Toxic and Nutrient Elements

ELEMENTS	SOURCES	NUTRIENT INTERACTIONS	PHYSIOLOGIC EFFECTS	CLINICAL SIGNIFICANCE
Aluminum (Al)	Found in virtually all food and food additives, water, air, and soil. Also found in antacids, antiperspirants, cosmetics, astringents, cans, pots, pans, siding, roofing, and foil.[1,2]	Calcium deficiency, citric acid, and low gut pH causes increased Al absorption.[1,3,4] Low iron intake increases Al absorption (rat study).[5] Selenium may be protective against Al.[4] Al reduces phosphorus and fluoride absorption. Al disrupts lipid membrane fluidity, altering Fe, magnesium, and calcium homeostasis, causing oxidative stress.[6]	Accumulates in bone, liver, kidney, and spleen.[5] Causes mitochondrial dysfunction due to Krebs cycle enzyme activity disturbance and electron transport chain alterations.[6] Alters the enzymes in the glutamate system, which may be one of the causes of aluminum-induced neurotoxicity.[7] Parathyroid hormone levels and osteoclast activity are disrupted by Al.[8] Al can also slow calcification of new bone and deposits in the bone matrix in place of calcium.[5] Disrupts normal iron homeostasis and iron-dependent cellular metabolism.[5]	Anemia, CNS functional, sensory and cognitive alterations, and bone abnormalities like osteodystrophy.[2,5]
Antimony (Sb)	Found naturally in the environment, air, soil, water. Found in lead storage batteries, solder, sheet and pipe metal, pewter, bearings and castings, paints, ceramics, fireworks, plastic enamels, metal and glass. Sometimes used medically to treat parasites.[9]	Unknown	Highest accumulation in the lungs, GI tract, RBC's, liver, kidney, bone, spleen, and thyroid. It is excreted in urine and feces, and partially in bile after conjugation with glutathione. Trivalent antimony is predominantly excreted in feces while pentavalent antimony in urine.[10,11] Binds to sulfhydryl groups with subsequent inhibition of enzymes involved in cellular respiration and carbohydrate/protein metabolism.[12]	Lung and skin irritation, cardiac and EKG alterations, GI symptoms such as nausea, vomiting, ulceration. In animal studies, antimony can decrease serum glucose levels.[9,11]

Toxic and Nutrient Elements

ELEMENTS	SOURCES	NUTRIENT INTERACTIONS	PHYSIOLOGIC EFFECTS	CLINICAL SIGNIFICANCE
Arsenic (As)	Found in water, air, soil, cigarettes, and cosmetics. Food grown in contaminated water sources, such as rice and vegetables, or fish, are a common source.[13] Major sources of occupational exposure is the manufacture of pesticides, herbicides, and agricultural products.[14] 90% of all arsenic produced is used as a preservative for wood to prevent rotting and decay. Copper chromated arsenate (CCA), also known as pressure-treated wood, was phased out for residential use in 2003, but wood treated prior could still be in existing structures. CCA-treated wood is still used in industrial applications. Organic arsenic found in seafood is relatively nontoxic, while the inorganic forms are toxic.[15]	Folate, SAM, vitamin B12, and choline are needed to optimize methylation. Arsenic is metabolized by a series of methylation reactions to dimethylarsenic and methylarsonic acids. There are some highly reactive intermediates in its trivalent form which are toxic.[16] Magnesium may have protective effects against As toxicity, and Zinc may increase As excretion.[4] Vitamin C, α-tocopherol, flavonoids, polyphenols, and selenium have been shown to decrease arsenic-induced toxicity.[16]	The absorption rate of arsenic in the GI tract is 90%. (Though arsenic compounds of low solubility are not absorbed as efficiently.) As binds to RBC's and deposits in the liver, kidneys, muscle, bone, hair, skin, and nails. It is excreted mainly through urine, with 50-80% excreted within three days.[14,17] Most of the arsenic in blood is rapidly cleared within hours. It is not possible to distinguish organic from inorganic arsenic in urine or blood.[18] Impairs cellular respiration by inhibiting mitochondrial enzymes and the uncoupling of oxidative phosphorylation. Reacts with protein sulfhydryl groups, producing inhibition in the oxidation of pyruvate and beta-oxidation of fatty acids. Inhibits DNA repair and induces chromosomal aberrations.[19]	Increased risk of cancer (skin, lung, bladder, liver, prostate). Associated with neurobehavioral changes, memory, intellectual function abnormalities, diabetes, cardiovascular disease, reproductive effects, skin hyperpigmentation, peripheral neuropathy, respiratory irritation, nausea, and hematologic effects.[14,17]

Toxic and Nutrient Elements

ELEMENTS	SOURCES	NUTRIENT INTERACTIONS	PHYSIOLOGIC EFFECTS	CLINICAL SIGNIFICANCE
Barium (Ba)	Radiologic testing contrast, paint, bricks, ceramics, glass and rubber. Air, water, and food. Fish and aquatic organisms can accumulate barium.[20]	Barium toxicity can induce severe hypokalemia.[21,22]	Barium is excreted mainly in feces and urine within 1-2 weeks. Can deposit in bones and teeth.[20] Barium is a competitive potassium channel antagonist blocking the passive efflux of intracellular potassium. Barium toxicity can cause hypokalemia.[23]	Barium compounds that do not dissolve well in water, such as barium sulfate, are generally not harmful. Water soluble forms can cause cardiac dysrhythmias, GI disturbances, muscular weakness, vomiting. Electrolyte abnormalities can induce cardiac dysrhythmia, muscle cramping/paralysis, and vomiting. Nephropathy is also possible based on direct renal toxicity.[20]
Bismuth (Bi)	Used in alloys, electronics, batteries, crystal ware, cosmetics, flame retardants, and in antimicrobial therapy (H. pylori), antiseptic dressings, paraffin paste.[24,25] Bismuth medical therapies exhibit high therapeutic effects and little side effects, though over-dosage can cause toxicity.[26]	Unknown	Very limited absorption in the GI tract. When absorbed, it binds mainly to transferrin and lactoferrin, interacts with enzymes due to a high affinity to cysteine residues, blocking the active site.[26] Can accumulate in the kidney, lung, spleen, liver, brain, and muscles, while being eliminated in urine and feces via bile and intestinal secretions.[27]	Nephropathy, GI complaints, encephalopathy, difficulty walking/standing, memory deterioration, behavioral change, insomnia, muscle cramping.[26,28] Decreased appetite, weakness, gingivitis, dermatitis, and diarrhea have also been seen clinically with chronic bismuth toxicity.[14]
Cadmium (Cd)	Found in food such as shellfish, leafy vegetables, rice, cereals, cocoa butter, dried seaweed, and legumes.[29] Also present in nickel cadmium batteries, cigarette smoke (including second-hand smoke), insecticides,	Iron deficiency is associated with higher cadmium burden and absorption of cadmium may increase during very early stages of iron deficiency.[29] Zinc deficiency is associated with an increase in Cd, as a result of the antagonistic relationship between the elements.[30]	Cd accumulates in the liver and kidneys and has a long half-life (17-30 years). The renal and skeletal systems are the main targets of Cd toxicity.[5] Urinary cadmium reflects integrated exposure over time and body burden. Urinary levels do not rise significantly after acute exposure. Elevated blood cadmium levels confirm recent acute exposure.[31-33]	Renal tubular toxicity, decreased bone density with increased bone turnover and fractures.[29] Chronic inhalation exposure is associated with emphysema. Acute oral ingestion leads to abdominal pain, nausea, vomiting, muscle cramps, and GI tract erosions.[19]

ELEMENTS	SOURCES	NUTRIENT INTERACTIONS	PHYSIOLOGIC EFFECTS	CLINICAL SIGNIFICANCE
	fertilizer, motor oil, emissions and exhaust.[19] Drinking water, air, and occupational exposures are also seen.	Dietary cadmium inhibits GI absorption of calcium and interferes with calcium and vitamin D metabolism. Low dietary calcium stimulates synthesis of calcium-binding protein which enhances Cd absorption.[5]		
Cesium (Cs)	Naturally occurring Cs can be found in a stable form (measured on Genova's tests). Radioactive Cs is produced by the fission of uranium in fuel elements, usually near nuclear power plants. These are unstable but eventually become stable through radioactive decay. Some Cs can be found in air, water, and soil (and thereby food) based on location near nuclear plants.[34]	Higher levels of vitamin D ($25(OH)D_3$) have been linked to enhanced absorption of radioactive isotopes like cesium.[4] Cs and potassium compete for uptake and cell membrane potential.	Cs acts like potassium, entering cells and altering electrical charges. It has a higher distribution in the kidneys, skeletal muscle, liver, and RBC's. In RBC's it decreases their ability to release oxygen in tissues. Additionally, the acute effects of Cs on cardiac tissues consists of membrane potential changes due the interaction within the electrical current and channel pore, causing dysrhythmia.[35] It is usually excreted by the kidney, but also in feces.	Stable Cs may not likely cause significant health defects. However, radioactive Cs could cause nausea, vomiting, diarrhea, or acute radiation syndrome, though most exposures are not large enough to cause these effects unless it's a significant industrial or occupational event.[34]
Gallium (Ga)	Used in integrated circuits, LED's, solar cells, laser diodes. It is also used in medicine, where the radioisotopes are used as imaging agents, and stable compounds are used in chemotherapy. Ga can be a antimicrobial agent, and used to treat life-threatening, malignancy-related hypercalcemia.[36] Can be found in ground water near mining, manufacturing and coal combustion plants. Most commonly seen in occupational exposures, while there is less data on consumer electronic exposures.[37]	Ga competes with iron for transferrin binding and inhibits receptor-mediated iron uptake by cells, rendering cells iron-deficient. Iron replacement has been shown to restore hemoglobin production in Ga exposed cells.[38] It was also found to interact with bone metabolism and to lower calcium levels in the blood.[36]	Ga binds to transferrin and interferes with protein synthesis and the heme pathway. It's use in medicine shows that it tends to localize to tumors and cause cell death via interference with iron metabolism.[37] Ga is excreted in the urine, and in rats, renal toxicity was noted with the formation of precipitates of gallium complexed with calcium and phosphate.[2]	In animal studies, toxicity is associated with pulmonary conditions, immunosuppressive effects, and renal toxicity. Direct exposure to Ga has been shown to cause skin rashes, and neurological pain and weakness.[37] Anemia is possible due to its interference with heme pathways.[38]

Toxic and Nutrient Elements

ELEMENTS	SOURCES	NUTRIENT INTERACTIONS	PHYSIOLOGIC EFFECTS	CLINICAL SIGNIFICANCE
Gadolinium (Gd)	Used as a nuclear MRI contrast agent (usually in its chelated form). Also used in magnets, compact discs, superconductors, magnets, and fluorescent materials. Can also be found in ground and drinking water.	Gd ions in chelates can be exchanged with cations like zinc, copper, calcium, or iron. Zinc is a major contributor, therefore adequate zinc levels improve Gd excretion.[39,40]	Gd can accumulate in tissue, bone, and brain. Usually removed via kidney.[39] Chelated Gd can dissociate under certain metabolic conditions and inhibit intracellular calcium signaling and disrupt the action of thyroid hormone.[41] Gd targets iron recycling macrophages, induces cellular iron import/export, and labile iron release, which participates in systemic fibrosis.[42]	In spite of past research, recent studies reveal brain deposition of Gd post MRI can occur, but information on adverse health effects in humans is lacking.[43-45] In chronic kidney disease however, there is risk of nephrogenic systemic fibrosis (cutaneous and visceral fibrosis with renal failure).[46]
Lead (Pb)	Found naturally in soil. More often found in fossil fuels, gasoline/exhaust, manufacturing, lead-acid batteries, ammunitions, metal solder and pipes, X-ray shields, paint, glass, pigments, and sheet lead.[19]	Iron and lead share a common transporter; therefore, iron deficiency increases lead absorption.[29] There is some evidence that higher amounts of dietary calcium are associated with lower blood lead levels.[29] Calcium and phosphorus supplementation decreases lead absorption and retention.[4] Selenium has been useful as an adjunct in chelation in lead intoxication.[4] Zinc deficiency enhances lead absorption and lead increases zinc excretion.[5] Zinc supplementation decreases tissue lead accumulation.[4] Vitamin D increases lead absorption.[4]	Mainly taken into the kidney, liver, and other soft tissues such as the heart and brain. However, lead in the skeleton is the major body fraction. The nervous system is a vulnerable target of lead toxicity.[19] Binds to sulfhydryl groups and amide groups of enzymes, diminishing their activity. This enzymatic inhibition can be seen in heme synthesis, neurotransmitter metabolism, and other sodium-dependent processes.[47] Produces reactive oxygen species, and competes with metallic cations for binding sites, altering the transport of cations such as calcium and interferes with calcium-dependent processes.[19] Lead replaces zinc on heme enzymes, and inhibits the enzyme needed to incorporate iron into the hemoglobin molecule by replacing iron. Copper and iron supplementation have been used to counter these heme synthesis effects.[5] Whole blood lead levels estimate recent exposure to lead, but it is also in equilibrium with bone lead stores.[48]	Headache, poor attention span, irritability, memory loss, and weakness are early CNS symptoms of exposure.[19] Reproductive effects, GI diseases, anemia, kidney damage, and adverse effects on vitamin D metabolism are also seen.[19,47] The CDC provides recommendations for follow-up and case management of children based on confirmed whole blood lead levels beginning at levels of 5 mcg/dL.[49] There are guidelines with specific cut-points for adults at risk for occupational lead exposure and for lead-exposed adults in general.[48,50] Urine lead is less validated than blood lead levels as a biomarker of external exposure or predictor of health effects.[48]

Toxic and Nutrient Elements

ELEMENTS	SOURCES	NUTRIENT INTERACTIONS	PHYSIOLOGIC EFFECTS	CLINICAL SIGNIFICANCE
Mercury (Hg)	Hg has three forms: Elemental (metallic)- older glass thermometers, fluorescent light bulbs, dental amalgams, folk remedies, combustion, electrical industry (switches, batteries, thermostats), solvents, wood processing Organic (methyl mercury)- seafood, thimerosal (preservative), fungicides Inorganic- skin lightening compounds, industrial exposure, folk medicine, lamps, photography, disinfectants[19,51]	Calcium, magnesium, and selenium, iron, and copper protect against acute toxicity of mercury.[4,5]	A major proportion of absorbed mercury accumulates in the kidneys, neurological tissues, and liver. Molecular mechanisms of toxicity involve oxidative stress. Once in a cell, Hg depletes intracellular antioxidants and therefore causes mitochondrial dysfunction.[19] Mercury releases intracellular calcium, disrupting neuronal transport, alters cell membrane integrity, interrupts microtubule formation, disrupts or inhibits enzymes, inhibits protein and DNA synthesis and impairs immune function.[52] Methyl mercury (organic) appears to be absorbed almost completely in the GI tract, and in this form is higher in the brain compared to other forms.[53] It is excreted fecally and can be measured in blood; urine is not a reliable indicator of organic mercury.[52] Inorganic mercury accumulates in the kidneys. It is excreted in the urine and both inorganic and elemental Hg can be measured in urine and blood.[51,52] Blood and urine mercury levels correlate fairly well with each other, but not with total body burden; blood and urine mercury reflects recent exposure.[54]	GI symptoms, neurotoxicity (headaches, tremor, decreased mental concentration), and nephrotoxicity are common, as well as iron deficiency.[4,19] Inhaling elemental Hg vapors causes acute symptoms including cough, chills, fever, shortness of breath, nausea, vomiting, diarrhea, metallic taste, dysphagia, salivation, weakness, headaches and visual disorders. Chronic inhalation may cause cognitive impairment and personality changes.[52]
Nickel (Ni)	Used in making metal coins and jewelry, valves and heat exchangers, and stainless steel. Also used for nickel plating, color ceramics, cosmetics, tobacco, and batteries. Can be found in the soil, air, and water. There are also nickel-containing foods such as almonds, chick peas, cocoa, tomato, lentils, oats, peanuts, and walnuts.[55]	Iron is a competitive inhibitor of nickel absorption, therefore absorption is enhanced with iron deficiency.[55] Vitamin C works as an antioxidant to counter ROS from nickel, and may also inhibit nickel absorption.[55]	Nickel can affect the lungs via inhalation and if ingested, pass through the GI tract to be excreted in feces. Nickel that is absorbed through the skin or GI tract can either be excreted in urine or deposit anywhere, though mainly the kidneys. In vitro and in vivo studies demonstrate that divalent nickel promotes lipid peroxidation at DNA bases.[55]	Allergic dermatitis/skin rash, asthma/lung inflammation, stomach aches, proteinuria and kidney diseases are seen with exposures. There is some carcinogenic potential.[53]

Toxic and Nutrient Elements

ELEMENTS	SOURCES	NUTRIENT INTERACTIONS	PHYSIOLOGIC EFFECTS	CLINICAL SIGNIFICANCE
Niobium (Nb)	Niobium is sometimes found in jewelry, and is used with other alloys, like titanium, to make surgical implants and dental applications.[2] It is also a component of superconducting magnets and nuclear reactor cores.	Unknown	Niobium is poorly absorbed from the GI tract.[2]	It is a moderate eye and skin irritant. Due to poor GI absorption, it has a low order of toxicity. Lethargy and respiratory depression have only been seen with parenteral administration.[2]
Platinum (Pt)	Can be found in soil and river sediments, air, and jewelry. Used as a catalyst in the automotive, chemical, and pharmaceutical industries. It's resistance to oxidation makes it important in the manufacturing of laboratory equipment. It is also used as a chemotherapeutic agent.[2]	Unknown	Platinum binds to DNA and interferes with transcription and replication resulting in apoptosis.[56]	Metallic forms are inert, but the complex salts can produce conjunctivitis, urticaria, dermatitis, and eczema with dermal exposure.[2] Nephrotoxicity and thrombocytopenia are seen with platinum chemotherapeutic agents. Respiratory exposures can produce wheezing and shortness of breath.[14]
Rubidium (Rb)	Soil, rocks, vegetation, water, contrast agent for PET scans, atomic clocks, photoelectric cells, magnetometers, GPS systems, fireworks.[57-61]	Rubidium resembles potassium, and these two elements are metabolically interchangeable.[62]	Rb is rapidly and completely absorbed by the GI tract when ingested and is excreted mainly through the kidneys.[61] Urinary excretion is consistent with a 50-day half-life.[63] Physiologically, rubidium most resembles potassium, and these two elements are metabolically interchangeable.[62] In the myocardium it is an active participant in the NA/K pump.[58] Rubidium and lithium are often studied for CNS dysfunctions including mania and depression, and may work through the NMDA/nitrergic pathways.[64]	Rb chloride was used historically to treat cardiac issues, syphilis, epilepsy and more recently has been studied for depression.[65] Excess rubidium chloride was associated with weight gain, diarrhea, nausea/vomiting, polyuria, confusion, excitement/agitation and dermatitis.[61] In rats, rubidium chloride administration led to hypokalemia.[66]

Toxic and Nutrient Elements

ELEMENTS	SOURCES	NUTRIENT INTERACTIONS	PHYSIOLOGIC EFFECTS	CLINICAL SIGNIFICANCE
Thallium (Tl)	Fish, shellfish, plants, cigarettes, soil, air, water, electronic devices, switches and closures for the semiconductor industry, glass for medical procedures.[67]	Some of its toxic effects results from interference with biological functions of potassium.[14]	Thallium is absorbed through the skin and GI tracts. Highest concentrations are found in the kidney. Large amounts are excreted in the urine within 24 hours, then excreted via feces. Tl undergoes enterohepatic circulation.[14] Tl can accumulate in bones, renal medulla, liver and CNS.[68] Thallium has a similar charge and radius as the potassium ion. Some of its toxic effects results from interference with biological functions of potassium. Additionally, it binds to sulfhydryl groups in the mitochondria interfering with oxidative phosphorylation. With these mechanisms, cardiac dysfunction, mitochondrial dysfunction, abnormal protein synthesis and heme synthesis are seen.[14]	GI irritation, paralysis, alopecia, and psychological disturbances are seen.
Thorium (Th)	Rocks, soil, water, plants, ceramics, gas lantern mantles, metals in the aerospace industry and nuclear reactions, fuel for nuclear energy, and mining.[69]	Unknown	Th can damage chromosomes.[69]	Exposure may lead to increased risk of certain cancers including gallbladder, liver, and leukemia, as well as cirrhosis. Inhaled Th (mainly among workers exposed to Th dust) can cause lung damage many years after being exposed.[69]
Tin (Sn)	Found in manufacturing, food packaging, solder, bronzing, dyeing textiles, plastics, PVC pipes, fungicides, toothpaste, perfume, soap, food additives, electronic cigarette aerosol, and dyes. Naturally present in rocks and nearby air, water, and soil.[70,71] Seafood is the primary route of human exposure to organotin compounds.[72] Tin is found in both organic and inorganic forms. Inorganic tin is generally regarded as safe (GRAS) by the FDA as a food additive for human consumption.[73]	Tin disturbs copper, zinc, and iron metabolism.	Very limited GI absorption of inorganic tin orally, with 90% excreted in feces, and therefore non-toxic. When absorbed, it deposits in the liver and kidneys. Organic tin is better absorbed and concentrates in blood, liver, muscles, brain, and heart.[2,14]	Headaches, visual defects, depression, skin and eye irritation – rarely hepatotoxicity and neurotoxicity.[74] Organic tin compounds have been identified as environmental obesogens and urinary tin levels are associated with diabetes.[73,75]

Toxic and Nutrient Elements

ELEMENTS	SOURCES	NUTRIENT INTERACTIONS	PHYSIOLOGIC EFFECTS	CLINICAL SIGNIFICANCE
Tungsten (W)	Found naturally in soil and rocks or airborne emissions from industries using W. Used in high speed and cutting or forming tools (tungsten carbide), welding electrodes, turbine blades, golf clubs, darts, fishing weights, gyroscope wheels, phonograph needles, bullets, armor penetrators, x-ray tubes, light bulbs, ceramic pigments, fire retardant for fabrics, color-resistant dye for fabrics, generally mixed with other metals to make alloys.[76]	W ions antagonize the normal metabolic action of the molybdate ion, therefore molybdenum deficiency promotes W affects.[2]	W is not metabolized in the body and 90% of inhaled W is eliminated in urine after 14 hours.[77] Toxicity of W is enhanced when present in a metal mixture. The synergistic effect promotes oxidative stress and DNA damage.[77]	Exact effects in humans is unknown, however animal models suggest a connection with cancer. A cluster of patients with leukemia in Nevada was shown to have higher urine levels of W, however causation has not been established.[78] Memory and sensory deficits, and lung issues were observed in workers when exposed to hard metal dusts containing 79-95% W, 10% cobalt and other metals.[77]
Uranium (U)	Largely limited to use as a nuclear fuel. Present naturally in air, water, food, and soil. The uranyl ion forms water-soluble compounds and is an important component in body fluids. Three different kinds are defined: natural, enriched, and depleted uranium (DU). The radiological and chemical properties of natural and DU have similar chemotoxicity, though natural is 60% more radiotoxic.[79]	U is reactive. It can combine with and affect the metabolism of lactate, citrate, pyruvate, carbonate, and phosphate, causing mitochondrial damage.[79] It replaces calcium in bone.[80]	On average, only 1-2% of ingested U is absorbed via the GI tract. It rapidly enters the bloodstream and forms a diffusible ionic complex. Once in the bloodstream, it has a very short half-life and approximately 60% is eliminated within 24hrs.[79] The skeleton and kidney are the primary sites of U accumulation. Under alkaline conditions, uranium can be excreted in the urine and feces. Inhalation exposure is toxic to the lungs, though less toxic to distal organs.[79]	The soluble U present in plasma as the uranyl ion complexed with bicarbonate can cause renal toxicity. Nephritis is the main chemically induced effect of U ingestion.[80] Uranyl ion is most concentrated intracellularly in lysosomes, which explains its association with β-microglobulinuria and amino aciduria.[14] Osteopenia, weight loss, hemorrhages in the eyes, legs, and nose have also been seen.[80]

NUTRIENT	SOURCES	ABSORPTION FACTORS	BIOCHEMICAL ACTIONS	SYMPTOMS OF IMBALANCE
Calcium (Ca)	Dairy products, vegetables, legumes, grains, fish, eggs, dietary supplements, and many other foods which have been fortified with calcium.[81]	Active Ca absorption depends on calcitriol and intestinal vitamin D receptors. Passive diffusion in the intestine relies on luminal: serosal electrochemical gradients.[81] Ca can interfere with the absorption of iron and zinc. Protein intake enhances calcium absorption, but also increases urinary Ca excretion. Alcohol, caffeine, high sodium and phosphorus increase urinary excretion or reduce absorption. Foods with high levels of phytates (whole grain products, wheat bran, beans, seed, nuts, soy isolates) and oxalates (spinach, collard greens, sweet potatoes, beans) bind calcium and interfere with absorption.[82]	Necessary for teeth and skeletal structure, vascular contraction and vasodilation, muscle function, nerve transmission, intracellular signaling and hormonal secretion.[81,82]	Hypercalcemia can cause renal insufficiency, vascular and soft tissue calcification, nephrolithiasis, and is most often associated with hyperparathyroidism or malignancy. Inadequate dietary intake does not produce obvious symptoms in the short term, but in the long term may lead to osteoporosis. Hypocalcemia generally results from renal failure and medication use and includes numbness and tingling in the fingers, muscle cramps, convulsions, lethargy, poor appetite and arrhythmias.[82]

Toxic and Nutrient Elements

NUTRIENT	SOURCES	ABSORPTION FACTORS	BIOCHEMICAL ACTIONS	SYMPTOMS OF IMBALANCE
Chromium (Cr)	Ubiquitous in foods at low concentrations. Derived from processing of food with stainless steel equipment.[83] Also present in tobacco smoke, chrome plating, dyes and pigments, leather tanning, and wood preserving and is deposited into air, water and soil.[84] There is debate as to whether chromium is an essential trace element. Hip prosthesis bearing surfaces are made from cobalt and other materials including chromium.[85] Welding produces fumes that may contain chromium and other metals (Mn, As, Fe, Ni).[86]	Dietary chromium absorption is low. Chromium is bound to the protein transferrin in the bloodstream.[83] Conditions that increase circulating glucose and insulin increase urinary chromium output.[87] Blood distribution of chromium appears to be equally divided between plasma and RBCs, making whole blood chromium the sample type for total Cr measurement. Cr (VI) is more concentrated in the RBCs, while Cr (III) does not enter the RBCs. Therefore, it is possible to distinguish sources and types of exposure to indicate toxic (Cr[VI]) exposure versus benign (Cr[III]) by measuring RBC chromium.[88-90] Chromium rapidly clears from the blood and measurements relate to recent exposure. Urinary Cr excretion reflects absorption over the previous 1-2 days.[89,90]	Often given as a supplement to treat glucose intolerance by improving insulin sensitivity.[83]	Currently, no symptoms of chromium deficiency exist. Compounds containing hexavalent chromium (Cr [VI]) are mutagenic and carcinogenic in large quantities. No adverse effects have been associated with trivalent chromium (Cr[III]), the form in food and supplements.[83] Inhaled chromium may cause irritation to the lining of the nose, nose ulcers, runny nose, and breathing problems including asthma, cough, shortness of breath or wheezing. Dermal contact with chromium may cause skin ulcers, redness and swelling. Ingested chromium (in animals) may cause irritation and ulcers in the stomach and small intestine and anemia.[84] The FDA recommends testing chromium in whole blood in patients with metal on metal hip implants who have symptoms. These symptoms may include localized pain due to damaged bone and/or tissue surrounding the implant and joint.[91]

NUTRIENT	SOURCES	ABSORPTION FACTORS	BIOCHEMICAL ACTIONS	SYMPTOMS OF IMBALANCE
Cobalt (Co)	Cobalt is a hard silvery-bluish metal widely dispersed in nature in low concentrations. Diet, environment and supplements are the main sources of cobalt for the general public. The highest Co concentration in foods include chocolate, butter, coffee, fish, nuts, green leafy vegetables and cereals. Vitamin B12 (contains Co) is found in meat and dairy. Cosmetics, jewelry and electronics may be other sources of exposure. Industrially, workers may be exposed to cobalt powders in hard metal production (often combined with tungsten), construction, electronic waste recycling, diamond polishing and paint. Contamination from these industries may affect the general public through water, soil or air.[92] Hip prosthesis bearing surfaces are made from cobalt and other materials including chromium.[85]	Binds to albumin.[93] Iron deficiency can be associated with increased absorption of Co. The GI absorption of Co is approximately 25%. Once absorbed, Co disseminates to serum, whole blood, liver, kidneys, heart and spleen and to a lesser extent bones, hair, lymph, brain and pancreas. The kidneys are responsible for Co excretion.[92]	Cobalt is a necessary element for the formation of vitamin B_{12} (cyanocobalamin).[94] The B_{12} RDI is 2.4 mcg/d and contains 0.1 mcg Co.[92] Elevated cobalt can result in generation of reactive oxygen species (ROS) and lipid peroxidation, interruption of mitochondrial function, alteration of calcium (Ca) and iron (Fe) homeostasis, interactions with body feedback systems triggering erythropoiesis, interruption of thyroid iodine uptake, and induction of genotoxic effects and possible perturbation of DNA repair processes.[92]	Excessive administration produces goiter and reduced thyroid activity. Industrially, exposure can cause a contact dermatitis or occupational asthma. Polycythemia has been observed in some studies.[92,94] Cobalt toxicity from a hip prosthesis is determined by monitoring blood measurements. Symptoms include peripheral neuropathy, sensorineural hearing loss, cognitive decline, visual impairment, hypothyroidism and cardiomyopathy.[85,92]

NUTRIENT	SOURCES	ABSORPTION FACTORS	BIOCHEMICAL ACTIONS	SYMPTOMS OF IMBALANCE
Copper (Cu)	Legumes, mushrooms, chocolate, nuts and seeds, shellfish and liver are high in copper (all >2.4 µg/g).[95,96] Food (Cu^{+}), water (Cu^{2+}) and air (via combustion of fossil fuels and agriculture) are sources of copper.[97] Copper pipes and fixtures in household plumbing may allow copper to leach into water.[96]	Cu absorption occurs in the upper small intestine and compared to other elements, has a relatively high absorption rate at 55-75%.[95] Copper levels in the body are homeostatically maintained by copper absorption from the intestine and copper release by the liver into bile to provide protection from copper deficiency and toxicity. Most copper is excreted in bile/feces and a small amount excreted in urine.[96] Urinary copper declines only when dietary copper intake is very low. A 24-hour urinary copper provides a screening for suspected cases of toxicity or copper deficiency anemia.[98,99] Correlation was seen in Wilson's disease using first morning or 24-hour urine.[100] Grains contain phytates that may inhibit copper absorption in the intestines.[98] Intestinal iron absorption is a copper-dependent processes.[95] Iron, vitamin C, zinc, lead poisoning, hemochromatosis, excessive soft drink ingestion, bariatric surgery and Zn-containing denture creams adversely affect Cu bioavailablity.[95] Cadmium exposure may result in increased urine excretion of copper due to possible renal tubular damage.[101] Increased Mo intake may elevate urinary copper excretion.[102] Serum and 24-hour urine copper excretion was similar in long-term copper IUD users as in a control group that did not have an IUD.[103]	Cu is a cofactor for more than 20 enzymes, particularly those involved in cellular respiration and energy metabolism, neurotransmitter and hormone biosynthesis, iron metabolism, gene transcription, melanin formation and antioxidant defense. Copper is also involved in blood coagulation and blood pressure control, myelination, and connective tissue cross-linking.[95,97] Ceruloplasmin (CP) carries the predominance of copper in the blood, so alterations in blood copper likely reflect the amount of circulating CP. Plasma Cu and CP can increase during an acute phase response to infection and inflammation, pregnancy and other hormonal perturbations, some carcinogenic phenotypes, and smoking. Plasma Cu may be elevated in these states while tissue Cu could be low. Low plasma Cu indicates physiological impairment.[95]	Copper deficiency is associated with osteoporosis, hypochromic, microcytic anemia, impaired cholesterol and glucose metabolism, cardiovascular disease, connective tissue abnormalities, CNS disorders, and impaired immune function.[95,98] Reductions in plasma copper and ceruloplasmin (CP) activity are noted in severely copper-deficient individuals.[95] Copper toxicity is rare due to adequate homeostatic control, however an upper tolerable intake level of 10 mg/day has been established. Wilson's disease is an inherited disease that results from decreased biliary Cu excretion due to biliary atresia or biliary cirrhosis.[95] Signs and symptoms include jaundice and abnormal LFTs, ascites, Kayser-Fleischer rings, and neurological and psychiatric symptoms. Copper dyshomeostasis involving either deficiency or excess has been implicated in Alzheimer's disease and cognitive decline.[97]

NUTRIENT	SOURCES	ABSORPTION FACTORS	BIOCHEMICAL ACTIONS	SYMPTOMS OF IMBALANCE
Iron (Fe)	Iron from food comes in two forms: heme and non-heme. Heme iron sources include meat and seafood. Non-heme iron sources include nuts, beans, vegetables, and fortified grains.[104]	Gastric acid plays an important role in the absorption of nonheme iron from the diet. Proton pump inhibitors can reduce iron absorption.[105] Iron is absorbed at the brush border of duodenal enterocytes.[106] Heme iron is more bioavailable than non-heme iron. Vitamin C enhances the bioavailability of non-heme iron whereas calcium inhibits bioavailability of both heme and non-heme iron. Phytates and polyphenols can inhibit non-heme absorption.[104]	Iron-containing proteins are required for oxygen transport, mitochondrial respiration, xenobiotic metabolism, nucleic acid replication and repair, host defense and cell signaling.[107] Under normal physiological conditions, circulating iron can be filtered by the glomerulus and is almost completely reabsorbed by the tubular epithelium to prevent urinary iron wasting.[108] In a cohort of chronic kidney disease patients, increased urinary iron was associated with increased urinary 8-OHdG, indicating oxidative stress in renal tubules.[106]	Iron deficiency can result in anemia. Associated symptoms include fatigue, GI symptoms, weakness, difficulty concentrating, impaired cognition, impaired immune function, poor exercise tolerance or issues with body temperature regulation.[104] Urinary iron excretion is increased in patients with systemic iron overload (such as in hemochromatosis), renal tubular dysfunction, and hemolytic anemia.[108,109] A blood iron study or ferritin measurement is recommended as appropriate for patients with suspected iron deficiency or excess.
Lithium (Li)	Cereals, fish, nuts, potatoes, tomatoes, cabbage, mineral water, tap water, nutmeg, coriander seeds, cumin, medication. Naturally found as a trace element in the earth's crust and water sources. Not officially considered a micronutrient, although it is recognized as important.[110] Industrial use includes lithium-based batteries, dessicants.[111]	Li is rapidly absorbed, has a small volume of distribution and is excreted in the urine unchanged (lithium is not metabolized).[112] Pregnancy and increased sodium, xanthines (theophylline and caffeine), nifedipine, and carbonic anhydrase inhibitors (e.g., acetazolamide) increase lithium excretion in the urine.[110]	Li modulates the activity of norepinephrine, serotonin, dopamine, glutamate, GABA, acetylcholine and glycine. It can resynchronize circadian rhythms by modulating the expression of clock genes and HPA axis regulation. Li stimulates the production of neural stem cells and is protective against oxidative stress.[110]	Lithium excess from overmedicating can result in interstitial nephritis, cardiac abnormalities and seizures.[112] It is hypothesized that low Li intake can cause mood worsening and increase impulsiveness and nervousness.[110] Li is prescribed for bipolar disorder and major depressive disorder due to its impact on neurotransmission. It is also prescribed for vascular headaches and neutropenia.[112]

Toxic and Nutrient Elements

NUTRIENT	SOURCES	ABSORPTION FACTORS	BIOCHEMICAL ACTIONS	SYMPTOMS OF IMBALANCE
Magnesium (Mg)	Green leafy vegetables, legumes, nuts, seeds, whole grains, medicines (e.g., Milk of Magnesia), Epsom salt. Over the last 60 years, the Mg content in fruits and vegetables has decreased by 20-30%, and 80-90% of Mg is lost during food processing.[113]	The intestine, bone and kidney maintain magnesium homeostasis.[114] Unlike other minerals, Mg can be absorbed along the entire length of the GI tract.[115] Soft drinks, low protein diets, foods containing phytates, polyphenols and oxalic acid, fluoride, antibiotics, and oral contraceptives bind to magnesium and produce insoluble precipitates or complexes, negatively impacting Mg availability and absorption. Caffeine, alcohol and diuretics (e.g., furosemide, bumetanide) increase renal excretion of Mg. Antacids (e.g., omeprazole) affect Mg absorption due to the increase in GI pH.[115]	Mg plays a role in hundreds of enzymatic reactions involved in hormone receptor binding, muscle contraction, neural activity, neurotransmitter release, vasomotor tone, blood glucose control, mitochondrial energy production, and cardiac excitability.[114,116] RBC magnesium is often cited as preferable to serum and plasma levels due to their higher magnesium content (0.5% vs 0.3%). Serum is used to assess hyper- or hypomagnesemia. Urinary Mg may not correlate with Mg status in the body due to the variable degree of renal reabsorption and secretion. Variables affecting this include dietary intake, existing Mg status, mobilization from bone and muscle, hormones (estrogen, parathyroid, calcitonin, glucagon), medications (diuretics, chemotherapy), diabetes. Anywhere between 5% to 70% of filtered Mg may be excreted in the urine. 24-hour urine levels may be more reliable than spot urine.[115] Normal or high urinary excretion is thought to indicate renal Mg wasting, whereas low Mg excretion suggests reduced intestinal absorption.[113]	Low magnesium is associated with hypertension, coronary heart disease, diabetes, osteoporosis, neurological disorders (migraine, depression, epilepsy), asthma, muscle cramps, sleep disorders, fibromyalgia, and chronic fatigue.[113,115] Elevated magnesium is associated with nausea, vomiting, lethargy, headaches, flushing, bradycardia, hypotension and cardiac abnormalities.[113]

NUTRIENT	SOURCES	ABSORPTION FACTORS	BIOCHEMICAL ACTIONS	SYMPTOMS OF IMBALANCE
Manganese (Mn)	Whole grains (wheat germ, oats and bran), rice, and nuts (hazelnuts, almonds, and pecans) contain the highest amounts of Mn. Other food sources include chocolate, tea, mussels, clams, legumes, fruit, leafy vegetables (spinach), seeds (flax, sesame, pumpkin, sunflower, and pine nuts) and spices (chili powder, cloves and saffron).[117] Airborne exposure can occur through automobile exhaust, unleaded gasoline and occupational exposure (mining, welding, ferroalloy and steel industry, battery manufacturing). It is also present in fungicides, textile bleaching, manufacture of glass and ceramics, paint, matches and fireworks, leather tanning, hydroquinone, potassium permanganate and other chemical production. Soil manganese concentrations can contaminate well water.[117,118]	Only about 1 to 5% of dietary Mn is absorbed in the gut. Absorption is influenced by intestinal pH, the presence of divalent metal transporter DMT1, other divalent metals competing for absorption (iron, copper, zinc, calcium) and phytic acid.[119] The absorption of Mn is tightly regulated in the gut and therefore toxicity from diet has not been reported.[117] Iron deficiency increases Mn absorption.[119] Supplemental magnesium (200mg/day) may decrease Mn availability by decreasing absorption or increasing excretion.[120] Mn is eliminated mainly via bile.[118]	Required for immune function, regulation of blood sugar and cellular energy, reproduction, digestion, bone growth, blood coagulation, hemostasis, wound healing and antioxidant. Mn is incorporated into metalloproteins, such as superoxide dismutase and others.[117,120]	Mn deficiency is rare and results in impaired growth, poor bone formation and skeletal defects, abnormal glucose tolerance, altered lipid and carbohydrate metabolism, dermatitis, slowed hair/nail growth.[117,118] Diseases reported with low blood Mn concentrations include epilepsy, Mseleni disease, Down's syndrome, osteoporosis and Perthest disease.[118] Individuals with increased susceptibility to manganese toxicity include patients with chronic liver disease, newborns and children, iron-deficient populations, patients on parenteral nutrition, and occupational exposure.[118,120] Mn is neurotoxic and excess levels have been associated with Parkinson's-like symptoms. A blood Mn level may provide the best estimate for brain Mn levels when exposure is recent. Mn toxicity is generally due to environmental or occupational exposures including airborne (inhaled) and drinking water.[117] Periods of occupational exposure of 6 months to 2 years may lead to manganism and the motor and neuropsychiatric symptoms may remain several years after the exposure. Symptoms include dystonia, bradykinesia and rigidity (due to damage to dopaminergic neurons) and gliosis.[86] Additional symptoms include tremors, muscle spasms, tinnitus, hearing loss, ataxia, mania, insomnia, depression, delusions, anorexia, headaches, irritability, lower extremity weakness, changes in mood or short-term memory, altered reaction times and reduced hand-eye coordination.[121]

NUTRIENT	SOURCES	ABSORPTION FACTORS	BIOCHEMICAL ACTIONS	SYMPTOMS OF IMBALANCE
Molybdenum (Mo)	Beans (lima, white, red, green, pinto, peas), grains (wheat, oat, rice), nuts, vegetables (asparagus, dark leafy, Brassicas), milk, cheese.[102,122]	Mo absorption is passive in the intestines. Urinary excretion is a direct reflection of dietary Mo intake, not necessarily Mo status.[102] Increased Mo intake may elevate urinary copper excretion.[102]	Four enzymes require Mo as a cofactor: sulfite oxidase, xanthine oxidase, aldehyde oxidase and mitochondrial amidoxime-reducing component (mARC). These enzymes are important in detoxification. Sulfite oxidase converts sulfite to sulfate.[122] Mo has been used clinically to treat Wilson's disease to bind copper and prevent absorption. Because of the copper-chelating property, Mo has been studied as an antitumor therapy as well as its ability to inhibit profibrotic and proinflammatory cytokines for the treatment of arthritis and MS.[122]	Mo deficiency is quite rare and a case report shows an acquired deficiency due to long-term parenteral nutrition.[122] The potential for Mo toxicity is low and may be associated with aching joints, gout-like symptoms, hyperuricosuria, elevated blood Mo, hallucinations and seizures.[122]
Potassium (K)	Fruits and vegetables especially potatoes, apricots (dried), prunes, citrus juices, tomatoes, beet greens, avocadoes, bananas, leafy greens, legumes, yogurt, salt substitutes.[123-126]	Approximately 90% of the daily K intake is excreted in the urine and 10% by the GI tract.[124] Salting foods, then discarding the liquid reduces the potassium content.[127] Approximately 98% of K is found within cells and 2% in the extracellular fluid.[124] A standard metabolic panel includes serum potassium to assess hyper or hypokalemia. RBC potassium indicates intracellular levels. The correlation between dietary K intake and urinary K is high.[125] Increased urinary potassium loss may result in hypokalemia. While the 24-hour urinary collection is considered gold standard for assessing urinary potassium excretion, a spot urine adjusted to creatinine correlates with a 24-hour urine collection.[128] Thiazide diuretics have a common side effect of lowering serum potassium leading to hypokalemia.[127]	Potassium is critical for normal cellular function. All cells possess a sodium-potassium exchanger that pumps Na out of and K into cells, creating a membrane potential. Excitable tissues such as nerve and muscle rely on this gradient. Insulin, catecholamines and aldosterone are responsible for maintaining the regulation of K distribution between the intracellular and extracellular space. Additionally, the kidneys play a role in maintaining K homeostasis.[124] The potassium: sodium intake ratio has decreased from early to modern times and contributes to the negative effect on blood pressure.[123]	Anorexia nervosa, crash diets, alcoholism, excessive sweating, intestinal malabsorption and diarrhea are clinical situations associated with K deficiency. Hypokalemia is characterized by low serum K and can lead to glucose intolerance via impaired insulin secretion, cardiac arrhythmias, and muscle weakness. Mild hypokalemia is characterized by constipation, fatigue, muscle weakness, and malaise.[124-127] Adequate potassium intake is important for heart and bone health, reduces the risk of stroke and coronary heart disease, and is associated with a reduction in recurrent kidney stones. The primary health outcome used to evaluate potassium intakes for dietary guidelines is blood pressure.[123] Hyperkalemia is characterized by elevated serum K and symptoms include paresthesias, fasciculations in the arms and legs, ascending paralysis with eventual flaccid quadriplegia, respiratory failure (rare), ECG changes, ventricular fibrillation and asystole.[124]

NUTRIENT	SOURCES	ABSORPTION FACTORS	BIOCHEMICAL ACTIONS	SYMPTOMS OF IMBALANCE
Selenium (Se)	The selenium content of grains and vegetables depends on the Se content of the soil. In meats, Se content is dependent on the diet of the animals. Foods with higher selenium content include Brazil nuts, seafood (especially tuna), chicken, beef, pork, lamb.[129,130] Also present in air, water, soil, metallurgy, airborne coal/oil emissions, dandruff shampoo, paints, photo cells, drums, photocopiers, glass, ceramics, rubber, pharmaceuticals.[129]	Selenium tends to be well absorbed and the bioavailability of Se in the form of selenomethionine is greater than 90%.[130] Sulfur, lead, arsenic, calcium and iron (Fe3+) reduce the absorption of Se.[129] Urine is the main route of excretion and reflects recent dietary intake. Plasma is useful for assessing nutritional selenium status.[129,130]	Selenium is part of selenoproteins that are important for antioxidant defense, thyroid hormone formation, DNA synthesis, and reproduction. Deiodinases in the thyroid incorporate Se and are important for conversion of thyroxine to active T3. Glutathione peroxidase is a selenium-dependent antioxidant enzyme that neutralizes hydrogen peroxide.[129] Some research suggests that plasma glutathione peroxidase levels may be a good indicator of selenium status.[130]	Symptoms of selenium deficiency occur in extreme cases of deprivation and include necrotizing cardiomyopathy, peripheral myopathy, decreased muscle tone, thinning hair, opaque nails, and anemia. The disease associated with selenium deficiency is called Keshan disease. Selenium deficiency may be a cancer promoting factor.[129] Selenium toxicity symptoms include hair and nail brittleness and loss (selenosis), GI disturbances, skin rash, garlic breath odor, fatigue, irritability and nervous system abnormalities.[130]
Strontium (Sr)	Sr is found in fish, grains, leafy vegetables, dairy, soil, water, air, and is also used in the manufacturing of televisions, fireworks, paints, glass, ceramics, fluorescent lights, medicines, magnets.[111,131]	Vitamin D, calcium, and protein reduces the absorption of Sr.[131] Sr is eliminated mainly through urine.[111]	Sr is considered a trace mineral that is similar to calcium, accumulates in bone and is involved in bone metabolism. Sr promotes calcium uptake into the bone and has been used as a prescription drug in the treatment of osteoporosis.[111,132]	Toxic levels may be associated with rickets especially in children.[111] Urinary Sr levels were associated with breast cancer risk.[133]
Sulfur (S)	Protein (specifically amino acids methionine and cysteine as organic sulfur), eggs, meat, fish, dairy, garlic, onion, broccoli and other cruciferous vegetables, supplements (chondroitin sulfate, glucosamine sulfate, MSM, etc.), sulfiting agents (inorganic sulfur) as food additives in processed meats, wine, beer, dried fruits, seafood.[134,135]	Unknown	Sulfur is involved in cartilage synthesis. Sulfation is a major detoxification pathway.[135] The sulfur-containing amino acids cysteine and methionine are not stored in the body. Any dietary excess is oxidized to sulfate, excreted in the urine, or stored in the form of glutathione.[135] Sulfur deficiency is involved in the development of oxidative tissue damage.[136]	Nutritional deprivation of sulfur is associated with cardiovascular disease and stroke.[136]

NUTRIENT	SOURCES	ABSORPTION FACTORS	BIOCHEMICAL ACTIONS	SYMPTOMS OF IMBALANCE
Vanadium (V)	Mushrooms, shellfish, black pepper, parsley, dill seed, beer, wine, grains, sweeteners, infant cereals.[102] Fossil fuels, welding, catalysts, steel alloys, batteries, photographic developer, drying agent in paints/varnishes, reducing agent, pesticides, black dyes/inks/pigments in ceramics, printing and textile industries.[137,138]	The absorption of V is <5% and most ingested V is found in the stool.[102] V is transported mainly in the plasma. It is found in large amounts in the blood initially and at trace levels 2 days after exposure.[139] V has a half-life of around 10 days. Body clearance occurs directly via urinary excretion.[138]	Vanadium mimics insulin and has been used as a supplement for diabetic patients. V stimulates cell proliferation and differentiation. The highest concentrations are found in the liver, kidney and bone.[102] V is studied in the treatment of diabetes, cancer, and diseases caused by parasites, viruses and bacteria, and for anti-thrombotic, anti-hypertensive, anti-atherosclerotic, and spermicidal properties.[138] Vanadium-induced cytotoxicity can be mitigated by glutathione, ascorbic acid, or NADH to convert oxidized vanadium (5+) into its reduced (4+) form.[140]	Acute toxicity is rare. V exposure is through ingestion or inhalation. Vanadium may cause abdominal cramps, loose stools, green tongue, fatigue, lethargy, focal neurological issues. Animal studies show renal toxicity with high doses.[102] Urinary vanadium concentrations during pregnancy were associated with preterm delivery and impaired fetal growth. Cardiovascular and respiratory symptoms may be present.[140]
Zinc (Zn)	Red meat, seafood (oysters), whole grains (in the germ and bran portion). As much as 80% of total Zn is lost during the grain milling process.[102] Denture cream and galvanized steel or iron also contain Zn.[141,142]	The majority of Zn is absorbed in the jejunum via a transcellular process and at high Zn intakes paracellular transport may occur. Iron and calcium supplements, phosphorus-containing salts, phytates (grains, legumes), phosphorus-rich proteins (milk casein, nucleic acids), and long-term alcohol consumption may decrease Zn absorption.[102] Zn decreases the concentration of copper.[143] Occupational silica exposure may lead to increased urinary loss of copper and Zn.[144] Increased urinary Zn levels may be seen with muscle catabolism, cirrhosis, long-term alcohol consumption, and use of thiazide diuretics.[102,145-147] A drop in urinary Zn occurs before a decrease in plasma Zn in Zn-	Zinc is important for immune function, cell division, cell growth, wound healing, breakdown of carbohydrates, enhancing insulin action, sense of smell and taste and as an antioxidant. During pregnancy, infancy, and childhood, zinc is a requirement for proper growth and development.[143] There are over 300 active Zn metalloproteins and more than 2000 Zn-dependent transcription factors involved in gene expression of various proteins.[143] Some of the well-known metalloenzymes include RNA polymerases, alcohol dehydrogenase, carbonic anhydrase, and alkaline phosphatase (ALP).[102] Over 85% of total body Zn is found in skeletal muscle and bone.[102]	Zinc deficiency is associated with lymphopenia, frequent infection, hair loss, diarrhea, poor appetite, problems with taste and smell, slow growth, hypogonadism in males, nighttime vision loss, dermatitis, delayed wound healing, depression, schizophrenia, multiple sclerosis.[102,143] Acrodermatitis enteropathica is a rare inherited condition that results in low zinc.[151] Excess intake of Zn can result in copper or iron deficiency, nausea, vomiting, epigastric pain, lethargy, fatigue and headaches.[102,143]

NUTRIENT	SOURCES	ABSORPTION FACTORS	BIOCHEMICAL ACTIONS	SYMPTOMS OF IMBALANCE
Zinc (Zn)		deficient diets, indicating that urinary Zn responds more rapidly than plasma to dietary changes. Plasma Zn is useful for assessing the exchangeable pool of Zn between tissues, and can be low due to stress, inflammation, infection, low albumin or other metabolic conditions, as well as extreme dietary deficiency. Homeostatic mechanisms are effective in maintaining plasma Zn concentrations for many weeks of even severe dietary Zn restriction.[102,148-150]		

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