VITAMINS

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Originally, most **vitamins** were **used** for the **prevention** of **deficiency** syndromes **associated** with **inadequate nutritional** intake.

It was **encouraged** by the **misinformation** that if **vitamins** are **important** for maintenance of **health**, then **greater ingestion** must necessarily provide **better health**.

Vitamins **deficiencies** may be **higher** in the following **individuals**:

(i) Those living **below** the **poverty level**.
(ii) Patients with **malabsorption** syndromes.
(iii) Patients undergoing **treatment** with **antibiotics** that **alter normal** vitamin-synthesizing **bacterial flora**.
(iv) Individuals with **behavioral problems** that encourage **poor dietary** intake.
(v) Inadequate intake of nutritionally **rich foods** that **lead** to **decreased ingestion** or **poor absorption** of **vitamins** (poorly planned vegetarian diets, reducing diets in the elderly, etc.).

FAT-SOLUBLE VITAMINS

Vitamin A and Retinoic Acid Derivatives

Vitamin A, and its **derivatives**, is essential for proper **maintenance** of **vision** acuity, for **dental** development, **skeletal muscle** and **bone** growth, **corticosteroid** synthesis, and **reproduction**.

Derivatives of vitamin A include **retinol**, **retinal**, **retinoic acid** and **β-carotene**.

These **physiologically** important factors **support** proper functioning of the **reproductive** cycle, **visual** acuity, **somatic growth** and **differentiation**, and **visual adaptation** to darkness, **respectively**.

A balanced **diet consisting** of fish, liver, meat, carrots and dairy products provides the **RDA** for **vitamin A**.

Hypervitaminosis A syndrome develops with **chronic ingestion** of **megadoses** of the vitamin **or** in the **presence** of **hepatic disease**.

In general, doses of **25,000 IU/kg** result in **acute** toxicity.

Prolonged excessive consumption of vitamin A for **6** to **15** months (**4000 IU/kg**) also produces a toxic syndrome.

The **retinoids** are **derivatives** of **retinoic acid** that **promote** epithelial **cell differentiation**, **keratinization**, and **local inflammation**.

Therapeutically, the desired **effect** results in the **reduction** of the **severity** and **formation** of **microcomedones** characteristic of **acne**.

Adverse effects of **most** of the **topical products** are related to transient or **temporary local inflammatory** responses.

Contraindicated in **women** of **childbearing** potential (**teratogenic risk**).

Human **fetal abnormalities** with oral **isotretinoin** ingestion, including **skeletal**, **neurological** and **cardiovascular** anomalies.

Vitamin D

Vitamin D is a **fat-soluble** vitamin with **hormone**-like **activity**.

Calcitriol is the **most active** form of **vitamin D3**.

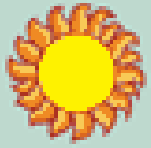
In **conjunction** with parathyroid hormone (**PTH**), calcitriol **maintains blood calcium** levels by **promoting** GI **absorption** of **calcium** and **phosphorus**, and **decrease magnesium** absorption.

Calcitriol stimulates **renal** tubular **reabsorption** of **calcium**.

Negative feedback of **blood calcium** controls **secretion** of **calcitonin** from the **thyroid gland** and **PTH** from the **parathyroid gland**.

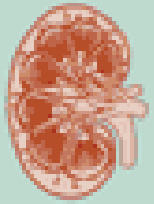
Vitamin D Metabolism

7-dehydrocholesterol



cholecalciferol (vitamin D_3)

calcidiol (25[OH] D_3)



calcitriol
(1α,25[OH]$_2$$D_3$ and 24R,25[OH]$_2$$D_3$)

Effects of Calcitriol

Intestines
- Increased calcium absorption
- Increased phosphorus absorption
- Decreased magnesium absorption

Parathyroid gland
- Increased mineralization indirectly via increased calcium absorption in intestinal lumen
- At high doses, increased osteoclastic bone

Kidneys
- Autoregulation of calcitriol production

Years of research have led to an in-depth understanding of the metabolism of vitamin D. But the moniker of "vitamin" is not correct in the classic sense. In reality, vitamin D is a prohormone that has many effects.

Oral or parenteral **administration** of the **active forms** of **vitamin D** is indicated in the **management** of **hypocalcemia**.

The **condition** is **prevalent** in **renal dialysis** patients and individuals with **hypoparathyroidism** (treated with **calcitriol**), refractory **rickets**, and **hypophosphatemia** (treated with **vitamin D2**).

The compounds are **used** as **dietary supplements** or in the management of **vitamin D deficiency** (**vitamin D3**).

Deficiency states of **vitamin D** result in **rickets** in growing **children** and **osteomalacia** in **adult**s.

Limited exposure to **sunlight** is probably the **most** important **reason** for development of a **deficiency** state **leading** to **hypocalcemia**.

Hypocalcemia, in turn, **stimulates PTH secretion**, which **promotes renal α1-hydroxylase** activity (responsible for **conversion** of precursors to **D2** and **D3** in **kidney**).

Causes and Effects of Rickets in Children and Osteomalacia in Adults (Vitamin D Deficiency)

Metabolic, physiologic, or behavioral cause	Pathologic or net effect on vitamin D
Inadequate exposure to sunlight; races or descendants of African or other dark-skinned nations	Reduced endogenous synthesis
Poor or inadequate nutrition (poor diet)	Poor GI absorption
Cytochrome P-450–inducing drugs[a]	Enhanced degradation
Liver, renal disease	Impaired synthesis
Chronic antacid ingestion; renal disease	Phosphate depletion

Administration of **vitamin D** in **excess** of **daily** requirements may **cause** clinical **signs** of acute or chronic overdosage (**hypervitaminosis D syndrome**), **most** of which are **related** to **elevated calcium** levels.

Concomitant **high intake** of **calcium** and **phosphate** may cause the development of **similar abnormalities**.

Treatment of **accidental overdose** requires **general supportive** measures.

Treatment of **hypervitaminosis D** with **hypercalcemia** consists of prompt **withdrawal** of **vitamin D supplements**, **low calcium diet**, **laxatives**, and **attention** to serum **electrolyte imbalances** and **cardiac function**.

Major blood vessels, the **myocardium** and **kidneys** are at **risk** of developing **ectopic calcification**.

Hypercalcemic crisis with **dehydration**, **stupor** and **coma** requires more immediate attention, such as prompt **hydration**, **diuretics**, short-term **hemodialysis**, **corticosteroids** and **urine acidification**.

Vitamin E

The most biologically **active form** of **vitamin E**, a fat-soluble vitamin, is **α-tocopherol**.

The **antioxidant** properties of **vitamin E** help to protect cells from **oxidative processes**.

For **example**, it **preserves** the **integrity** of the **red blood cell** membrane, stimulates **production** of **cofactors** in **steroid metabolism**, and **suppresses prostaglandin synthesis** and **platelet aggregation.**

Vitamin E has numerous **unlabeled uses**, including the **prevention** of **cancer**, **preservation** of **ageless skin**, and **stimulation** of **sex drive**.

However, it is **only indicated** for the treatment of nutritional states related to **vitamin E deficiency**.

It is **widely** distributed in **nature**, predominantly found along with **polyunsaturated fatty acids** in **vegetables** and their oils, **meat**, **dairy**, **wheat**, **soy** and **nuts**.

Its **ubiquitous presence**, coupled **with** a **low RDA**, makes clinical **deficiency** of **vitamin E** a **rare** phenomenon.

Premature infants and **patients** with **malabsorption** syndromes, however, are more **likely** to **develop deficiency**, defined as having **tocopherol** levels **less** than **0.5 mg/dL**.

Signs and **symptoms** of deficiency, particularly **in premature infants**, include **hemolytic anemia**, **thrombocytosis** and **increased platelet aggregation**.

Hypervitaminosis E are usually at doses **greater** than **3000 IU**.

Vitamin K

Vitamin K, and its equally active synthetic analog **K1** (**phytonadione**), is a **fat soluble** vitamin.

Vitamin K **promotes** the **hepatic synthesis** of **coagulation factors II** (prothrombin), **VII** (proconvertin), **IX** (plasma thromboplastin), and **X** (Stuart factor).

The vitamin **acts** as a **cofactor** for **hepatic post-translation carboxylation** of **glutamic acid** residues to the active **γ-carboxyl glutamate** moieties of the **clotting proteins**, as well as **anticoagulant proteins** C, S and **osteocalcin** (bone matrix).

Phytonadione is indicated in the **treatment** of **coagulation disorders related** to vitamin K–associated decreased **synthesis** of **coagulation factors**.

It is **also** valuable in the **treatment** of **prothrombin deficiency** (hypoprothrombinemia) **induced** by oral or parenteral **anticoagulants**, **salicylates** or **antibiotics**.

Sources of the vitamin are provided in various **foods**, particularly green vegetables, dairy products, meats, grains and fruits.

In addition, it is **synthesized** by **normal intestinal bacterial flora**.

Vitamin K **deficiency** is **uncommon**, **except** in **premature** and breast-fed **newborns**, patients with **malabsorption** syndromes, and **patients receiving** chronic **anticoagulant** or **broad-spectrum antibiotic** therapy.

Hypervitaminosis K is **rare** because the drug is **not available OTC**.

Fat-Soluble Vitamins and Toxic Manifestations of Excessive Consumption or Administration

Vitamins	Derivatives	Proprietary name	Deficiency state	Common ADRs
Vitamin A	Retinol, retinal, retinoic acid	Palmitate A 5000 tablets, Aquasol A injection, various tablets and capsules	Kwashiorkor, xerophthalmia, keratomalacia	Acute: anorexia, nervousness, increased intracranial pressure, blurred vision Chronic: hepatomegaly, allopecia, dry scaly skin, bone pain and demineralization, cheilitis[a]
	β-Carotene	Various capsules		Yellow-orange skin discoloration
Retinoids	Adapalene	Differin gel	None	Erythema, scaling, dryness, pruritis, burning, photosensitivity, skin discoloration
	Tretinoin	Retin-A gels, creams		
	Tazarotene	Tazorac gel, cream		
	Isotretinoin[b]	Accutane capsules	None	Major human fetal malformations involving neurological, skeletal, muscular, hormonal, and CV systems; ADRs including pancreatitis, psychiatric disorders, visual impairment, dermatologic, CNS, GI, GU, IBS
Vitamin D	Calcitriol (D_3)	Rocaltrol	Rickets (children)	Acute: weakness, headache, NV, constipation, bone pain
	Cholecalciferol (D_3)	Delta-D	Osteomalacia (adults)	Chronic: anorexia, polydipsia, polyuria, nephrocalcinosis, vascular calcification
	Ergocalciferol (D_2)	Drisdol, Calciferol		Chronic OD: hypercalcemia, hypercalciuria, hyperphosphatemia
Vitamin E	DL-α-Tocopherols	Aquavit-E, various products and dosage forms	Anemia, thrombocytosis, increased platelet aggregation (uncommon)	Hypervitaminosis E: NVD, weakness, thrombophlebitis, increased lipids and hormone levels, breast tumors, gynecomastia, altered immunity
Vitamin K	Phytonadione (K_1)	Mephyton, AquaMEPHYTON	Hemorrhagic disorders (uncommon)	Severe allergic reactions, especially upon injection; transient flushing, pain at site; hemolytic anemia in infants; scleroderma-like lesions, hyperbilirubinemia

WATER-SOLUBLE VITAMINS

Thiamine

Thiamine (vitamin B1) is **essential** for normal **aerobic metabolism** and **tissue development**, proper transmission of **nerve impulses** and **synthesis** of **acetylcholine**.

It **combines** with adenosine triphosphate (**ATP**) to form **thiamine pyrophosphate**, the **active** form of **thiamine**.

Thiamine is **indicated** in the oral or parenteral treatment of **B1 deficiency** syndromes (**beriberi**) and in **neuritis of pregnancy**.

Sources of the vitamin **include** brewer's yeast, meat, nuts, grains, and dairy products.

Beriberi is the classic deficiency syndrome frequently **associated** with **chronic alcoholism**, renal **dialysis patients**, and individuals with **liver and biliary dysfunction** or **poor diets**.

The syndrome is **characterized** by **peripheral neuritis**, **muscle wasting** (dry beriberi), and **cardiac failure and edema** (wet beriberi).

Hypersensitivity reactions, **anaphylactic shock**, and **hypervitaminosis** syndrome are **rare** with oral or IV doses.

Riboflavin

Vitamin B2 is a **component** of flavin mononucleotide (**FMN**) and flavin adenine dinucleotide (**FAD**).

These two coenzymes **catalyze** a variety of **oxidation reduction reactions**, including **glucose oxidation** and **amino acid deamination**.

The vitamin **found** in fish, poultry, dairy products and leafy vegetables.

Poor intestinal **absorption** of riboflavin **limits** its **toxicity**.

Deficiency state (**ariboflavinosis**) is **rare** and often masked by other nutritional insufficiency.

Early **symptoms** include **cheilosis** (fissures in the mouth), **glossitis** (inflammation of the tongue), interstitial **ophthalmic keratosis** and **dermatitis**.

Niacin

Vitamin B3 (nicotinic acid) is a **component** of nicotinamide adenine dinucleotide (**NAD**, coenzyme I) and nicotinamide adenine dinucleotide phosphate (**NADP**, coenzyme II).

The two coenzymes **catalyze oxidation-reduction reactions** that act as electron acceptors and hydrogenases.

Niacin is **derived** from **niacinamide** or **tryptophan** and **occurs** naturally in most red meats, fish, poultry, dairy products, nuts and vegetables.

Niacin deficiency (**pellagra**, Italian rough skin) is **characterized** by dermatitis, dementia, and diarrhea (**3Ds**).

It is often **seen** in **chronic alcoholism**, **malabsorption syndrome**, and in patients **receiving isoniazid** (an antituberculosis antibiotic).

Pharmacologically, **nicotinic acid**, but **not nicotinamide**, is effective in **reducing serum lipids**.

In addition, it triggers **peripheral vasodilation** and **increases blood flow** by stimulating **histamine release**. These properties are distinct from its nutrient role.

Consequently, nicotinic acid is **useful** in the **treatment** of **hypercholesterolemia** and **hyperlipidemia** and in the management of **niacin deficiency** and pellagra.

Folic Acid

Folate (Pteroylglutamic acid) is **found** in **leafy vegetables**, **organ meats** and **yeast**.

Physiologically, folic acid is **required** for **nucleoprotein synthesis** and **maintenance** of **hematopoiesis**.

It is **converted intracellularly** to **tetrahydrofolic acid**, which acts as a **cofactor** in the **biosynthesis** of **purines** and **thymidylates** of **nucleic acids**.

Consequently, **deficiency** of folic acid (along **with** vitamin **B12**) is often seen during **pregnancy** and in **malabsorption** conditions and is **responsible** for **defective DNA synthesis**.

The **condition** is **manifested** by the **production** of **enlarged immature red cells** characteristic of **megaloblastic anemia**.

Cyanocobalamin

Dietary **deficiency** of vitamin B12 is **rare** since the nutrient is **found** in all meats and dairy products but is **absent** from plant foods.

Strict **vegetarians** and individuals with **malabsorption** syndrome, especially those experiencing atrophic gastritis who cannot absorb B12, are prone to developing **pernicious anemia**.

Presence of **intestinal parasitic infections** has been noted to induce **B12 deficiency**.

Signs and **symptoms** of the syndrome, however, **may not** be evident for **three** to **five years**.

Pernicious anemia develops principally **because** of the **lack** of secretion of **intrinsic factor** in the **stomach**, which is **necessary** for **absorption** of **cyanocobalamin** in the ileum.

Vitamin B12 is **essential** for **cell growth**, **hematopoiesis**, and **nucleic acid** and **neuronal myelin synthesis**.

Several preparations of cyanocobalamin are available and are **indicated** for the **management** of **B12 deficiency** (all dosage forms) and **pernicious anemia** (injection).

Ascorbic Acid

Vitamin C is **abundant** in citrus fruits, strawberries, tomatoes, and leafy vegetables.

It is **involved** in numerous **oxidation-reduction reactions**, including the **synthesis** of **connective tissue** components, such as **chondroitin** sulfate and **collagen**.

In addition it **improves** the **absorption** of **iron** from the GI tract, **promotes** the **synthesis** of **catecholamine** neurotransmitters, and is an important **cofactor** in the **wound-healing** process.

Deficiency of ascorbic acid (**scurvy**) is well documented and **occurs** in individuals with **inadequate dietary** intake, **chronic alcoholism** and the **elderly**.

Some **suppression** of **ascorbate blood levels** appears in **situations** such as extreme cold, heat, fever, physical trauma, tuberculosis, and cigarette smoking and in women taking oral contraceptives.

Scurvy is **characterized** by **impaired wound healing**, **petechial hemorrhage** (pinpoint, minute spots in the skin), and **perifollicular hemorrhage** (surrounding the hair follicles).

It is **also** demonstrated by inflammatory **bleeding gums**, **loss of teeth**, **arrested skeletal development** (in children), **dry skin**, **joint pain** and increased **susceptibility** to **infections** and **fatigue**.

Although the **incidence** is **low**, long-term effects of **doses greater** than the **DRI** are associated with **cataracts** and **coronary artery disease**, **increased iron absorption**, and development of **renal oxalate stones**.

Interestingly, **sudden curtailing** of vitamin C ingestion **after chronic** megadoses administration **may** precipitate **signs** of **scurvy**.

Pyridoxine

Found primarily in vegetables, peanuts, eggs, soy, and cereals.

Vitamin B6 (pyridoxal, pyridoxamine) appears to enact a significant **role** in **neuronal development**.

It is particularly **important** in the **formation** of **pyridoxal dependent decarboxylase** necessary for the **synthesis** of the neurotransmitter γ-aminobutyric acid (**GABA**).

In fact, pyridoxine **deficiencies**, although **rare**, are **characterized** by **unremarkable** features of **dermatologic**, **hematologic** and **nervous system anomalies**.

Vitamin B6 deficiencies **occur** in individuals who are also susceptible to deficiencies of other B-vitamins, including **chronic alcoholism** and **malabsorption** syndrome.

Patients receiving **isoniazid**, **cycloserine** (antituberculosis antibiotics), **hydralazine** (antihypertensive), and oral **contraceptives** are also prone to **B6 deficiency**.

Pyridoxine is **indicated** solely for the management of **pyridoxine deficiency** states.

Sensory **neuropathies**, **ataxia**, and **numbness** are possible in subjects **receiving megadoses** for **several months**.

Pantothenic Acid

Vitamin B5 is important as a **cofactor** in **enzyme-catalyzed** reactions involving **carbohydrates**, **gluconeogenesis**, **fatty acids**, and **steroids**.

It is **distributed** in **many food** products and is **nontoxic**, and **deficiencies** are seen only in association with **severe** multiple **B-complex malnutrition**.

Vitamin	Compound	Proprietary name	Deficiency state	ADRs associated with excessive ingestion
Vitamin B_1	Thiamine	Thiamilate, various	Beriberi, lactic acidosis, *Wernicke–Korsakoff*	Pruritis, weakness, nausea, urticaria, hypersensitivity, anaphylactic shock
Vitamin B_2	Riboflavine	Various	Ariboflavinosis (rare) cheilosis[a]	No toxicity noted, limited absorption
Vitamin B_3	Niacin	Various	Pellagra	Dermatologic: cutaneous flushing, rash, dry skin; GI: ulcer, NVD, abdominal pain; hepatoxicity, hyperglycemia
Vitamin B_6	Pyridoxine HCl	Various	Dermatologic, hematologic, CNS	Sensory neuropathy, ataxia, digital and perioral numbness, paresthesias
Folic acid	Pteroylglutamic acid (folate)	Folvite, various	Megaloblastic anemia	CNS: altered sleep patterns, irritability, confusion; GI: N, anorexia, abdominal distention
Vitamin B_{12}	Cyanocobalamin	Various (oral)	Pernicious anemia	Nontoxic
		Nascobal (IN)		Paresthesia, headache, glossitis, nausea
		LA-12 (injection)		Pulmonary edema, CHF, itching, anaphylactic shock
Vitamin C	Ascorbic acid	Various	Scurvy	GI disturbances, poor wound healing, urinary calculi

DRIs Daily Allowances of Vitamins and Minerals

Nutrient	Infants	Children	Males	Females	Pregnant/ lactating
Protein (g)	9.1–11	13–19	34–56	34–46	71
Fat-soluble vitamins					
Vitamin A (μg)	400–500	300–400	600–900	600–700	750–1300
Vitamin D (μg)	5	5	5–15	5–15	5
Vitamin E (mg)[a]	4–5	6–7	11–15	11–15	15–19
Vitamin K (μg)	2–2.5	30–50	60–120	60–90	75–90
Water-soluble vitamins					
Vitamin C (mg)	40–50	15–25	45–90	45–75	80–120
Thiamine (B_1, mg)	0.2–0.3	0.5–0.6	0.9–1.2	0.9–1.1	1.4
Riboflavine (B_2, mg)	0.3–0.4	0.5–0.6	0.9–1.3	0.9–1.1	1.4–1.6
Niacin (B_3, mg)	2–4	6–8	12–16	12–14	18/17
Pyridoxine (B_6, mg)	0.1–0.3	0.5–0.6	1.0–1.7	1.0–1.5	1.9–2.0
Folic acid (μg)	65–80	150–200	300–400	300–400	600/500
Vitamin B_{12}[b] (μg)	0.4–0.5	0.9–1.2	1.8–2.4	1.8–2.4	2.6–2.8
Minerals					
Calcium (mg)	210–270	500–800	1300/1200	1300/200	1300/1200
Phosphorus (mg)	100–275	460–500	1250–700	1250–700	1250–700
Magnesium (mg)	30–75	80–130	240–420	240–320	400–320
Iron (mg)	0.27–11	7–10	8–11	8–18	27–9
Zinc (mg)	2–3	3–5	8–11	8–9	11–13
Iodine (μg)	110–130	90	120–150	120–150	220–290
Selenium (μg)	15–20	20–30	40–55	40–55	60–70