantothenic%20acid) (vitamin B5), and [adenosine triphosphate](https://en.m.wikipedia.org/wiki/Adenosine_triphosphate) (ATP)

**DISCOVERY OF COENZYMES**

Coenzyme A was identified by [Fritz Lipmann](https://en.m.wikipedia.org/wiki/Fritz_Lipmann) in 1946, who also later gave it its name. Its structure was determined during the early 1950s at the [Lister Institute](https://en.m.wikipedia.org/wiki/Lister_Institute), London, together by Lipmann and other workers at [Harvard Medical School](https://en.m.wikipedia.org/wiki/Harvard_Medical_School) and [Massachusetts General Hospital](https://en.m.wikipedia.org/wiki/Massachusetts_General_Hospital). Lipmann initially intended to study acetyl transfer in animals, and from these experiments he noticed a unique factor that was not present in enzyme extracts but was evident in all organs of the animals. He was able to isolate and purify the factor from pig liver and discovered that its function was related to a coenzyme that was active in choline acetylation. The coenzyme was named coenzyme A to stand for "activation of acetate". In 1953, Fritz Lipmann won the Nobel Prize in Physiology or Medicine "for his discovery of co-enzyme A and its importance for intermediary metabolism"

**BIO SYNTHESIS**

Coenzyme A is naturally synthesized from [pantothenate](https://en.m.wikipedia.org/wiki/Pantothenic_acid%22%20%5Co%20%22Pantothenic%20acid) (vitamin B5), which is found in food such as meat, vegetables, cereal grains, legumes, eggs, and milk. In humans and most living organisms, pantothenate is an essential vitamin that has a variety of functions. In some plants and bacteria, including [Escherichia coli](https://en.m.wikipedia.org/wiki/Escherichia_coli), pantothenate can be synthesised *de novo* and is therefore not considered essential. These bacteria synthesize pantothenate from the amino acid aspartate and a metabolite in valine biosynthesis

**Details of the biosynthetic pathway of CoA synthesis from pantothenic acid.**

1. [Pantothenate](https://en.m.wikipedia.org/wiki/Pantothenate) (vitamin B5) is phosphorylated to 4′-phosphopantothenate by the enzyme [pantothenate kinase](https://en.m.wikipedia.org/wiki/Pantothenate_kinase%22%20%5Co%20%22Pantothenate%20kinase) (PanK; CoaA; CoaX). This is the committed step in CoA biosynthesis and requires ATP.[[10]](https://en.m.wikipedia.org/wiki/Coenzyme_A#cite_note-:3-10)
2. A [cysteine](https://en.m.wikipedia.org/wiki/Cysteine%22%20%5Co%20%22Cysteine) is added to 4′-phosphopantothenate by the enzyme [phosphopantothenoylcysteine synthase](https://en.m.wikipedia.org/wiki/Phosphopantothenoylcysteine_synthetase%22%20%5Co%20%22Phosphopantothenoylcysteine%20synthetase) (PPCS; CoaB) to form 4'-phospho-N-pantothenoylcysteine (PPC). This step is coupled with ATP hydrolysis.
3. PPC is decarboxylated to [4′-phosphopantetheine](https://en.m.wikipedia.org/wiki/4%27-phosphopantetheine) by [phosphopantothenoylcysteine decarboxylase](https://en.m.wikipedia.org/wiki/Phosphopantothenoylcysteine_decarboxylase%22%20%5Co%20%22Phosphopantothenoylcysteine%20decarboxylase) (PPC-DC; CoaC)
4. 4′-Phosphopantetheine is adenylated (or more properly, [AMPylated](https://en.m.wikipedia.org/wiki/Adenylation%22%20%5Co%20%22Adenylation)) to form dephospho-CoA by the enzyme phosphopantetheine adenylyl transferase (PPAT; CoaD)
5. Finally, dephospho-CoA is phosphorylated to coenzyme A by the enzyme dephosphocoenzyme A kinase (DPCK; CoaE). This final step requires ATP.

**USE IN BIOLOGICAL RESEARCH**

Coenzyme A is available from various chemical suppliers as the free acid and [lithium](https://en.m.wikipedia.org/wiki/Lithium) or [sodium](https://en.m.wikipedia.org/wiki/Sodium) salts. The free acid of coenzyme A is detectably unstable, with around 5% degradation observed after 6 months when stored at −20 °C, and near complete degradation after 1 month at 37 °C. The lithium and sodium salts of CoA are more stable, with negligible degradation noted over several months at various temperatures. Aqueous solutions of coenzyme A are unstable above pH 8, with 31% of activity lost after 24 hours at 25 °C and pH 8. CoA stock solutions are relatively stable when frozen at pH 2–6. The major route of CoA activity loss is likely the air oxidation of CoA to CoA disulfides. CoA mixed disulfides, such as CoA-*S*–*S*-glutathione, are commonly noted contaminants in commercial preparations of CoA.Free CoA can be regenerated from CoA disulfide and mixed CoA disulfides with reducing agents such as [dithiothreitol](https://en.m.wikipedia.org/wiki/Dithiothreitol%22%20%5Co%20%22Dithiothreitol) or [2-mercaptoethanol](https://en.m.wikipedia.org/wiki/2-mercaptoethanol).