Essential & Toxic Elements

A Reference Guide for Practitioners

Rocky Mountain Analytical
Changing lives, one test at a time

Element Analysis

Although single element analysis is often used to assess potential toxicity of elements such as mercury, cadmium and lead; doubts about the clinical utility of multi-element analyses of hair or urine have been expressed.

Hair Elements

For hair element analysis, clinicians have questioned whether individual element levels accurately reflect what is being transported through blood. An extensive review of thousands of hair element results led Dr. Andrew Hall Cutler, an expert in the field of hair element analysis, to conclude that assessing the *pattern* of essential element distribution is crucial when interpreting hair element results. Dr. Cutler found that with a statistically normal distribution of essential elements, both essential and toxic element results could be taken at face value. However, when essential element distribution is abnormal (too many high, low, or too few normal levels), it's likely that the ability of hair to simply incorporate what flows by in blood has been compromised. Factors that may perturb element transport into hair include: presence of a toxic element in excess, genetic abnormalities, and/or poor digestion. Thus, an abnormal distribution pattern of essential elements may prove a useful indicator for the presence of toxic elements in excess, as it suggests something (e.g. mercury) is affecting element transport into hair tissue.

External contamination of hair samples via direct exposure to elements is also a concern (e.g. metalworker). Rocky Mountain Analytical uses a standardized wash procedure to reduce or eliminate particulate contamination and maintain consistent results.

Urine Elements

Measurement of elements in urine typically reflects recent exposure rather than total body burden. Consequently, many clinicians administer chemical chelating agents to facilitate the elimination of toxic elements stored in tissue. Although accepted for treatment of poisoning, some clinicians consider chelation for other conditions to be controversial.

Clinical Effects of Element Toxicity

Toxic elements impact a number of physiologic systems, but their clinical significance can vary significantly from person-to-person and with degree of exposure. Nevertheless, it is clear that even relatively low levels of some elements can negatively impact health. Health issues associated with elevated levels of toxic elements include (but are not limited to): cancers, neurological conditions, renal failure, psychological issues, hematological and dermatological conditions.

Gastrointestinal

Contamination of food or drink by toxic elements may cause acute gastroenteritis. Symptoms may develop shortly after consumption of contaminated foodstuffs, and could be mistaken for food poisoning. Vomiting and diarrhea may be followed by circulatory collapse and multi-system involvement. Chronic gastroenteritis may occur with repeated ingestions of low doses of toxic elements over time. Toxic elements implicated in gastroenteritis include: antimony, cadmium, lead, bismuth, silver, thallium, and mercuric salts. Excessive exposure to essential elements may also cause GI toxicity. For example, canned fruit juices contaminated with zinc and/or tin have led to chronic GI symptoms. Other essential elements implicated in gastroenteritis include: chromium, phosphorus, copper, iron, and vanadium.

Respiratory

Inhalation of fumes from toxic elements has caused chemical pneumonitis and pulmonary edema. In some cases, the inhalation of fumes can produce symptoms resembling an acute respiratory infection. Chronic exposure to metal dusts may lead to pulmonary fibrosis, bronchitis and/or asthma. Elements implicated in respiratory conditions include: aluminum, antimony, beryllium, cadmium, chromium, platinum, iron, lithium, mercury, nickel, selenium, titanium, vanadium, and zinc. In addition, dusts of tungsten and titanium carbides with cobalt have also been implicated in respiratory disease.

Cardiovascular

Cardiovascular toxicity occurs primarily after acute poisoning. Specifically, acute poisoning with antimony, barium, cobalt or lithium could lead to arrhythmias or cardiomyopathy. Chronic exposure to some elements may affect red blood cell production. Hemolysis may result from acute exposure to gases of arsenic or antimony, and from ingestion of large amounts of soluble copper salts. Chronic lead poisoning destroys red blood cells, while cobalt may cause polycythemia.

Central Nervous System

Acute exposure to toxic elements frequently leads to convulsions and coma. Barium, iron, lithium, thallium and organic tin compounds have all been implicated.

Delusions, hallucinations and acute psychosis are also potential CNS consequences of acute toxicity. Lead poisoning, either acute or chronic, is extremely toxic to the central nervous system. Other possible CNS effects of element toxicity include: peripheral neuropathy, motor neuropathy, paresthesias, sensory neuropathy (including the trigeminal nerve), and degenerative changes in the brain basal ganglia, cortex, and cerebellum. Elements known to cause CNS toxicity include: antimony, bismuth, copper, manganese, mercury, and thallium.

Renal

Kidney damage may occur subsequent to gastrointestinal symptoms. Renal symptoms manifest as acute tubular necrosis, oliguria, anuria or renal failure. Antimony, arsenic, bismuth, copper, uranium and vanadium compounds have all been implicated in renal toxicity.

Hepatic

Hepatoxicity can manifest as abnormal liver enzyme levels or jaundice. Antimony, arsenic, bismuth, copper, chromium, iron and selenium have all reportedly caused hepatoxicity.

Treatment of Element Toxicity

The most important step in the treatment of toxicity, regardless of type or length of exposure, is to eliminate the source of the toxic element. In the workplace, exposure usually comes via inhalation, while outside of work, exposure is usually through ingestion.

Mercury is a commonly ingested toxic element, and therefore most likely to disrupt essential element transport in hair or be found in urine. Chelation can be used in the treatment of most toxic element poisonings, including mercury, but chelation may deplete essential elements, or redistribute toxic elements to other tissues (e.g. redistribution of mercury from body to brain).[2] Therefore, chelation should be only carried out by health professionals certified in its use.

Summaries of commonly used chelating agents are provided for information only and are not intended as treatment suggestions.

Dimercaprol (BAL) is a toxic chemical that forms a stable chelate with arsenic. It has been used in treatment of acute and chronic arsenic toxicity. Dimercaprol has also been used to remove antimony and bismuth, but is contraindicated in mercury toxicity because it forms lipid-soluble complexes with organic mercury and redistributes mercury to the brain.[2]

DMPS (2,3-dimercapto-1-propanesulfonic acid sodium) is a synthetic amino acid chelating agent. DMPS forms a water soluble complex with toxic elements and is believed to eliminate heavy metals through the kidneys, liver, gastrointestinal tract. DMPS is less toxic than dimercaprol, and has shown an ability to accelerate excretion of inorganic and organic mercury, arsenic, bismuth and lead. Mobilization of toxic elements after DMPS treatment may aggravate metal-related symptoms.

DMSA (meso-2,3-dimercaptosuccinic acid) is less toxic than DMPS, and is preferred for treatment of lead poisoning. DMSA also binds with arsenic and mercury, excreting them through the liver, kidneys and bowel. It is given orally or intravenously and must be accompanied by 6 to 8 glasses of water throughout the day.

Prussian Blue (potassium ferricyanoferrate) given orally may enhance fecal excretion of an insoluble complex of absorbed cesium.[3]

Diethyldithiocarbamate has proven effective in treating acute nickel carbonyl poisoning.[2]

Penicillamine effectively chelates copper, iron, lead, mercury and zinc, and is used for ongoing treatment of Wilson's disease. It has also been used to chelate bismuth.

Triethylenetetramine (TETA) is used to chelate copper in Wilson's disease if tolerance to penicillamine has developed.

Desferrioxamine is the agent of choice for iron excess.

Calcium EDTA (Ethylene diamine tetraacetate) given intravenously chelates lead (replacing it with calcium), but may redistribute lead to the brain. Also available in suppository and oral form, but only about 5% is absorbed orally.

N-acetylcysteine (NAC) is used to support detoxification of the liver after exposure to toxic elements.

In some cases, symptomatic relief is the only accepted treatment for element toxicity. For example, systemic corticosteroids have been shown to improve pulmonary symptoms of chronic beryllium disease.

About this Reference Guide

At Rocky Mountain Analytical, we believe the treating healthcare professional is best qualified to determine which information to share with a patient. Therefore, we do not include detailed toxicity information in our report interpretation. Instead, we have created this guide to provide you with specifics on the potential hazards of the various elements. In the reference guide you will find :

A brief description of the physiologic effects of toxic and essential elements.

- Toxicity data is usually specific to a particular form of an element (soluble salt, isotope etc), and so you must consider that not all forms of the element are necessarily equally toxic.

Elements appear in alphabetical order,

- Essential/non-toxic elements in green, and toxic/potentially toxic elements in purple.

Elements are categorized as either essential or toxic for the purposes of the test interpretation.

- However, not all the elements categorized as essential are necessarily essential for health, some are merely non-toxic in commonly consumed amounts.

Data on sources of elements.

- All elements, whether toxic or essential, are present to some degree in food and/or water. Where data are available, the estimated daily intake of the element is presented.
- Note that levels of the various elements can differ by geographic area. Therefore, as we gather data and geographic patterns emerge for specific elements, that information may be included in the interpretation.

Information on common sources of both toxic and essential elements.

- Note: the list of potential sources of each element is not warranted to be complete.

Up to 45 Elements

Essential / Non-Toxic	Toxic / Potentially Toxic
Barium	Aluminum
Boron	Antimony
Calcium	Arsenic
Chromium	*Beryllium
Cobalt	Bismuth
Copper	Cadmium
*Germanium	Cesium
Iron	Gadolinium
Lithium	*Gallium
Magnesium	Indium
Manganese	Lead
Molybdenum	Mercury
Phosphorus	Nickel
Potassium	*Platinum
Rubidium	*Silver
Selenium	Tellurium
Silicon	Thallium
Sodium	Thorium
Strontium	Tin
Sulphur	*Titanium
Vanadium	Tungsten
Zinc	Uranium
Zirconium	

*Elements included in hair element analysis, but not part of urine element analysis.

Aluminum

Aluminum is poorly absorbed, with oral bioavailability estimated at between 0.1 and 0.3%.[2] After absorption in the upper intestine, aluminum concentrates in skeleton and lungs. Daily aluminum intake ranges from 5 to 10mg.[2]

Effects: Aluminum inhibits the formation of alpha ketoglutarate, which is needed to eliminate ammonia formed from amino acid metabolism. Increased serum ammonia could result in impaired brain function with poor memory, confusion and in extreme cases delirium.[1] *In vitro* studies also show decreased levels of succinate dehydrogenase and other enzymes involved in the tricarboxylic acid (TCA) cycle. Dysfunction in the TCA impairs ATP production and may contribute to fatigue symptoms.[4] Aluminum is a known neurotoxin.[2] Inhalation of aluminum salts has been linked to asthma.[2]

Elevated aluminum has been correlated with poorer scores on tests of memory function, concentration and motor function. Aluminum is also frequently elevated in the presence of behavioural and learning disorders such as ADD, ADHD and autism. Children absorb aluminum more readily than adults and are also more sensitive to its toxic effects, exhibiting toxicity at lower levels.[1] Because it is a neurotoxin, aluminum may be a factor in Alzheimer's disease and other dementias, resulting in confusion, disorientation, poor memory and poor coordination. A relationship between aluminum and Alzheimer's disease is suggested by some epidemiological studies, but other studies show no relationship. It is possible that neurofibrillary tangles in the brain bind up aluminum and concentrate it in the brain.[2]

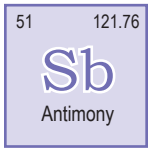
High doses of aluminum inhibit bone remodeling and produce osteomalacia. Some renal dialysis patients develop hypochromic, microcytic anemia due to aluminum toxicity. An increased risk of coronary heart disease has been observed in aluminum production workers. Sufficient evidence exists for an association between lung and bladder cancer and aluminum toxicity.[2]

Aluminum levels are commonly elevated in patients on renal dialysis, as it tends to accumulate in the presence of renal failure. Aluminum toxicity may also cause cardiomyopathy and microcytic anemia.[2] Aluminum may be a possible trigger for sarcoidosis, an autoimmune condition.[1]

Aluminum may interfere with absorption of calcium, iron and phosphate.[1]

Sources: Aluminum cans, baking powders, processed cheese, antacid preparations, antiperspirants, and baking pans are common sources of aluminum. Foods cooked in uncoated aluminum cookware may absorb aluminum, depending on the acidity of the food. Aluminum is also used as a flocculating agent in water treatment plants.

Antimony



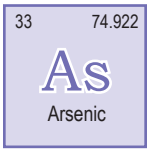
Animal studies estimate absorption of antimony after ingestion at 2 to 7%. After oral or parenteral exposure, the highest concentrations of antimony are found in the thyroid, adrenals, liver and kidney.[2] Trivalent antimony (3^+) has a longer biological half-life than pentavalent (5^+) antimony, and is generally more toxic.[1] Elemental analysis measures total antimony and does not distinguish between the trivalent and pentavalent forms. The estimated adult intake of antimony from diet is 4.6 to 7.4 µg per daily.[2]

Effects: Elevated antimony may cause liver damage or even liver failure.[1,5] Antimony can suppress white blood cells, particularly neutrophils. Cardiotoxicity is the most significant long term risk associated with antimony exposure. Antimony concentrates in the heart, and may cause heart problems by impairing magnesium utilization.[1] Antimony toxicity may contribute to cardiomyopathy, heart failure, myocardial infarcts, arrhythmias, myocardial depression and fainting due to heart slowing (Stokes-Adams attacks).[1,5] Inhalation of antimony has resulted in pneumoconiosis, obstructive lung changes and focal fibrosis.[2]

Early symptoms of antimony toxicity include: fatigue, lethargy, malaise, headaches, aches and pains, and other nonspecific symptoms.[1]

Sources: Flame retardants in plastics and textiles; including clothing and upholstery are common sources of antimony. Antimony is also used as solder for waterpipes, in pottery glazes and sun resistant paints, batteries, semiconductors and as a catalyst for plastics. PETE plastics may contain antimony. Loading ammunition and spending time at firing ranges may increase risk of antimony exposure.

Arsenic



Arsenic is very well absorbed from the gastrointestinal tract. Average daily intake of arsenic from food and water is around 0.01 to 0.02 mg daily, but may be considerably higher (~0.37 mg) in areas where fish consumption is very high.[2]

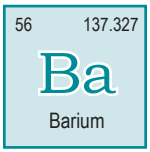
Absorbed arsenic is distributed widely throughout the body and tends to remain longest in the skin, GI tract, thyroid and skeleton. It is excreted primarily through the kidneys. The highest levels of arsenic are typically found in the hair, nails and skin.[2]

Effects: Arsenic causes cell injury or death by inhibiting mitochondrial respiration and creating reactive oxygen species (ROS), which may ultimately play a role in causing cancers, diabetes, and cardiovascular disease (hypertension, atherosclerosis, stroke, ischemic heart disease, microvascular disease). Arsenic affects multiple organ systems by interfering with the action of enzymes, essential cations and cellular transcription.[2] The severity of these effects depends on the duration and magnitude of arsenic exposure. Acute poisoning with arsenic can result in neuropathies, but this is an inconsistent finding in chronic exposure at low concentrations.[2]

Early symptoms of arsenic toxicity are non-specific and may include: headaches, fatigue, restlessness, insomnia, drowsiness, vertigo and dizziness, listlessness, malaise, abdominal pain, and aches and pains.[1] The World Health Organization includes peripheral neuropathy, numbness and tingling in extremities, muscle cramps and weakness as symptoms and signs of arsenic toxicity.[2] Arsenic causes imbalances in DNA methylation that likely contribute to the development of cancers.[2]

Sources: Arsenic has been used in rodenticides and pesticides, and is found in dust from burning coal. Consequently, arsenic is widely dispersed in the environment, and is frequently found in fish and crustaceans and in fruits and vegetables living and growing in contaminated waters. Rice is also often contaminated with arsenic.[6] Commercially-raised pigs and poultry are sometimes given arsenic-containing feed additives (e.g. roxarsone), which can concentrate arsenic in their flesh or organs, particularly the liver. Pressure treated lumber is often treated with chromate copper arsenate, so exposure may come from playground structures, decks and fences.[7]

Barium



Although not truly an essential element, barium is normally present in food, with daily intake estimated in the range of 0.3 to 1.8mg.[2]

Barium is poorly absorbed through the GI tract. However, some studies have shown statistically significant increases in serum and urine barium levels after consumption of barium sulphate in diagnostic radiographic examinations of the GI tract.[1] Presence of 'leaky gut' could theoretically result in increased absorption of barium-containing contrast agents. Inhalation of barium salts may cause a pulmonary reaction, but without pulmonary function abnormalities or symptoms.

Effects: Animal studies showed no clear neurobehavioural or reproductive toxicities associated with barium. However, ingestion of non-pharmaceutical grade barium sulphate has caused nausea, abdominal pain, diarrhea and vomiting. Barium may be associated with motor neuron disease and amyotrophic lateral sclerosis, although these effects may have been due to concomitant cesium exposure, rather than barium.[8]

Deficiency: There are no demonstrated deficiency states for barium.

Excess: Ingestion of water-soluble barium compounds (e.g. barium nitrate) can be acutely toxic. In acute poisoning, cardiac arrhythmias, and general muscular paralysis (including respiratory) may ensue.[1]

Sources: Brazil nuts, pecans and dry cocoa are food sources of barium. Barium is also found in depilatories, insecticides and rodenticides. In industry, barium is used in drilling mud; pharmaceuticals; oil additives; and in the manufacturing of alloys, glass, cement, fireworks and ceramics.[2] Barium is also found in white pigments used for paper, paint and ceramics.[1]

Beryllium

Animal studies show beryllium is poorly absorbed from the gastrointestinal tract. Inhalation can result in long-term deposition of beryllium in lung tissue. The average daily intake of beryllium is estimated to be between 5 and 100µg.[2]

Effects: Beryllium has direct and indirect chemical toxicity through antigen-specific stimulation of T-cells. Beryllium exposure can cause dermatitis, acute pulmonary inflammation and chronic beryllium disease (CBD), which is a T-cell mediated condition. Individuals with an abnormal blood

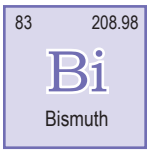
beryllium lymphocyte proliferation test (BeLPT) have about a 10% chance of developing CBD per year of follow-up.[9] Accumulation of specific T-cells is associated with the development of granulomatous inflammation.[2,9] In addition to the lung, granulomatous lesions may develop in other organs including: liver, kidney, bone marrow, spleen, lymph nodes and skin.

People with the HLA-DPβ1-Glu69 genotype are 8 times more likely to contract CBD on exposure to beryllium, but almost one-third of the general population has this genotype. Consequently, routine screening for the genotype is not useful for prevention of CBD.[2]

Elevated levels of beryllium are most likely due to direct exposure, but there are no clinical data on whether or not reducing or eliminating exposure relieves symptoms or improves outcomes.

Sources: Beryllium is found primarily in metal alloys: particularly those with copper, nickel and aluminum.[2] Beryllium is light, strong, transparent to x-rays and a good conductor of heat and electricity. Consequently, beryllium is frequently used in medical-dental, computer, aerospace, military and electronic applications. Beryllium is also found in tobacco smoke.

Bismuth

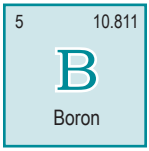


Bismuth compounds are generally poorly absorbed after inhalation or ingestion.[2] Absorbed bismuth concentrates primarily in the kidneys, but also appears in liver, spleen, colon, lung, brain and blood.[1,2] Bismuth crosses the placenta and can accumulate in glial cells and neurons in the brain. The average daily intake of bismuth from food and water is estimated to be around 20 µg.[2]

Effects: Early signs of bismuth toxicity include difficulty standing, walking or writing, memory deterioration, behaviour changes, insomnia, muscle cramps as well as psychiatric disturbances.[10] Bismuth toxicity is part of the differential diagnosis for Parkinson's disease. Neurotoxic effects include: clumsiness, tremors, confusion, myoclonic jerks and gait disturbances as well as paranoid ideation, memory impairment, altered taste, dysarthria, and progressive dementia. The administration of bismuth compounds has also led to colitis, GI bleeding, purpura, agranulocytosis and aplastic anemia.[1,2] Ingestion of colloidal bismuth can cause acute renal failure.[2] Bismuth pigmentation has been found in colon, vagina and skin tissues.[2]

Sources: Bismuth is found in pharmaceuticals (e.g. bismuth subsalicylate in Pepto-Bismol®) and cosmetics.[2] Elimination from blood occurs via multi-compartment pharmacokinetics, with the shortest half-life in humans recorded at 3.5 minutes and the longest being around 20 years.[10]

Boron



Although essentiality has yet to be proved, boron is nevertheless an important trace element in humans. Boron is well absorbed from the gastrointestinal tract,[9] and animal data indicates fairly uniform distribution of boron across various tissues. However, lower concentrations tend to be found in fat and higher concentrations in bone.[11] The average intake is estimated at 0.5 to 3.1 mg per day.[11]

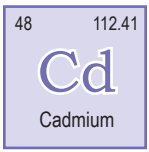
Effects: Boron appears to modulate cell signaling via effects on transport of ions across membranes, thereby influencing cellular responses to hormone signals.[12] Boron is required for activation of vitamin D to assist in calcium absorption. Boron also enhances estrogen activity in bone, thereby protecting against bone loss.[12]

Deficiency: True boron deficiency has not been demonstrated, but experimental research has shown that depriving humans of boron can affect the metabolism or utilization of calcium, magnesium, copper, nitrogen, glucose, reactive oxygen species and estrogen.[11] Communities with low levels of boron have been shown to have a higher incidence of osteoarthritis.[13]

Excess: High boron intake (300mg per day) has produced symptoms of nausea, vomiting, diarrhea, dermatitis and lethargy. However, boron supplementation is usually in the range of 3 to 10mg per day.[12]

Sources: Boron comes primarily from fruits and vegetables when adequate boron is present in soil.[12] Borax is found in laundry products, and boron-based products are used in flame retardants. Boric acid is used medicinally.[1]

Cadmium



Cadmium is well-absorbed through the lungs, with inhaled particles depositing in alveoli and tracheobronchial mucosa. Poorly absorbed inhaled particles are transported to the pharynx and can be swallowed. The estimated daily intake of cadmium from food and water ranges from 10 to 60µg, but is

higher in contaminated regions.[2]

After absorption, cadmium is transported primarily in blood cells, where it is bound to metallothionein (MT). The Cd-MT complex is taken up into renal tubular cells where MT can be catabolized, causing release of cadmium ions. MT is made in the liver, so cadmium initially tends to concentrate in liver tissue prior to redistribution.[2]

In humans, iron deficiency has been shown to increase cadmium absorption. Adequate zinc levels may protect against cadmium toxicity by synthesizing MT in the liver, which can then be used to bind up cadmium ions. Animal studies show that low intake of iron, zinc, calcium or protein may significantly increase absorption of cadmium.[2] Cadmium toxicity is increased in the presence of arsenic.

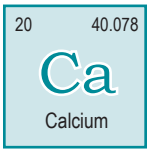
Effects: Acute cadmium inhalation toxicity results in irritation, dryness of nose and throat, coughing, headaches, chills, fevers and chest pains. Severe cases may result in pulmonary edema or chemical pneumonitis. Ingestion of cadmium stimulates gastric mucosa; causing nausea, vomiting, abdominal pain and diarrhea within minutes of ingestion.[2]

Chronic cadmium poisoning may result in impaired pulmonary function including: shortness of breath, emphysema, and chronic obstructive pulmonary disease. Early signs of renal damage include increased urinary excretion of low molecular weight proteins. Epidemiologic evidence shows that type II diabetics are at increased risk for cadmium induced renal dysfunction. Osteomalacia and osteoporosis are rare, but can manifest as *Itai-Itai* disease, which is also associated with iron-deficiency anemia and renal anemia. There is no proven association between cadmium toxicity and hypertension. Cadmium exposure is not significantly correlated with the development of cancer, with the possible exception of lung cancer.[2]

Cadmium is a mitochondrial toxin and as a consequence, toxicity may manifest primarily as fatigue.

Sources: Cadmium is obtained as a by-product in the mining of zinc. It is used as an electroplating agent to protect iron from rust, as a pigment in some oil paints, in rechargeable batteries, some types of solders, in the glaze on certain ceramics used for cooking and eating, as a stabilizer in some plastics, and as a coloring agent in denture plates. Cadmium is also present in welding fumes, cement dust and particulates from coal-fired power plants. Cigarettes contain significant amounts of cadmium.[1]

Calcium



Calcium is the most abundant element in the body, with 95 to 99% of body calcium stores used in forming the matrix of bone tissue.[12] The remaining 1 to 5% is found in blood, extracellular fluid, muscle, and other tissues. Calcium requirements vary according to age, gender and reproductive status, but it is uncommon for the average North American diet to provide the full daily requirement of calcium. Depending on the geographic region, dietary intake of calcium is between 50 and 90% of recommended levels.

Calcium absorption varies based on environmental and dietary conditions, age, and race; with Asians and Africans absorbing calcium more efficiently than Caucasians.[14] Calcium undergoes active transcellular transport in the duodenum and jejunum, while positive paracellular transport occurs in the ileum.[12] When calcium levels are low, PTH and vitamin D act synergistically to mobilize calcium from bone. When calcium levels rise, the hormone calcitonin acts to reduce serum levels. Calcitonin and PTH maintain calcium homeostasis by controlling deposition and absorption of bone, kidney excretion of calcium, and gastrointestinal absorption.

Cadmium can interfere with calcium metabolism in kidney and bone; affecting calcification, decalcification and bone remodeling.[2] Aluminum can replace calcium in soft bone tissue. Low dietary calcium can result in higher levels of lead in tissues. Lead can also compete with calcium for uptake by calcium channels, and disturb neurotransmitter kinetics. Nickel toxicity can increase free intracellular calcium.[2]

Effects: Calcium is essential for nerve transmission, muscle contraction, vascular contraction, vasodilation, glandular secretion, cell membrane and capillary permeability, enzyme reactions, respiration, renal function, and blood coagulation. It also plays a role in neurotransmitter and hormone release and storage, uptake and binding of amino acids, cyanocobalamin (vitamin B12) absorption, and gastrin secretion.

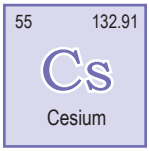
Skeletal, smooth and cardiac muscle all require calcium to trigger ATP production to provide energy for muscle contraction. Neurotransmitters release calcium at the synaptic cleft to enable nerve transmission. Calcium also helps regulate ion transport in cell membranes.[12] Other calcium functions are activation of prothrombin, conversion of fibrinogen to fibrin, and activation of various enzymes.

Deficiency: Calcium deficiency can lead to muscle cramps, twitches, possible hypertension and osteoporosis.

Excess: Calcium homeostasis is very well-controlled, so calcium excess is rarely toxic. However, ingestion of very high doses of calcium accompanied by supplemental vitamin D may result in calcification of body tissues.

Sources: Calcium is found in dairy foods, the Brassica family of vegetables (kale, Swiss chard, turnip greens etc), Brazil nuts, almonds, sunflower seeds, carob flour, Barbados molasses, dried figs and Brewer's yeast.

Cesium



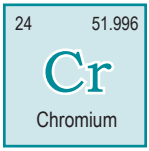
In vitro studies show that cesium can be actively transported into cells.[15]

Effects: Cesium is suggested to have both cardiotoxic and neurotoxic effects. Cesium and potassium ions are of a similar size, therefore replacement of potassium ions by cesium may be a mechanism by which cardiotoxicity occurs. There are at least six published reports of arrhythmias (prolonged QT-intervals) induced by use of cesium chloride. It is believed that cesium acts by inhibiting delayed rectifier potassium channels in the myocardium. Cesium has been shown to cause hypokalemia.[16]

The neurotoxic effects of cesium have been studied in animals and humans. Progressive paralysis has been observed in animals after injections of cesium chloride.[17] In humans, cesium levels in postmortem samples of brain and spinal cord of ALS patients were almost twice as high as controls.[17] However, other data suggests that cesium can have a neuroprotective effect by preventing neuronal cell death.[18] In general, the non-radioactive form of cesium being measured, cesium-133, is considered to be relatively non-toxic. Cesium chloride has been used to treat cancer, as it is believed to preferentially enter cancer cells, raise pH, and cause cancer cell death.[19]

Sources: Cesium is found in specialized glass conductors. Radioactive cesium is used in nuclear medicine. Cesium chloride is used in the centrifugation of DNA and has been studied as a cancer treatment.

Chromium



Chromium is poorly absorbed from the GI tract.[2] Absorption is increased by amino acids, ascorbic acid and starch; and decreased by zinc and calcium-magnesium antacids.[9] Chromium is transported by transferrin into insulin-sensitive cells in response to increased plasma insulin.[14] Average daily intake of chromium is in the range of 0.03 to 0.1mg.[2]

Effects: Chromium is essential for normal glucose tolerance, and is a key element of the glucose tolerance factor (GTF). GTF is a complex of glycine, cysteine, glutamic acid, and two molecules of nicotinic acid bound to chromium. Chromium potentiates the effects of insulin by increasing receptor numbers and affinity, and increasing insulin binding to cells. In animal models, a chromium-containing peptide called chromodulin potentiates the actions of insulin at its receptors, including activation of receptor tyrosine kinase activity. In diabetes patients, these effects result in decreased insulin resistance, improved glucose tolerance, and lower blood glucose levels.[14]

Deficiency: Symptomatic chromium deficiency is uncommon, but can arise from malnutrition, pregnancy, stress, or long-term use of chromium deficient total parenteral nutrition (TPN). Deficiency symptoms may include severe glucose intolerance, weight loss, and metabolic encephalopathy.[14]

Excess: Symptoms of chromium excess may result in non-specific symptoms such as fatigue and malaise, abnormal liver function tests and anemia. Hexavalent chromium (Cr VI) is 100 times more toxic than the trivalent dietary form chromium (Cr III). Elemental analysis measures total chromium and does not distinguish between the III and VI forms. Cr VI can cause liver, kidney and heart failure in addition to being carcinogenic in humans.[14]

Sources: Chromium is found in Brewer's yeast, beef, calf's liver, whole wheat bread, wheat bran, rye bread and fresh chili.[12] Hexavalent chromium is used industrially in stainless steel manufacture, certain wood finishes, leather tanning, handling cement, glass cleaners and radiator cleaners.[1]

Cobalt

Cobalt is an essential trace element, and 85% of cobalt in the body exists in the form of vitamin B_{12}. Dietary cobalt intake is highly variable, ranging from 5 to 50 µg per day, most of which is consumed in inorganic form (not as vitamin B_{12}).[2]

Gastrointestinal absorption of cobalt varies from 5 to 45% depending on the individual. After absorption, cobalt is distributed systemically, with the liver and kidney containing the highest concentrations.[2]

Effects: Cobalt helps increase blood volume and total numbers of erythrocytes. Cobalt given to anephric patients resulted in a 46% increase in hemoglobin concentration.[2] Reduced cobalt intake has been associated with improvement in dyshidrotic eczema.[20]

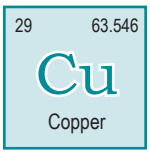
Cobalt appears to inhibit tyrosine iodinase, thereby decreasing iodine concentration and leading to goiters.[2] Vitamin B_{12} is used to regenerate folic acid, and as a consequence many B_{12} deficiency symptoms are resolved upon supplementing with folic acid.

Deficiency: Cobalt deficiency is essentially a vitamin B_{12} deficiency. Deficiencies can lead to increased methylmalonic acid (MMA) and/or homocysteine levels. MMA is a myelin destabilizer and high levels of homocysteine are associated with increased risk of stroke and heart attack. Clinically, the signs of B_{12} deficiency may include fatigue, and numbness and tingling in extremities. Severe deficiencies may lead to pernicious anemia, depression, mania, suicidal tendencies and paresthesias.

Excess: High intake of cobalt has been associated with polycythemia, cardiomyopathy and thyroid lesions.[2] Excess cobalt may also affect cytochrome p450 enzymes in the liver, with both induction or inhibition possible.

Sources: Vitamin B_{12} is found in beef, mollusks, turkey, chicken, eggs, fish, nuts, green leafy vegetables, and cereals. A 1995 Canadian analysis of food products found that waffles, corn cereal and potato chips had the highest levels of cobalt.[21] Cobalt is used in metal alloys for the aerospace industry, and in blue pigments and glazes.[1]

Copper



Copper is an essential trace element. Dietary copper is absorbed across the mucosal membrane of the small intestine. Copper is bound to albumin and transcuprein in the portal circulation, and is incorporated into ceruloplasmin for excretion into blood.[2] Daily copper intake from food ranges from 1 to 2.5 mg.[2]

Estrogens increase serum copper concentration. Copper shares an absorption carrier with zinc and calcium, which means excess of these

elements may antagonize copper absorption. Rarely, iron may interfere with copper absorption. Amino acids and citrate in the diet may chelate copper and enhance its absorption, while fibre and bile may inhibit absorption.[12] High intake of zinc, antacids, or molybdenum may interfere with copper utilization or absorption. Cadmium and lead may also interfere with transport or availability of copper.[2]

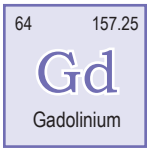
Effects: Copper is found in numerous enzyme systems including superoxide dismutase (SOD), ferroxidases and cytochrome oxidase. Hemoglobin synthesis is also dependent on copper, and copper is used in aerobic energy production to facilitate electron transfer and to oxidize cytochrome c.[12] Erythrocuprein binds copper in red blood cells and exerts an antioxidant effect.[12]

Deficiency: Symptoms of copper deficiency include: poor immune function, reduced skin pigmentation, CNS impairment, poor collagen structure, lipid abnormalities, iron deficiency anemia, and osteoporosis.

Excess: At high doses, copper causes epigastric pain and emesis, headaches, diarrhea and hemolytic anemia. Toxic doses cause severe liver, kidney, and brain damage. Copper is excreted primarily through bile. Mercury toxicity may impair production or excretion of bile, thereby increasing copper retention.

Sources: Copper is found in oysters, nuts, soy lecithin, beef liver, buckwheat, cod liver oil and lamb chops. Supplementation with more than 2 to 4 mg copper may result in copper accumulation. Copper sulphate is used to prevent algae growth. Copper is commonly used in electrical and plumbing applications. Copper is gradually replacing arsenic salts for treating wood products.[1]

Gadolinium



Free gadolinium is extremely hepatotoxic, which is why only chelated gadolinium is used medically as a contrast agent. Even with chelated forms though, some free gadolinium may be released, with linear chelates posing the greatest risk. After administration of two different gadolinium chelates, deposition of gadolinium in bone was 4 times higher for gadodiamide (linear chelate) than for gadoteridol (cyclic chelate).[2]

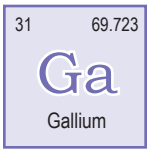
Effects: Renal dialysis patients are at greatest risk of gadolinium toxicity; specifically a condition called nephrogenic systemic fibrosis (NSF). The proposed cause of NSF is deposition of free gadolinium in tissue. Once in tissue, gadolinium cannot be cleared readily by the kidney. NSF can also lead to waxy thickening and hardening of the extremities and torso, giving skin a

wood-like texture with plaques and subcutaneous nodules. [2,22]

Gadolinium chelates may cause pseudohypocalcemia through binding of gadolinium to reagents used in colorimetric assays of calcium concentration.[2] This effect may persist for up to 50 hours.

Sources: The primary source of gadolinium exposure is from intravenous injections for MRI imaging.[1]

Gallium



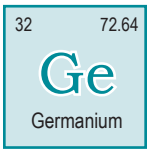
Gallium is relatively common in the earth's crust and occurs naturally in food; but food-sourced gallium is unlikely to be toxic. Gallium concentration in the body is estimated to be less than 0.01 µg/g. Absorbed gallium is bound to transferrin in circulation and concentrates in liver, bone and bone marrow, kidneys, and spleen. Gallium transfer via breast milk has been reported. Gallium is excreted primarily via the kidney.[2]

Effects: Pulmonary, hematopoietic, renal, immunological and reproductive effects have been demonstrated in animals. In particular, alveolar and bronchioalveolar tumors, suppressed IgM production, and decreased sperm count were observed. Limited correlative human data is consistent with animal findings. Gallium arsenide is classified as carcinogenic to humans, but toxicity may be related to arsenic content rather than gallium.[2]

Gallium competes with iron for transferrin. Because it can interfere with delivery of iron to cells, gallium has been used therapeutically to inhibit tumour cell growth in cancer patients.[2] Gallium has an affinity for bone and gallium nitrate has been used to reduce serum calcium levels in cancer patients with bone involvement.

Sources: Gallium isotopes are used for organ screening, and gallium is also used in the manufacture of semi-conductors.[2]

Germanium



Although not a true essential element, germanium has been used nutritionally to treat cancers and AIDS. Both inorganic and organic forms of germanium are well-absorbed from the gastrointestinal tract and lungs. The estimated dietary intake of germanium ranges from 0.4 to

3.4 mg per day.[2]

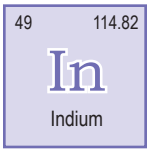
Effects: An organic form of germanium, spirogermanium, had non-significant benefits on regression of advanced renal cell cancers.[2] Organogermanium supplements are also purported to improve immune function, increase oxygen delivery to tissue and reduce fatigue.

Deficiency: No deficiency states of germanium have been reported.

Excess: High intake of inorganic germanium has resulted in nephrotoxicity. Discontinuation of germanium led to improvement in renal function, but recovery was incomplete.[23] High intake of both organic and inorganic forms (including Ge-sesquioxide: Ge-132) in humans has led to weight loss, cardiac dilation, lactoacidosis, chronic renal failure and hepatotoxicity. [2,23] Muscle weakness, peripheral neuropathy and anemia have also been observed.[24] Use of spirogermanium in cancer treatment has resulted in neurotoxicity and pulmonary toxicity.[23]

Sources: Germanium is found in raw clams, canned tuna, dried pan fish, canned baked beans and tomato juice.[2] Germanium is used in specialized electronic and infrared applications.[1]

Indium

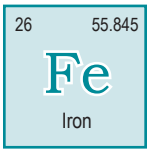


Like gallium, indium is bound to transferrin in circulation. Animal studies indicate indium arsenide is deposited mainly in liver, kidneys, and spleen, with lesser amounts in the lungs. Ionic indium is excreted primarily in urine, while colloidal indium is mainly excreted in feces.[2] The average daily intake of indium from food and water is estimated to be in the range of 8 to 10 µg.[25]

Effects: Indium chloride causes necrosis of the renal proximal tubules in rats, and colloidal indium oxide causes necrosis of liver and spleen cells. Reduced hemoglobin and neutrophil counts as well as lung damage have also been observed. In humans, pulmonary fibrosis from inhalation exposure to indium-tin oxide has been reported in one patient. The IARC has classified indium phosphide as a probable human carcinogen. Indium salts are marketed as a nutritional supplement for hormone balancing and energy.

Sources: Indium is used with gallium in nanotechnology and the manufacture of semiconductors. Indium is also used as a hardening and anti-corrosion agent in the manufacture of automobile bearings. Radioisotopes of indium are used in organ scanning and in the treatment of tumors. Indium and gallium alloys are also being used as surface hardening agents in dental restorations.[2]

Iron



In general, 60 to 70% of total body iron exists in the hemoglobin of circulating eryrthrocytes.[2] Iron absorption occurs primarily in the duodenum, with heme iron more readily available than elemental iron. Elemental iron (Fe III) is virtually insoluble at neutral pH, therefore absorption is dependent on an acidic gut pH and reducing agents in the diet. Ascorbic acid enhances iron absorption as does cysteine. Phytic acid, polyphenolic compounds, calcium and partially digested proteins may inhibit iron absorption. Iron is delivered to cells when transferrin binds to receptors. Typical Western diets provide approximately 15 mg iron daily.

Effects: Iron is found primarily in the hemoglobin of red blood cells and in the myoglobin of muscle cells where it is required to transport oxygen and carbon dioxide. Iron is a biological catalyst and is used in the electron transport chain as an electron carrier in cytochromes. It is also found in the functional groups of most enzymes in the Krebs cycle. Iron is an essential cofactor in the synthesis of neurotransmitters.

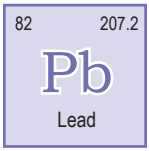
Nickel, cobalt and aluminum have all been shown to interfere with specific iron-dependent processes.[2]

Deficiency: Iron deficiencies can result in severe anemia, fatigue, decreased immunity and learning disabilities. Iron deficiency leads to microcytic and hypochromic blood cells. Iron deficiency anemia of chronic disease may be a result of iron sequestration in ferritin due to increased ferritin synthesis resulting from inflammatory processes.[2]

Excess: Iron exacerbates oxidative damage by free radicals, which is believed to be responsible for the increased cardiovascular disease risk and possible increased cancer risk associated with iron excess.[2,12,14] Iron overdose is the most common cause of poisoning deaths in children. Initial symptoms of iron toxicity include: abdominal pain, vomiting, diarrhea and GI hemorrhage.[2] Death from iron poisoning occurs from circulatory shock, metabolic acidosis, and/or acute hepatic necrosis.[2]

Sources: Good food sources of iron include: kelp, Brewer's yeast, blackstrap molasses, wheat bran, pumpkin and squash seeds, wheat germ, beef liver and sunflower seeds.[12] Iron is found in many plant fertilizers. [1]
Iron is used in the steel industry and in iron-based pigments. [2]

Lead



The skeleton absorbs approximately 90% of ingested lead, which also concentrates in teeth. Blood measurement of lead tends to underestimate exposure and risk in highly toxic individuals.[2] Exposure to lead can come via ingestion of contaminated foods, or through inhalation and industrial exposure. Average daily intake of lead is estimated to be between 30 and 60 µg.[26]

When lead is ingested or inhaled, it eventually moves into the GI tract where it is reabsorbed. Lead binds to erythrocytes and inhibits enzyme activity. It concentrates in the liver and kidneys, and passes through the blood/brain barrier. Lead toxicity is extremely challenging to treat because mobilizing lead from bone is difficult.[2]

Alcohol, vitamin D and milk increase lead absorption, while phytates, calcium and phosphate decrease absorption.[2]

Effects: Lead toxicity affects virtually all organ systems, but often manifests clinically in the gastrointestinal system first. Initial symptoms can include: protracted constipation, indigestion, loss of appetite and occasional diarrhea. Abdominal cramps and vomiting are also common. GI effects are likely a result of interference with calcium in smooth muscle, so i.v. adminstration of calcium may provide temporary relief from cramps.[2]

Severe lead toxicity may lead to renal dysfunction, which causes hypertension, hyperuricemia and gout, and eventually chronic renal failure.[2]

Central nervous system toxicity is common. Low levels of exposure may result in mild distal weakness, tingling or numbness in arms and legs, muscle pain, and decreased peripheral sensory perception.[2] Severe exposure can cause peripheral motor neuropathy with paralysis. Symptoms of lead toxicity are more pronounced in children. In children, encephalopathy can occur, with severe toxicity resulting in ataxia, coma and convulsions. Chronic low level exposure results in higher prevalence of symptoms of irritablility, hostility, anxiety, fatigure, tension, depression, difficulty concentrating and interpersonal problems.[2]

Lead toxicity has been associated with lower IQ and cognitive performance test scores. Even low levels of lead have been associated with intellectual impairment. Nevertheless, the effect of lead on the total variation in IQ is estimated to only be about 1 to 4%, compared to around 40% for social and parenting factors. U.S. studies of children age 4 to 15 showed an association

between ADD and lead toxicity. There is a slight, but statistically significant association between increased bone lead and delinquent behaviour. [2]

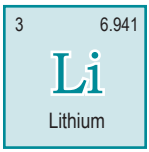
Lead toxicity may also affect the autonomic nervous system, causing postural instability and impairment in visual and auditory functions. Lead toxicity has been associated with poor neuromotor assessments in children.

Severe lead toxicity may cause anemias and interfere with iron transport, heme synthesis, sideroblasts in bone marrow, and shorten the life of red blood cells. Lead inhibits the aminolevulinic acid (ALA) dehydratase enzyme, resulting in increased levels of ALA. ALA is a neurotoxin and induces free radical formation. Inhibition of ALA dehydratase activity in blood cells occurs at low levels of lead exposure and may be a sensitive indicator of lead uptake, although inter-individual variation is high. It has been estimated that 2% of cardiovascular disease worldwide is due to lead exposure. There is also evidence that exposure to low levels of lead is associated with hypertension in humans.[2]

Lead toxicity may also reduce fertility in men and women. Women have greater difficulty conceiving and an increased incidence of miscarriages and still births. Sperm quality in men may be affected.[2]

Sources: Lead is found in solders, alloys, weights, crystal, batteries, ammunition and as a stabilizer in polyvinyl chloride (PVC). Lead is commonly used in the roofing, plumbing, flooring, construction, stained glass, and pottery industries. Lead constitutes up to 40% of the dried weight of some paints. It is also found in some pesticides. Lead solder in plumbing can continually release lead into the drinking system. At its peak in the early 1970's, over 250,000 tons of lead per year were added to gasoline.[2]

Lithium



Although believed to be an essential micronutrient; no lithium deficiency diseases have been identified. The average adult daily intake ranges from 0.65 to 3.1 mg.[14]

Lithium salts are almost completely absorbed from the small intestine via sodium channels. Lithium is found in all organs and tissues with the highest concentrations in brain and kidneys. It is excreted primarily through kidneys. Lithium is fairly evenly distributed in the body, with only minor differences between extracellular and intracellular levels.

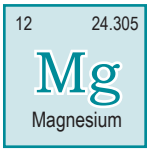
Effects: The powerful polarizing effect of lithium's small atomic radius allows it to replace sodium, potassium, magnesium, and calcium at various binding sites, which may explain its beneficial effects. Lithium appears to affect dopamine and serotonin activity and may increase monoamine oxidase (MAO) activity. It has also been shown to enhance folate and vitamin B12 transport into brain cells, which might also benefit mood.[14]

Deficiency: Although lithium deficiency states have not been identified, there is epidemiological evidence that lower lithium content in tap water is associated with increased psychiatric hospital admissions and criminal behaviour. Animal studies suggest that lithium deficiency can adversely affect mortality and reproduction. Lithium appears to be essential for fetal blood cell development, particularly during the first trimester of gestation.[14]

Excess: Signs of lithium toxicity include increasing diarrhea, vomiting, anorexia, muscle weakness, lethargy, giddiness with ataxia, lack of coordination, choreoathetosis, tinnitus, blurred vision, coarse tremor of the extremities and lower jaw, muscle hyperirritability, dysarthria, and drowsiness. Severe toxicity can cause toxic psychosis, syncope, renal failure, dehydration, circulatory failure, coma, and occasionally death.[14]

Sources: Lithium is found in grains and vegetables, with smaller amounts obtained from animal-derived foods.[14] In some geographical areas, drinking water may contribute significantly to lithium intake. Lithium is also present in tobacco smoke.

Magnesium



Magnesium is absorbed in the lower intestine and colon, and is found primarily in bone and soft tissue. Approximately 50 to 60% of body magnesium resides in bone, where approximately 1/3 acts as a reservoir for the maintenance of extracellular magnesium levels.[14,27] The remaining 2/3 is a component of the bone mineral hydroxyapatite and is not readily available as a source of magnesium.[14,27]

Effects: In tissue, magnesium is involved in over 300 enzyme systems including energy metabolism, protein synthesis, RNA and DNA synthesis, and maintenance of cell membrane potentials.[14] Magnesium is also required for the enzyme sodium-potassium ATPase, which regulates cellular energy metabolism and vascular tone. Insufficient magnesium may therefore result in vasoconstriction of blood vessels or muscle contraction.[12] On average,

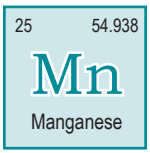
Canadians consume between 200 and 300mg of magnesium daily.[28]

Deficiency: Magnesium deficiency symptoms include weakness, heart irregularities, muscle cramps or twitches, insomnia, lethargy, irritability, anorexia and mental confusion.[12,27] There is evidence that suboptimal magnesium levels may be a contributing factor in cardiovascular disease.[27] Magnesium deficiency leads to depletion of muscle potassium.[27] As magnesium levels decline, intracellular calcium levels rise, leading to vasoconstriction and inhibition of cardiac and smooth muscle relaxation. Low magnesium levels are associated with an increased risk of developing metabolic syndrome.[14]

Excess: Diarrhea is often the first sign of excess magnesium supplementation. Toxicity symptoms may include: drowsiness, lethargy, and weakness. Overconsumption of magnesium-containing laxatives is a common source of toxicity, particularly in the elderly.[12]

Sources: Good food sources of magnesium include kelp, wheat bran, wheat germ, almonds, cashews, Blackstrap molasses, Brewer's yeast, buckwheat, Brazil nuts, dulse, filberts, peanuts, millet, wheat grain, pecans, walnuts, rye, tofu and beet greens.[12]

Manganese



Manganese is considered an essential trace element. Manganese is poorly absorbed, with only about 5% absorbed from the gastrointestinal tract.[2] Most of the absorbed manganese is taken to the liver, and then transported to other tissues by transferrin.[12] The estimated daily intake of manganese from food ranges from 2 to 8.8 mg per day.[2]

Effects: Manganese is involved in amino acid, cholesterol, and carbohydrate metabolism. Enzymes requiring manganese include arginase, glutamine synthetase, phosphoenolpyruvate decarboxylase, and manganese superoxide.[12,14]

Manganese competes with iron for transferrin, therefore manganese deficiencies may arise from excess iron, or conversely, manganese excesses may lead to functional iron deficiencies.[12]

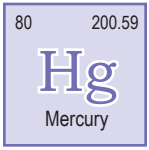
Deficiency: Manganese deficiency has resulted in reddening of black hair, scaly dermatitis, slow growth of hair and nails, decreased serum cholesterol and decreased levels of clotting proteins; all of which resolved

when manganese was restored to normal.[2]

Excess: Manganese in excess causes a form of neurotoxicity called manganism, which is characterized by Parkinsonian-like extrapyramidal symptoms. High levels of manganese have been found in brains of patients with amyotrophic lateral sclerosis.[12] Significantly elevated manganese was found in the hair of violent offenders versus nonviolent controls.[29]

Sources: Good food sources of manganese include nuts, legumes, seeds, tea, whole grains, and leafy green vegetables.[14] Manganese is also used in some blue-purple pigments.[1]

Mercury



Mercury exists in three chemical forms: elemental (pure mercury), inorganic (mercury salts: e.g. mercuric chloride), and organic (with an alkyl group attached: e.g. methylmercury). All forms of mercury are toxic to humans. Most mercury is ingested as an alkylmercury from food, or as mercury vapor from dental amalgams. In the absence of occupational exposure, dietary intake usually does not exceed 10 µg per day.[2]

Effects: Ingested mercury is a potent cell toxin that binds to sulfhydryl and selenohydryl groups of plasma proteins like glutathione, cysteine, NAC and homocysteine. The alteration of these proteins affects receptors, ion channels and intracellular signalization. The conjugation of methylmercury to thiol-containing biomolecules is the likely mechanism by which mercury molecules cross the blood-brain barrier. The toxic effects of methylmercury manifest primarily in neurons and glia cells. The central nervous system is also affected more significantly because the half-life of mercury in the brain is several years, compared to a couple of months in the body.

Mercury toxicity also affects the functioning of the peripheral nervous system, kidneys, immune system, endocrine system and muscles.[2] Signs of chronic mercury toxicity may include weakness, fatigue, paresthesias in extremities or tongue and lips, ataxia, extrapyramidal symptoms, anorexia and weight loss, and gastrointestinal disturbances.[2] CNS symptoms from *in utero* exposure include ataxic motor disturbances and mental symptoms or psychomotor retardation.

With continued exposure, tremors, spasms, severe behavioural and personality changes, memory loss, insomnia, depression or excitability may develop. Other symptoms may include dermatitis, gum inflammation and excessive salivation,

hypertension due to elevated catecholamines, and acute polyarthritis. Mercury can also cause hypothalamic intoxication, which affects mood, emotions, sleep, appetite, heart rate and thirst.[2]

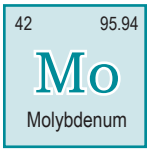
Mercury from amalgams can be released as vapor, which is highly lipophilic and therefore readily absorbed through the lungs. Amalgam particles can also be swallowed and oxidized in the digestive tract, but less than 10% is reabsorbed as mercury. The fetuses of mothers with mercury amalgams have approximately twice the mercury concentrated in the brain and kidneys compared to fetuses of mothers with no mercury amalgams.[2]

Acute poisoning by mercury vapor can cause bronchitis and interstitial pneumonitis and eventually respiratory insufficiency. Acute poisoning from mercuric salts causes gastric pain, vomiting, and necrosis of the intestinal mucosa. Even if the patient survives the GI damage, renal failure occurs within 24 hours.[2]

Occupational exposure comes mainly from the chloralkali and mining industries. Dental and medical professionals may also experience occupational exposure from spills or contamination.[2]

Sources: Mercury is used in chlorine-caustic soda manufacture, which accounts for approximately half the mercury produced annually. The other half is found in dental amalgams, mercury switches, fluorescent lamps and other electronic devices. Mercury has been used in pharmaceuticals, paints, and as a fungicide and algicide. Most of these former mercury products have been banned.[2] Alkylmercury is formed in ocean sediment, and is passed up the ocean food chain, with larger fish like tuna having the greatest concentrations. High fructose corn syrup is another common food source of mercury, due to the use of caustic soda in its manufacture.[30]

Molybdenum



Molybdenum is an essential trace element. Molybdenum is well-absorbed from the gastrointestinal tract, although the efficiency of absorption varies depending on the food source (e.g. 57% absorption from soy versus 87% from kale). In the United States., the estimated daily intake of molybdenum ranges from 50 to 126 µg.[2]

Molybdenum has important interactions with sulphur and copper: tetrahydromolybdate has been used to treat copper toxicity, and

thiomolybdates (sulphur containing molybdenum compounds) have powerful effects on copper metabolism. Molybdenum may antagonize copper uptake, which means that decreased copper may become apparent before direct toxicity from molybdenum is evident.

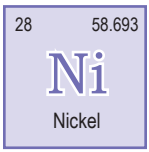
Effects: Molybdenum is required as a cofactor for numerous enzymes including aldehyde oxidase (alcohol detoxification), xanthine oxidase (formation of uric acid) and sulphite oxidase (detoxifies sulphites). A genetic deficiency of molybdenum cofactor has also been identified that prevents detoxification of sulphites, leading to severe brain damage and early death.[2] Molybdenum supplementation may reduce or eliminate symptoms associated with inadequate detoxification, particularly alcohol and sulphites. Molybdenum supplementation may also be useful in cancer prevention, with some evidence indicating it may reduce incidence of esophageal cancer.[12]

Deficiency: Molybdenum insufficiency may contribute to sulphite sensitivity, cancer risk and inadequate detoxification of alcohol.[12]

Excess: High intake of molybdenum has been associated with a significant incidence of gout-like disease, likely as result of increased xanthine oxidase activity and subsequent uric acid formation.[2]

Sources: Molybdenum is found in lentils, beef liver, split peas, cauliflower, green peas, Brewer's yeast, wheat germ and spinach. Molybdenum disulphide is used as a lubricant, and some red pigments contain molybdenum. [1]

Nickel



Although essential in animal health, nickel is not considered essential for humans. However, it may be beneficial in small amounts. The average daily intake of nickel from food and water is about 300 µg.[2]

Nickel undergoes intestinal absorption, and is transported in the blood by the iron transport proteins transferrin and divalent metal transporter-1 (DMT1). As a consequence, adequate iron intake may limit nickel absorption. Nickel is also absorbed by the lungs, which is where the highest concentrations of retained nickel are found.[2]

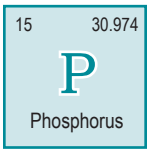
Effects: Acute inhalation exposure to nickel carbonyl or soluble nickel compounds can cause headache, vertigo, nausea, vomiting, nephroxicity, pneumonia followed by pulmonary fibrosis. Chronic exposure to nickel can cause allergy symptoms including rhinitis, sinusitis, and asthma. It is also hepatotoxic, but presence of adequate zinc may prevent nickel toxicity and

help maintain normal liver enzyme function.

Up to 30% of people with skin exposure to nickel-containing metals experience allergic contact dermatitis. Nickel refinery workers show reduced numbers of pregnancies, increased numbers of spontaneous abortions and more birth defects than construction workers. Nickel is considered a carcinogen, with sinus and respiratory cancers predominating.[2]

Sources: Nickel is found most often in jewelry and body-piercings. Nickel is resistant to corrosion by water, air and alkali, is inexpensive and has a metallic sheen. As a consequence, it is a popular jewelry alloy and is also used in steel production, electroplating, nickel-cadmium batteries, dental appliances and various electronic components. It is also found in common household items like cooking utensils, buttons, eyeglass frames, watches, and coins. Some hair dyes and popular multi-vitamin preparations also contain nickel. Nickel is also found in cigarette smoke.

Phosphorus



After calcium, phosphorus is the next most abundant element in the body, with body stores of just under 1 kg for an average adult. Adults consume approximately 1 to 3 grams of phosphorus daily.

Approximately 70% of dietary phosphorus is absorbed. Regulation of phosphorus occurs via renal absorption and interaction with calcium, parathyroid hormone and vitamin D.

Effects: Phosphorus is essential to life: as a key component of nucleic acids in DNA and RNA; for transporting energy via adenosine triphosphate (ATP); supplying phosphates for phospholipid cell membrane layers; and for regulating numerous enzymes. Phosphate ions also function as buffers in the body. Like calcium, most phosphorus (85%) is found in bones and teeth, where it forms part of the bone mineral complex apatite.[12]

Absorption of phosphorus is inhibited by excessive iron intake, and aluminum can bind phosphorus in the intestine and prevent its absorption.[12]

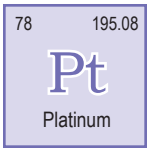
Deficiency: Deficiencies of phosphorus may occur as a result of excess calcium intake or deficiency of vitamin D. Symptoms of deficiency include weakness, joint stiffness, anorexia, and fragile bones.[12] Symptoms of hypophosphatemia include muscle and neurological dysfunction, and

disruption of muscle and blood cells from lack of ATP.

Excess: Too much phosphorus can disrupt calcium balance. Consumption of carbonated beverages can disrupt the balance between calcium and phosphorus.[12] Too much phosphate may cause diarrhea and calcification of organs and soft tissue, and interfere with iron, calcium, magnesium, and zinc utilization in the body.

Sources: Phosphorus is present in Brewer's yeast, wheat bran, pumpkin and squash seeds, wheat germ, sunflower seeds, sesame seeds, almonds, soy beans, cheddar cheese, pinto beans, and peanuts.[12]

Platinum



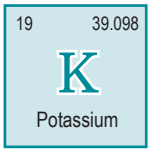
Platinum metal is essentially non-reactive and is very poorly absorbed. Platinum salts are also poorly absorbed after oral or inhalation exposure. Estimated total daily intake of platinum from food, water and air, is 0.02 µg.[2]

Absorbed platinum concentrates in the kidney. The acute toxicity of platinum depends on solubility, with more soluble compounds having greater toxicity. Cisplatin is a soluble platinum based compound used as a chemotherapeutic agent in cancer treatment. It is nephrotoxic, and has mutagenic and possibly carcinogenic properties as well. Tinnitus and peripheral neuropathy are potential consequences of treatment with cisplatin. Platinum may impair intestinal absorption and kidney retention of magnesium.[1,2]

Effects: Exposure to platinum salts can cause platinosis, also called platinum salt sensitivity, which is an allergic rather than toxic reaction. Symptoms are primarily respiratory: wheezing, sneezing, and asthma; but may also include watering of eyes, eczematous and urticarial skin lesions, and inflammation of mucous membranes.[2] Platinum-salt sensitivity appears to be a Type-I IgE mediated hypersensitivity reaction, which generally resolve in about an hour. Smokers are more likely to react.

Sources: Approximately 80% of platinum produced is used in its metallic or oxide form for catalytic converters in automobiles. It is also used as a catalyst in the chemical industry: oil refining, paint manufacture, acids, fertilizers and explosives. Platinum metal is used in pharmaceuticals, dental appliances, jewelry, and in electronics.

Potassium



The upper small intestine is where absorption of potassium occurs, and balance is maintained by hormones as well as renal and autonomic nervous system mechanisms. Potassium crosses cell membranes more readily than sodium, and exists primarily in intracellular fluid.[12]

Effects: Potassium is essential to many body functions including acid-base balance, maintenance of cell membrane potentials, isotonicity, and various enzymatic reactions. It is required for physiological processes including nerve impulse transmission; cardiac, smooth, and skeletal muscle contraction; gastric secretion; renal function; tissue synthesis; and carbohydrate synthesis.[14]

Potassium deficiency often occurs alongside magnesium deficiency.[12] Treatment of severe megaloblastic anemia with parenteral vitamin B_{12} can result in transient hypokalemia. (The increased number of red blood cells drains extracellular sites of potassium.)[14]

Deficiency: Potassium deficiencies result in muscle weakness, bradycardia, bone fragility, CNS, and possible death. Potassium deficiencies may arise from diarrhea and vomiting, renal disease, starvation, burns, diuretic use and aging.[12] Inadequate dietary intake of potassium might play a role in the development of hypertension, stroke, and cardiovascular disease. It is likely that potassium works together with other nutrients to produce beneficial physiological effects.[14]

Excess: Hyperkalemia can cause paresthesia, generalized weakness, flaccid paralysis, listlessness, vertigo, mental confusion, hypotension, blood in the stool, cardiac arrhythmias, heart block, and death.[14]

Sources: Good food sources of potassium include dulse, kelp, sunflower seeds, wheat germ, almonds, raisins, parsley, Brazil nuts, peanuts, dates, figs, avocado, pecans, yams, Swiss chard, and cooked soybeans.[12] Potassium is a major ingredient in salt substitutes and low salt foods.

Rubidium

Although not considered essential, rubidium is rapidly absorbed after ingestion and appears to affect mood. The average intake of rubidium is between 1.5 and 3 mg daily.[31,32]

Effects: The body treats rubidium ions as if they were potassium ions, which means rubidium tends to concentrate in intracellular fluid. Rubidium ions are basically non-toxic, and are removed quite rapidly via sweat and urine. Rubidium may potentiate release of dopamine and noradrenalin into synapses by prolonging nerve action potential.[31,33]

Although lithium and rubidium are both alkali metals with similar properties, animal research suggests they have opposite effects in the brain. Lithium calms the manic phase of bipolar illness, while rubidium may be useful for treating the acute depressive phase of bipolar illness.

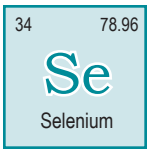
Rubidium isotopes are useful in nuclear medicine for brain tumor imaging as rubidium concentrates more in tumors than in normal brain tissue.

Deficiency: Lack of rubidium may contribute to symptoms of depression.

Excess: Rubidium can become toxic when erythrocyte or muscle cell concentrations reach 30% of the potassium concentrations.[33] Animal data showed high levels of rubidium caused neuromuscular hyperirritability symptoms and reproductive deficiencies.

Sources: Rubidium can be found in red meats.[31] Rubidium is sometimes used in fireworks and in laser applications.

Selenium



Selenium is an essential trace element. Daily intake of selenium varies considerably depending on the region. In Canada, the average adult intake of selenium ranges from 98 to 224µg daily.[34]

Both organic and water-soluble inorganic selenium compounds are well absorbed from the gastrointestinal tract.[2,12] Selenium in food is in the form of seleno-amino acids like selenomethionine and selenocysteine.

Effects: Selenium is essential for numerous enzyme systems including the five glutathione peroxidases, which function primarily as antioxidants. Selenium is also a catalyst for deiodinase enzymes, which are needed to convert the thyroid hormone T4 to its active T3 form.

Animal studies suggest that selenium is able to prevent acute damage from cadmium toxicity. Arsenic compounds increase the toxicity of methylated selenium compounds. Selenium decreases lead toxicity in rats. High copper levels in animals have resulted in symptoms of selenium deficiency. Selenite given with methyl mercury is protective against nephrotoxicity from mercury.

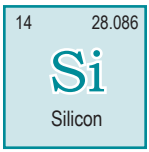
The toxcity of thallium, tellurium, silver and platinum may be lessened by administering selenium.[2]

Deficiency: Selenium deficiencies produce conditions related to poor antioxidant activity: cancers, cardiovascular disease, and immune dysfunction.[12] Incidence of cerebral palsy may be lowered by giving selenium in pregnancy.

Excess: Early signs of selenium toxicity include nausea, vomiting, diarrhea, abdominal pain, chills and tremor. Hair loss, garlic breath, skin lesions and depigmentation, and discoloured nails can occur with acute selenium intoxication.[2] Excess selenium interferes with sulphur enzyme systems and could cause liver disease and impaired bone and tooth growth.[12]

Sources: Food sources of selenium include: butter, smoked herring, smelt, wheat germ, Brazil nuts, apple cider vinegar, scallops, barley, whole wheat bread and lobster. Selenium is also found in anti-dandruff shampoos, use of which can lead to dramatically elevated hair selenium levels.[12]

Silicon



Silicon is a trace element that is converted to orthosilicic acid after ingestion, which increases its absorption. Approximately 40% of dietary silicon is bioavailable, with urine being the primary route of excretion. Most of the silicon in the body is contained in connective tissues such as in the aorta, trachea, bone, tendons, and skin.[14] The average adult intake of silicon is 14 to 21 mg per day.[14]

Effects: Although no definite biological role for silica has been established, it appears to have a role in bone and collagen formation. Orthosilicic acid has been shown to stimulate osteoblasts, and research suggests that supplementing with silicon helps inhibit bone resorption and stimulate bone formation. Since silicon interacts with aluminum, it may be able to prevent aluminum toxicity associated with Alzheimer's disease.[35] Silicon might also protect against atherogenesis.[14,35]

Deficiency: No human deficiency states have been proved, but animal studies show deformities resulting from structural abnormalities in skull and long bones (e.g. femur).[35]

Excess: No human data on the toxicity of orally administered silica has been published. However, inhalation of silica dust can cause silicosis, a

type of pulmonary fibrosis.

Sources: Silicon exists primarily as silicon dioxide, also known as silica, which is present in foods such as vegetables, whole gains, and seafood. Coffee, beer, and unfiltered drinking water are the major sources of dietary silicon, followed by grains, grain products, fruits and vegetables; especially bananas, raisins, beans, and lentils.[14]

Silver

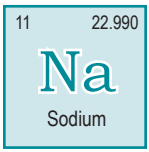
Silver is poorly absorbed orally. Most absorbed silver concentrates in the liver, with lower concentrations observed in lungs, brain and muscle. The estimated average daily intake of silver is 10 to 44 µg.[2]

Addition of selenium, copper and vitamin E has been shown to decrease the toxicity of silver in animals.[2]

Effects: Acute toxicity with water-soluble silver salts can be lethal. Autopsy findings have shown pulmonary edema, hemorrhage and necrosis of bone marrow, liver, and kidney.[2] Repeated ingestion of silver salts or colloidal silver can cause a condition called argyria. In argyria, the skin is discoloured to a grayish-blue, particularly in areas exposed to light. The discolouration occurs as a result of deposition of silver particles in the skin, but It is not clear whether argyria of the skin correlates with systemic toxicity. The concentration of silver in body organs of argyria cases is not known.[2]

Sources: Silver is used in pharmaceuticals, industry, and jewelry. Silver salts are used topically in medicine for the prevention of infections in burned tissue and to stop blood flow. Industrial applications include electroplating, in photographic processing, as conductors and switches, soldering, mirror, batteries, and as a chemical catalyst. Silver nanoparticles are in widespread use for various nanotechnologies. Silver is also found in coins, jewelry and cutlery.[2]

Sodium



The absorption and excretion of sodium and chloride ions is controlled by both active and passive transport mechanisms. Absorption of sodium occurs primarily in the upper small intestine. Cells are less permeable to sodium than to potassium.

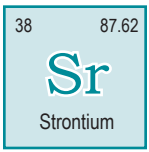
Effects: Sodium is essential for carbon dioxide transport, muscle contraction, nerve transmission and amino acid transport.[14] Active transport of sodium from the cell drives membrane transport proteins used to import glucose, amino acids and other nutrients into the cell. The balance between Na and K ions helps maintain cell volume. If cells begin to swell, the body will export sodium ions from the cell to create osmotic pressure to push excess fluid out.

Deficiency: Severe sodium deficiency, called hyponatremia, may cause osmotic shift of water from the plasma into the brain cells. Typical symptoms include nausea, vomiting, headache and malaise. As hyponatremia worsens, confusion, diminished reflexes, convulsions, stupor or coma may occur.

Excess: Sodium excess is called hypernatremia and may result in fluid imbalances due to a relative insufficiency of potassium. Clinical manifestations of hypernatremia can be subtle; consisting of lethargy, weakness, irritability, and edema. With more severe elevations of the sodium level, seizures and coma may occur.

Sources: Sodium is abundant in kelp, green olives, dill pickles, ripe olives, sauerkraut, cheddar cheese, scallops, cottage cheese, lobster, swiss chard, beet greens, buttermilk, celery, eggs, and cod.

Strontium



Ninety-nine percent of strontium in the body is found in bone.[14] Strontium chloride absorption is used to measure absolute intestinal bioavailability of calcium. The average adult intake of strontium from food is about 2 mg daily. [32]

Effects: Preliminary research suggests that strontium stimulates collagen and cartilage formation. Therapeutic doses of strontium ranelate have been found to stimulate bone formation and reduce bone resorption, but research is lacking for strontium chloride, the form found in most supplements. Strontium salts are used in toothpaste to relieve hypersensitivity by blocking fluid flow in dentinal tubules.[14]

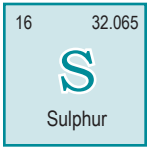
Deficiency: No strontium deficiency states have been identified in humans.[14]

Excess: Excesses of strontium may replace calcium in bone, thereby inhibiting hydroxyapatite formation and impairing mineralization. High

strontium levels may also interfere with vitamin D synthesis and calcium absorption, causing osteomalacia and rickets.[14]

Sources: Strontium is found in most fruits and vegetables, dairy, Brazil nuts, and seawater.

Sulphur



Although a key element of essential amino acids and enzyme systems, no deficiency or toxicity states related to sulphur have been identified. The average daily intake of sulphur from food is estimated to be around 930mg.

Sulphur is absorbed from the small intestine primarily as sulphur-containing amino acids (methionine and cysteine), or from sulphates in fruits, vegetables and water. Sulphur is stored in all cells, especially the skin, hair, and nails. Excess sulphur is eliminated through the urine or in the feces.[32]

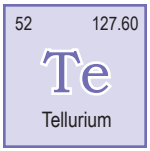
Effects: Sulphur containing supplements like methylsulphonylmethane (MSM) have demonstrated benefit in osteoarthritis and for seasonal allergies, although it is not clear whether sulphur is solely responsible for its benefits. Elemental sulphur is used topically to treat skin disorders like psoriasis, eczema and dermatitis.[32]

Deficiency: There are no defined sulphur deficiency states reported in the literature.[32] However, deficiencies of B vitamins, copper and iodine are thought to cause low hair sulphur levels.

Excess: No examples of sulphur toxicity have been reported, however sulphur-based additives (e.g. sulphites) may cause allergic reactions in susceptible individuals.

Sources: Sulphur is obtained primarily by consuming sulphur-containing amino acids found in meat, eggs and nuts.

Tellurium



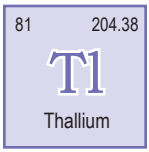
No quantitative information is available regarding respiratory or intestinal absorption of tellurium. Animal studies indicate that up to 25% of orally administered tellurium is absorbed in the gut within 2 hours of intake. Approximately 90% of absorbed tellurium enters erythrocytes, most probably bound

to hemoglobin. The highest concentrations of tellurium are found in the kidney.[2] The estimated daily intake of tellurium from food and water is approximately 100µg.[2]

Effects: Skin contact with tellurium compounds may cause skin burns or a bluish-black rash, followed by a garlic odor in the breath. It has been proposed that inhibition of squalene epoxidase enzyme may be responsible for the appearance of the garlic-like odor. Exposure to tellurium vapor may cause respiratory irritation. Workers exposed to tellurium dioxide reported garlic odor of breath, sweat and urine; metallic taste; decreased sweat production; anorexia; nausea; vomiting; depression; and somnolence. Temperature and pulse increases as well as moderate leukopenia, neutrophilia and leukocytosis have also been reported. Tellurium does not appear to have any mutagenic or carcinogenic properties, and at low doses may in fact be protective against cancer.[2]

Sources: Tellurium is used primarily in industry, with approximately 50% of production dedicated to providing additives to steel; 25% for chemicals and catalysts, 10% for non-ferrous alloys, another 10% for photoreceptor and thermoelectric applications and 5% for other uses. Specifically, tellurium is used in catalytic processes, pigments, metal coatings, semiconductors, solar cells, electroplating, curing of rubber and rechargeable batteries.[2]

Thallium



Thallium is widely distributed throughout the body after absorption.[2] Total intake in the general population from foodstuffs is estimated to be 5µg per day.

Effects: Thallium compounds are extremely toxic; uncoupling oxidative phosphorylation, affecting protein synthesis and inhibiting numerous enzymes. Thallium can also replace potassium in cardiac and muscle tissue. Investigation for thallium poisoning should be considered whenever peripheral neuropathy is accompanied by alopecia.[2]

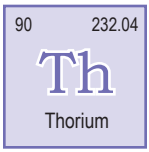
Acute poisoning begins within hours of absorption. Gastroenteritis, nausea and vomiting, diarrhea and abdominal pain are predominant early symptoms. After a few days, neurological symptoms appear and include: parasthesia, mental confusion, severe pain in the extremities, and

convulsion, respiratory and circulatory failure followed by death. If survival of acute poisoning extends beyond one week, headache, ataxia, tremor, and muscular atrophy develop. Cranial nerve involvement and autonomic nervous system toxicity also occur. Alopecia develops after several weeks, fingernail ridges appear and neurological defects remain in the form of ataxia, tremor and mental abnormality. Despite the grim prognosis, complete recovery has occurred in some cases.[2]

In chronic toxicity, symptoms may come on slowly and are usually more subtle. Mild to moderate chronic toxicities include a combination of hair loss, heart racing and high blood pressure; symptoms which might be misdiagnosed as hyperthyroidism.[1] Also, vague ill health and paresthesias have been observed with low level occupational exposure.[2]

Sources: Thallium is used primarily in infrared spectrometers, crystals, optical systems and glass colouring. Thallium ions (e.g. Tl^{201}) show nuclear magnetic resonance potential and have been used in myocardial imaging.[2] Thallium is a by-product of sulphuric acid and cadmium production. Thallous sulphate has been used as a rodenticide, and is regaining popularity due to the development of warfarin resistance in rats.

Thorium



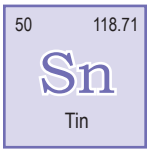
Thorium is chemically similar to uranium, and is a fairly reactive, metallic radioactive element that naturally produces low levels of gamma radiation and alpha particles.[36] However, radioactive elements like thorium undergo spontaneous decay, resulting in the formation of new radioactive elements. It is these 'daughter' elements of thorium that appear to be most toxic. Daily intake of thorium from food and water is estimated to be about 2µg.[37]

Effects: The toxic effects of thorium are due to its radioactivity rather than chemical toxicity.[35] After absorption, thorium concentrates in the spleen. The liver holds the next highest concentrations of thorium, at about 14% that of the spleen, then comes bone marrow at about 4%.[1] An intravenous thorium contrast agent (Thorotrast) used in the 1950', increased the incidence of bone and liver cancers 20 to100-fold.[36,38] Studies of workers with prolonged exposure to inhaled thorium showed an increased incidence of lung disease and cancers, but a causal relationship could not be established because the workers were mostly smokers and were exposed to other carcinogens.[36]

Sources: Thorium is a by-product of zirconium and titanium mining. It is used

most often in refractory applications (casting high-temperature metals and alloys for use in high-temperature vacuum or oxidizing furnaces); lamp mantles; magnesium-thorium alloys in aerospace; welding electrodes; nuclear weapon production; and other applications including ceramics and special use lighting. Natural thorium is also used in ceramic tableware glaze and in flints for lighters. Thorium can also be used as a fuel in nuclear energy generation.[1,36]

Tin



Tin forms a number of inorganic and organic compounds. Inorganic tin is insoluble and considered relatively non-toxic. Soluble inorganic salts of tin are divided into stannous (divalent) or stannic (quadrivalent) compounds. The estimated daily intake of tin from food and water is between 1 and 8 mg per day. Average intake is higher if canned foods are consumed.

Effects: The most common tin compounds are stannous fluoride, stannic chloride, stannous oxide and stannic oxide. Because of their solubility, tin salts may be toxic in high doses. Increased tin intake is associated with decreased copper status.[2] Organotin compounds (tribuyltin, triethyltin, triphenytin) are most toxic; their lipophilicity allows them to penetrate cell membranes, interrupt phosphorylation and disrupt mitochondrial function. They inhibit synthesis of heme oxygenase, and can be genotoxic. Tin hydride gas can be toxic to nerves.

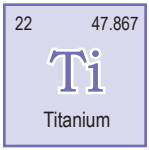
Long-term exposure to tin dust can result in stannosis: a benign pneumoconiosis. Consumption of food from unlacquered cans has resulted in gastric irritation, diarrhea, fatigue, headache and vomiting. Low levels of tin may cause fatigue, depression, suppressed adrenal function, shortness of breath, asthma, headaches, insomnia or reduced cardiac output. High intake of inorganic tin compounds may result in skin rash, gastrointestinal complaints, nausea, vomiting, diarrhea, headache and palpitations.[2]

Unlike inorganic tin compounds, tri-organotins are well-absorbed from the GI tract. Systemic toxicity can lead to anemia and renal and hepatocellular damage. Increased catecholamine production may also occur, causing hyperglycemia, blood pressure changes and damage to the immune system. Some organotins are highly neurotoxic. Skin contact

with organotins may cause epidermal necrosis, irritation, erythema and pustular lesions.[2]

Sources: Food stored in unlacquered tin cans has 24 times as much tin as food from lacquered tin cans. Of the 25 billion food cans produced in Europe annually, 20% have unlacquered tin-coated steel bodies. Inorganic tin is used in bronze, pewter and other alloys; as an alloy with titanium for aircraft engineering; solders; and dental amalgams.[2] Inorganic tin compounds are used in toothpaste; as a stabilizer in perfumes, in dyes and to coat glass. Organotins are used as heat stabilizers for polyvinylchlorides, and tri-organotins are used in marine applications as a biocide to prevent growth of barnacles on ships. Tri-organotins can leach into surrounding water; leading to reproductive failure and population decline in gastropods, mussels and oysters. Consequently, use of these compounds is restricted in some areas.[2]

Titanium



Although poorly absorbed in general, levels of titanium can be detected in blood, brain and parenchymatous organs. The highest concentrations are found in lymph nodes and lungs. Patients with titanium joint implants have higher serum levels of titanium compared to controls, although urine levels are comparable. Typical diets contain approximately 0.3 to 0.5 mg of titanium daily.

Effects: Ingested titanium is likely transported and distributed by transferrin. Titanium tends to accumulate over time in lung tissue, but not in other organs. However, no fibrotic changes in lung tissue have been attributed to titanium dioxide exposure, nor was any increase in mortality observed over several decades of exposure. There is no evidence of increased cancer risk with titanium dioxide. However, titanium tetrachloride may be responsible for significant lung effects including: chronic bronchitis, bronchoconstriction, wheezing, pneumonitis, and pulmonary edema. Titanium tetrachloride is also highly irritating to skin, eyes and mucous membranes.[2]

There are a few case reports of systemic side effects from tablets containing titanium dioxide. Symptoms disappeared when TiO_2 was removed from the tablets. It is thought that some individuals become sensitized to certain metals and develop immune dysfunctions.

Sources: Titanium is widely used in alloys because of its high tensile

strength, light weight, corrosion resistance and ability to withstand extreme temperatures. Titanium compounds are used in cosmetics and pharmaceuticals, and are also popular in implants like knee and hip joint replacements. Titanium dioxide is used as a paint pigment, as a sunscreen, and as a colour additive and clouding agent in foods and dry beverage mixes. Titanium dioxide is added to some cheeses as a whitener and aging accelerator.

Tungsten

Tungsten is closely related to molybdenum, and excesses of tungsten can interfere with utilization and retention of molybdenum.[1,2] Daily intake of tungsten is estimated at 8 to 13 µg per day.

Effects: Tungsten is considered relatively non-toxic. Patients given 25 to 80 grams tungsten powder as a substitute for barium in radiologic investigations suffered no ill effects. Pulmonary fibrosis has been found in tungsten carbide workers, however it is thought that the presence of cobalt in the alloy is the probable cause rather than tungsten.[2] Tungsten alloyed with nickel and cobalt resulted in increased DNA breakage and chromosomal aberrations in osteoblast cells.

Sodium tungstate antagonizes the normal action of molybdenum (as molybdate) in the enzymes xanthine dehydrogenase, sulfite oxidase, nitrate reductase and aldehyde oxidase.[2] Animal studies have shown that molybdenum deficient animals exposed to tungstate were more susceptible to sulfite toxicity.[2]

Sources: Tungsten has the highest melting point of all the metals, is a good conductor of heat and electricity, and maintains tensile strength at high temperatures. Therefore, it is used in drill bits as tungsten carbide, and in spacecraft for rocket nozzles and protective shields. Tungsten is used in incandescent light bulbs, fluorescent lamps, lasers, and as a pigment in some dyes and inks. Tungsten alloys are being used to replace lead in small-caliber ammunition. Thin layers of tungsten oxide are used in electronics.

Uranium

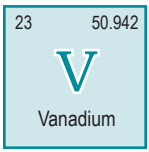
Uranium is ubiquitous in air, water and food, with average intake estimated to be 0.9 to 1.5 µg per day. Humans are typically exposed to uranium via inhalation or ingestion, or from fragment wounds in the military.[2]

Effects: Although radioactive forms of uranium exist, most of its adverse health effects are a result of chemical toxicity rather than radioactivity. In the lungs, uranium may irritate deep lung tissue to cause fibrosis and emphysema. However, most inhaled uranium particles are transported out of the lungs via mucociliary action and swallowed. Once ingested and absorbed, uranium tends to concentrate in lung, bone, liver, and kidney tissue. In kidneys, accumulation of uranium in tubular epithelia results in damage and necrosis, which is often reversible. Uranium may interfere with deposition of calcium in bone or with bone remodeling. Uranium also affects cytochrome p450 liver enzymes responsible for drug metabolism.[2] No reproductive toxicity or increased risk of cancer has been found with exposure to non-radioactive uranium.

Low iron tends to cause elevated uranium levels.[1] Washing of vegetables reduces the amount of uranium in final food products.[2]

Sources: Apart from its use for nuclear power, uranium is also used in glass tinting agents (apple green tint), ceramic glazes (some orange coloured glazes), gyroscope wheels, chemical catalysts, and in military and medical applications. Uranium dioxide extends the life of bulb filaments and is used for photographic toning. Uranium stains and dyes may be used in leather, wood and silk industries.[2] Elevated hair uranium levels appear in geographic areas with naturally higher groundwater uranium.

Vanadium



Vanadium is poorly absorbed, with only about 2% of an oral dose taken up from the upper GI tract.[2,12] Vanadium is excreted primarily in urine. In vivo, the vanadyl cation forms complexes with ferritin and transferrin. The highest concentrations of vanadium are found in the liver, kidney, and muscle tissue.[14] Daily intake of vanadium averages between 10 µg and 2 mg, depending on the geographic area.

Effects: No definite biological role for vanadium has been identified.

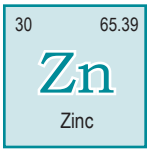
However, vanadium is a cofactor in various enzyme reactions, and is likely important for normal bone growth.[14] Vanadium appears to have insulin-like properties. Vanadium (as metavanadate 125 mg daily for 2 weeks, equivalent to 0.83 mg vanadium/kg/day) lowered the insulin requirements of Type I diabetics, and improved insulin sensitivity in Type II diabetes.[2,14] Although purported to have anabolic effects, research to date has been inconclusive.[2,39] Vanadium may offer some cardiovascular benefits by inhibiting cholesterol biosynthesis from mevalonic acid.

Deficiency: No vanadium deficiency states have been identified in humans, but animal studies show that lipid changes, growth impairment, thyroid metabolic changes, and increase rates of spontaneous abortions occur with low vanadium levels.[12]

Excess: Symptoms of excess vanadium may include hypertension, bipolar disorder, and decreased levels of coenzyme Q10 and coA.[12]

Sources: Good food sources of vanadium include grains and grain products, parsley, soybeans, dry mushrooms; shellfish; parsley. Drinking water can also contain trace amounts of vanadium. [2,12,14] Vanadium is used in industry to improve rust resistance, as a catalyst and in ceramics, fabric dyes and inks. [1]

Zinc



Zinc is fairly widely distributed in the body, with about 60% found in muscle, 30% in bone, and the remainder in skin, hair, liver, GI, pancreatic and other tissues. Dietary intake of zinc ranges from 5 to 14 mg per day.[2]

Zinc is absorbed primarily in the jejunum, but also in the colon.[9] Zinc absorption is increased when zinc status is low, and can be decreased by alcohol intake, infections, surgery, and other physiologic factors. Both calcium supplements and inorganic iron in the diet may decrease zinc absorption.[12]

Effects: Zinc has three broad functions: catalytic, structural and regulatory. Zinc catalyzes nearly a hundred enzymatic reactions, provides structural support for proteins and enzymes (e.g. SOD), and helps regulate metallothionein via binding to metal response element transcription factor (MTF1), which regulates gene expression.[39] Physiologically, zinc is important for protein and DNA synthesis, wound healing, bone structure, immune function and sebaceous glands. In men, zinc is essential for

healthy prostate tissue.[12]

Deficiency: Because of the ubiquity of zinc and its involvement in multiple systems, zinc deficiency symptoms are often non-specific: growth retardation, alopecia, diarrhea, delayed sexual maturation and impotence, eye and skin lesions, and impaired appetite being a few.[40] Chronic low levels may lead to sleep disturbances, poor wound healing, dandruff, rheumatoid arthritis, anorexia and inflammatory bowel disease.[12]

Excess: Zinc competes with copper for absorption, so excess zinc may lead to copper deficiency. Too much zinc is also immunosuppressant. Symptoms of toxicity may include vomiting, dizziness, lethargy and anemia.[12]

Sources: Fresh oysters, ginger root, meat, nuts and dairy are major sources of dietary zinc.[12] Zinc is also used in metal alloys, and is commonly included as an anti-corrosive agent in galvanized metals. Zinc oxide is used in white pigment and as a catalyst in rubber manufacture. Other zinc salts are used as pigments, as fire retardants, wood preservatives, and in laser applications.

Zirconium

Hypothesized to be an essential trace element in the 1960's, it now appears that zirconium is neither essential nor toxic. Human intake averages around 3.5 mg daily, but may be as much as 125mg.[41]

Like its chemical cousin titanium, gastrointestinal absorption of zirconium is minimal according to animal studies. However, zirconium is widely distributed in tissue, concentrating in muscle, liver and blood. In the liver, it concentrates in the mitochondria. The remainder is distributed in lung and spleen tissue. Zirconium crosses the blood-brain barrier, and deposition in human brain tissue has been documented.[41]

Effects: Animal studies show that zirconium can inhibit ATPase, alkaline phosphatase and peroxidase. It can also form chelates with amino acids, complexes with enzymes and can bind with acid mucopolysaccharides.[40]

Deficiency: No zirconium deficiency states have been identified in humans.

Excess: Toxicity related to zirconium is dependent on type of exposure: an admixture of radioactive elements in zirconium oxide and silicate dust has been shown to contribute to pulmonary fibrosis. However, zirconium metal workers over a period of 1 to 17 years showed no definite pathological effects. Cutaneous exposure to zirconyl sodium lactate has resulted in granulomas. Sarcoid-like

granulomas from allergic hypersensitivity to insoluble zirconium oxide have also been reported. Osteomalacia patients with histochemical evidence of zirconium metal were treated with desferrioxamine, after which decreased levels of zirconium and improvement in clinical, biochemical, histological and radiological parameters was observed.[41]

Sources: Zirconium is ubiquitous in the environment, and is present in foods. Oils and fats, cereals and grains, dairy foods, nuts, vegetables and meats contain measurable amounts of zirconium. Zirconium is used in metal alloys for its high conductivity and melting point.

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