VibrantWellness

Heavy Metals

Interpretive Guide

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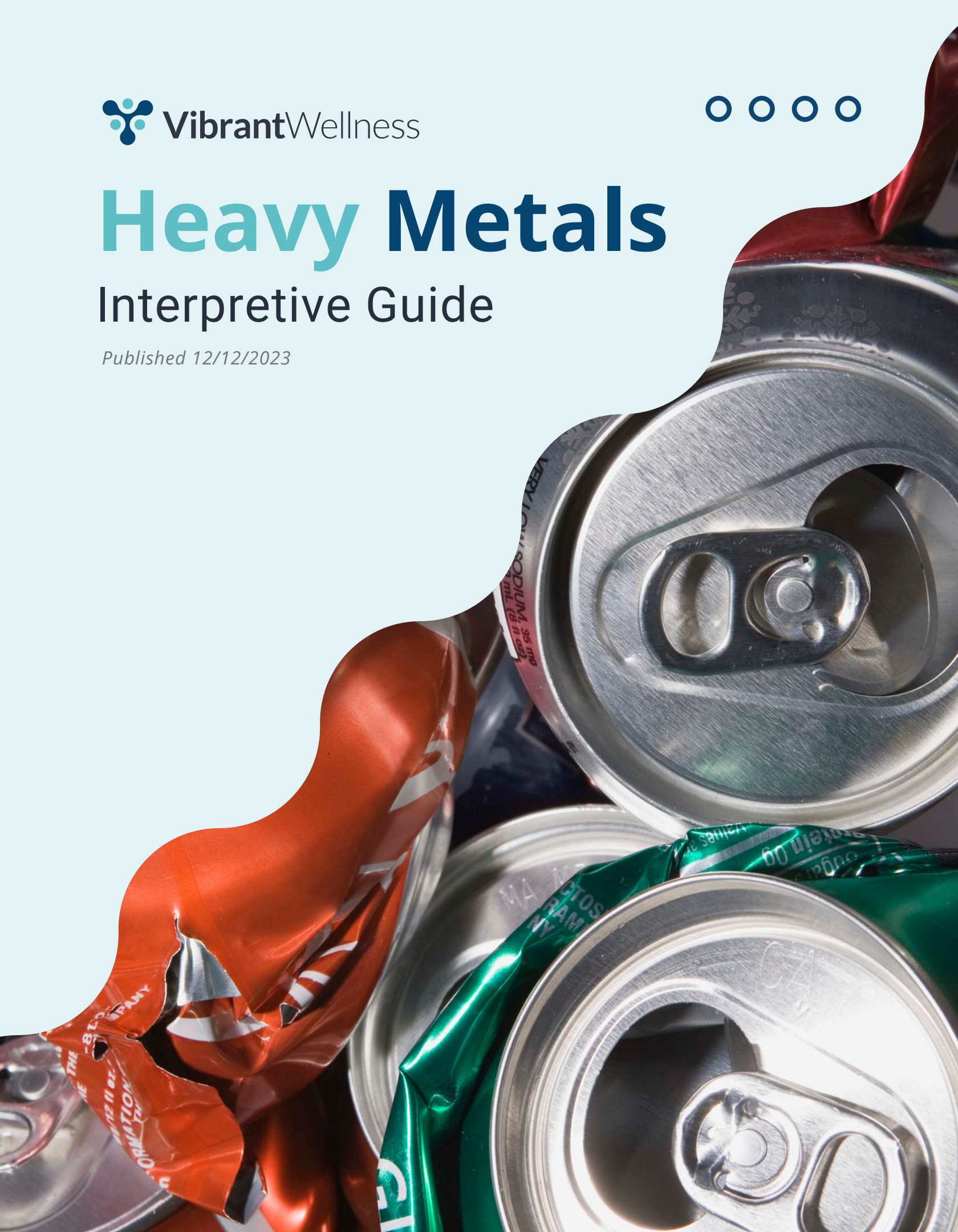

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Phase I and II
Detoxification Support

Supporting the Liver

As a critical piece of any detoxification protocol for heavy metal toxicity, the liver should be considered foundational. Because of its actions in removing environmental toxins for excretion by the body, the liver is often the site of inflammation and dysfunction in individuals affected by long term exposure to heavy metals and other environmental toxins. Within the liver, detoxification happens in two main phases, followed by a third elimination phase. The main goal of liver detoxification is to convert fat-soluble toxins into water-soluble substances that can be more readily excreted through the body's excretion pathways:

- urine (kidneys)
- bile (gallbladder/intestinal tract)
- sweat (exocrine glands)

Phase I

The first phase of liver detoxification involves the Cytochrome P450 enzyme system, and consists of the following reactions:

- Oxidation
- Reduction
- Hydrolysis
- Hydration
- Dehalogenation

Once a toxin is sent to the liver, hepatocytes use the above reactions to chemically transform the toxic element or substance into an intermediate metabolite. Intermediate metabolites can then be bound or conjugated in Phase II to prepare them for excretion. During these processes, there is some increased production of reactive oxygen species (ROS). This may lead to increased superoxide levels, as well as deplete NO— and other antioxidant compounds.

Phase II

In Phase II, the intermediate metabolites undergo one or more of the following steps to become a water-soluble compound, which can be excreted by the body:

- Acetylation
- Amino Acid Conjugation
- Glucuronidation
- Glutathione Conjugation
- Methylation
- Sulfation

The nutrients or cofactors needed for Phase II differ from those required in Phase I due to the differences in chemical reactions required. Phase II nutrients are incorporated into the final end product of the detoxification process, whereas Phase I nutrients are those that generally must be recycled or regenerated in an ongoing and continuous process of transformation.

Intermediate Nutrients Needed

In addition to the nutrients needed for both Phase I and Phase II detoxification, antioxidant nutrients are needed after Phase I to neutralize the reactive oxygen species (ROS) and free radicals produced during Phase I transformation. These include:

- Bioflavonoids
- Vitamin A
- Vitamin C
- Vitamin E
- CoQ10
- Copper
- Manganese
- Sycnogenol
- Selenium
- Silymarin
- Thiols (found in sulfurous veggies like Brussels sprouts, broccoli, cabbage, cauliflower, onions, garlic, leeks)

Nutrients And Cofactors For Phase I

- Riboflavin (Vitamin B2)
- Niacin (Vitamin B3)
- Pyridoxine (Vitamin B6)
- Folic Acid
- Cobalamin (Vitamin B12)
- Bioflavonoids
- Glutathione
- Branched chain amino acids (leucine, isoleucine, and valine)

Nutrients And Cofactors For Phase II

- Glutamine
- Glycine
- Taurine
- Cysteine
- Methionine
- N-acetyl cysteine (NAC)

Nutrients To Support Both Phases

- Silymarin (milk thistle)
- Selenium
- Copper
- Zinc
- Manganese
- Vitamin C
- Vitamin E/tocopherols
- Beta-carotene
- Vitamin A
- Bioflavonoids
- Coenzyme Q10
- Thiols/sulfur compounds found in garlic, onions, broccoli, cabbage, Brussels sprouts

Disclaimer

Please note regarding the chelating agents mentioned throughout this guide:

- Chelating agents mobilize toxins stored in body tissues/fat cells, moving them into circulation.
- Toxins stored in tissues can be largely unreactive, whereas circulating toxins tend to create more oxidative stress and damage.
- Only the ordering provider, who knows the patient's clinical history, can determine whether the patient can handle increased toxin circulation secondary to chelation.
- Therefore, it is up to the ordering provider's clinical discretion whether to recommend chelation for their patient or not.

Heavy Metal Descriptions

Aluminum

Aluminum (Al) is a trivalent cation found in its ionic form in most kinds of animal and plant tissues and in natural waters everywhere. It has no biological role. Aluminum is the most abundant metal in the earth's crust. It is always found combined with other elements such as oxygen, silicon, and fluorine. Aluminum as the metal is obtained from aluminum-containing minerals.

Clinical Manifestations of Toxicity

Aluminum's free metal cation, Al3+, is highly biologically reactive and biologically available aluminum is non-essential and essentially toxic. Biologically reactive aluminum is present throughout the human body; rarely, it can be acutely toxic. Chronic aluminum intoxication has been associated with many health conditions that include, but are not limited to, toxic myocarditis, ischemic stroke, granulomatous enteritis, Crohn's disease, Alzheimer's disease, dementia, autism, oligospermia and infertility, hepatorenal disease, breast cancer, pancreatitis, and diabetes mellitus (Igbokwe et al., 2019).

How it Gets Absorbed

Aluminum is present in significant amounts in air, water, and food, but a large amount of aluminum is not absorbed. Absorption depends on factors such as the levels of competing minerals and parathyroid hormone levels. Dermal absorption of aluminum is possible, such as by using antiperspirants and cosmetics containing aluminum. Aluminum can be absorbed orally through ingestion of foods cooked in cookware containing aluminum (especially from acidic foods being cooked in aluminum cookware), aluminum foil, soda cans, water supplies, baking powders containing aluminum, and antacids.

Sources of Aluminum Exposure

Small amounts of aluminum can be found dissolved in water. Aluminum is used for beverage cans, pots and pans, airplanes, siding and roofing, and foil. Aluminum compounds have many different uses, for example, as alums in water-treatment and alumina in abrasives and furnace linings. They are also found in consumer products such as antacids, astringents, buffered aspirin, food additives, and antiperspirants. Dietary aluminum is ubiquitous but, in such small quantities, that it is not a significant source of concern in persons with normal elimination capacity. Note aluminum is principally eliminated through urine therefore adequate kidney function is essential.

Dietary & Supplement Considerations

- Vitamin C has been used in combination with other chelating agents in the treatment of aluminum toxicity (Rahimzadeh et al., 2022).
- Bee propolis in combination with the potential chelator N-(2-hydroxyethyl) ethylenediaminetriacetic acid (HEDTA) may offer nerve protection, reduction of oxidative stress, and maintenance of cell membranes in the setting of aluminum toxicity (Rahimzadeh et al., 2022).
- Selenium in combination with HEDTA has also shown promise in reducing retention of aluminum while helping to regulate neurologic function in cases of antimony toxicity (Rahimzadeh et al., 2022).

Chelation Options

Deferoxamine, calcium disodium EDTA, and dimercaptosuccinic acid (DMSA), also known as succimer, have all been used as off-label chelating agents used for aluminum toxicity.

Antimony

Antimony (Sb) has no human physiological role. Antimony is released into the environment from natural sources and from industry. In air, antimony is attached to very small particles that may stay in the air for many days. Most antimony ends up in soil, where it attaches strongly to particles that contain iron, manganese, or aluminum. Antimony is found at low levels in some rivers, lakes, and streams.

Clinical Manifestations of Toxicity
Eye and lung irritation, skin irritation, stomach pain, diarrhea, vomiting, stomach ulcers, myocardial damage and alterations in EKGs have been observed in humans after exposure to antimony (ATSDR, 2019; National Center for Biotechnology Information, 2023).

How it Gets Absorbed
Antimony can be absorbed via inhalation, ingestion, and dermal routes via contaminated sources.

Sources of Antimony Exposure
Contaminated water and plant life are the most likely sources of exposure to antimony in humans. Another common source of exposure is through polyethylene terephthalate (PET) found in water bottles (ATSDR, 2019). Occupational exposure is possible via smelters, coal-fired plants, and refuse incinerators that process or release antimony.

Dietary & Supplement Considerations
- Avoid plastic water bottles and food storage containers.
- Support glutathione and methionine levels via diet or supplementation to provide sulfur-hydrogen groups which may help bind antimony.
- Selenium has been shown to help prevent antimony toxicity and stimulate antioxidant systems needed to combat toxicity in plant models and, therefore, may be a nutrient worth considering when addressing antimony toxicity in humans (Ding et al., 2015).

Chelation Options
Dimercaprol, also known as British anti-Lewisite (BAL), has been used as a chelating agent for antimony toxicity.

Arsenic

Arsenic (As) is a naturally occurring element. Arsenic is an essential element in small quantities. Arsenic's biological functions are not clear; however, it may play a function in growth and blood cell formation. Excess arsenic is an enzyme inhibitor and interferes with the uptake of folic acid. Acute high-level inhalation exposure to arsenic dust or fumes has resulted in gastrointestinal effects (nausea, diarrhea, abdominal pain).

Clinical Manifestations of Toxicity

Central and peripheral nervous system disorders have occurred in workers acutely exposed to inorganic arsenic. Chronic (long-term) inhalation exposure to inorganic arsenic in humans is associated with irritation of the skin and mucous membranes and deleterious effects in the brain and nervous system. Chronic oral exposure to elevated levels of inorganic arsenic has resulted in gastrointestinal effects, anemia, peripheral neuropathy, skin lesions, hyperpigmentation, and liver or kidney damage in humans. Inorganic arsenic exposure in humans, by the inhalation route, has been shown to be strongly associated with lung cancer, while ingestion of inorganic arsenic by humans has been linked to a form of skin cancer and to bladder, liver, and lung cancer. The EPA has classified inorganic arsenic as a human carcinogen.

How it Gets Absorbed

Arsenic can be absorbed via inhalation, ingestion, and dermal routes via contaminated sources. For many, fish and shellfish are a major source of exposure to arsenic due to bioaccumulation.

Sources of Arsenic Exposure

Organic arsenic (arsenate) is found in a variety of foods. Inorganic arsenate or arsenite is found in pesticides, beer, table salt, water, paint, cosmetics, pigments, rat poison, glass and mirror manufacture, fungicides, wood preservatives, and commercial chicken feed. Arsenic can also be found in rice (both organic and non-organically grown), and individuals who consume a lot of rice may consider limiting rice consumption if they have elevated arsenic levels in urine. Brown rice contains more arsenic than white rice, due to accumulation in the outer hull. Rice grown in the United States may contain higher levels of arsenic than in other countries due to soil contamination from previous farming practices. Due to the high prevalence of rice-based flour in gluten-free foods, practitioners should caution at-risk individuals on the use of gluten free foods with rice flour-based ingredients.

Dietary & Supplement Considerations

- Modified citrus pectin has been shown to significantly increase arsenic excretion (Eliaz et al., 2006).
- Garlic, onions, broccoli, cauliflower, cabbage, kale, Brussels sprouts, turnips, and kohlrabi can help clear arsenic from the liver via binding to sulfur compounds in these foods (Mehrandish et al., 2019).
- Curcumin has been shown to decrease liver toxicity secondary to arsenic toxicity (Mehrandish et al., 2019; Tunali-Akbay et al., 2007).

Chelation Options

Dimercaprol, DMPS, DMSA, and penicillamine have been used as chelating agents for arsenic toxicity.

Barium

Barium (Ba) is an alkaline earth metal that is typically found in food and groundwater. It serves no physiologic role in the human body. Barium and barium compounds have historically been used in electronic tubes, rodenticide, colorants in paint, and X-ray contrast medium. Individuals in certain parts of the country that use groundwater for drinking water, such as Pennsylvania, northern Illinois, Kentucky, and New Mexico may be exposed to higher levels of barium (up to 10X the MCL – maximum contaminated level).

Clinical Manifestations of Toxicity
There are reports of serious health effects of those exposed to barium chloride or barium carbonate. Possible side effects of exposure to high doses of barium include: hypokalemia, diarrhea, nausea, vomiting, ECG (heart rhythm abnormalities), muscle cramps, and kidney disease.

How it Gets Absorbed
Exposure to barium can happen through drinking groundwater, as well as through skin contact, ingesting it accidentally with polluted material/food, and from direct injection via X-ray contrast medium.

Sources of Barium Exposure
The main exposure source of barium in humans is groundwater, polluted material/food, and X-ray contrast medium.

Dietary & Supplement Considerations
Gentle laxatives may aid in the detoxification of barium.

Chelation Options
According to the CDC, there is no antidote to barium toxicity, although oral administration of soluble sulfates may limit absorption by causing precipitation of an insoluble form of barium (ATSDR, 2014). Standard of care treatment of acute barium toxicity involves regulation of serum potassium levels and respiratory and cardiovascular support as needed.

Beryllium

Beryllium (Be) is a hard, grayish metal naturally found in mineral rocks, coal, soil, and volcanic dust and has no biological role. Beryllium compounds are commercially mined, and the beryllium is purified for use in nuclear weapons and reactors, aircraft and space vehicle structures, instruments, x-ray machines, and mirrors. Beryllium ores are also used to make specialty ceramics for electrical and high-technology applications. Beryllium alloys are used in automobiles, computers, cell phones, sports equipment (golf clubs and bicycle frames), and dental bridges.

Clinical Manifestations of Toxicity

Beryllium produces health side effects ranging from sensitization without evidence of disease to clinically apparent pulmonary disease. Some individuals exposed to beryllium develop sensitization and are at risk of developing chronic beryllium disease (CBD). Immunologic tests can detect beryllium sensitization and help clinicians differentiate between CBD and other interstitial lung diseases.

How it Gets Absorbed

Most exposures to beryllium that cause disease are related to some aspect of beryllium processing. Beryllium particles are inhaled into the lungs and upper respiratory tract after a person breathes air containing beryllium mists, dusts, and fumes. Exposures not directly related to inhalation of workplace air, such as hand-to-mouth exposure, dermal contact with ultra fine particles, and resuspension following deposition of beryllium dust onto clothing may also occur.

Sources of Beryllium Exposure

Although beryllium is a naturally occurring substance, the major source of its emission into the environment is the combustion of fossil fuels (primarily coal), which releases beryllium containing particulates and fly ash into the atmosphere. Cigarette smoke is another source of beryllium exposure. Beryllium is relatively water insoluble and adsorbs tightly to soil, therefore, it is not often a drinking water contaminant. It has also been found in various foodstuffs, but bioaccumulation in the food chain is not significant.

Dietary & Supplement Considerations

- Moringa oleifera root extract and curcumin in combination have been shown to offer antioxidant protection against beryllium-induced oxidative stress and toxicity in rats (Agrawal et al., 2015).
- Bee propolis along with tiron (4,5-dihydroxy-1,3-benzene disulfonic acid) has also shown promise in attenuating systemic beryllium toxicity in rats (Nirala et al., 2008).

Chelation Options

In animal models, tiron has been found to be a significantly more efficacious beryllium chelating agent than calcium disodium EDTA (Sharma & Shukla, 2000). DMPS and penicillamine have also been used.

Bismuth

Bismuth (Bi) is a byproduct of iron ore manufacturing and is commonly used to replace lead in metal manufacturing due to its incredibly low toxicity profile. Bismuth is a commonly used supplemental product for the treatment of symptoms associated with gastric ulcers, excess abdominal gas, and diarrhea. Bismuth can adsorb gases produced by intestinal bacteria, such as hydrogen sulfide and methane, and is commonly used in SIBO protocols.

Clinical Manifestations of Toxicity

Small doses of bismuth may cause mild GI discomfort such as nausea or epigastric discomfort. Chronic ingestion of bismuth in higher doses or for longer periods of time than recommended on product labels may lead to symptoms of nausea, vomiting, encephalopathy (confusion, disorientation, possibly seizures), acute neurological symptoms such as ataxia, confusion, short term memory impairment, dysarthria, myoclonus, and paresthesias. Renal and hepatic failure may occur with high levels of toxicity. In chronic bismuth poisoning, individuals may also have a blue-black gum line and Lichen planus-like skin rashes.

How it Gets Absorbed

The most likely route of ingestion of elemental bismuth is oral. The most likely cause of elevated bismuth levels in the blood, outside of use of bismuth OTC products, is through inhalation of soldering fumes when working near lead-free pipes, which contain bismuth as a lead substitute.

Sources of Bismuth Exposure

The most common ingested sources of bismuth, besides what small amounts may be present in drinking water, are over-the-counter medicines that contain bismuth (chewable or liquid); bismuth oxychloride (BiOCl), an ingredient in some cosmetics, such as eye shadows, hair sprays and nail polishes; and bismuth subsalicylate, the active ingredient in such preparations as Pepto-Bismol.

Dietary & Supplement Considerations

Charcoal has been used as an adjunct treatment with DMPS for treatment of bismuth toxicity (Yang and Sun, 2011).

Chelation Options

Dimercaprol, DMSA, and DMPS have been used as chelating agents for bismuth toxicity.

Cadmium

Cadmium (Cd) is a naturally occurring element found in the earth's crust and has no human physiological role. It is a well-known human carcinogen.

Clinical Manifestations of Toxicity
Symptoms of cadmium toxicity include anemia, liver disease, vomiting, diarrhea, kidney disease, and impaired bone density.

How it Gets Absorbed
Cadmium can be absorbed via inhalation, ingestion, and dermal routes via contamination sources.

Sources of Cadmium Exposure
Common sources of exposure to cadmium include inhalation, ingestion, dermal contact through soil, water, and air by exposure to non-ferrous metal mining and refining, manufacture and application of phosphate fertilizers, fossil fuel combustion, and waste incineration and disposal. When taken up by plant life, cadmium enters the food supply. In general, leafy vegetables such as lettuce and spinach, potatoes and grains, peanuts, soybeans, and sunflower seeds contain high levels of cadmium. Aquatic organisms will bioaccumulate cadmium, possibly entering the food supply. People who consume fish from local waters should be cautious and abide by any advisories. Cadmium is also a component of tobacco smoke.

Dietary & Supplement Considerations

- Adequate zinc intake may reduce both cadmium absorption, as well as cadmium toxicity because intake of zinc also induces the synthesis of metallothionein (MT), a low molecular weight protein that has a high affinity for Cd and causes detoxification by binding Cd.
- Deficiency in essential metals such as zinc, calcium, or iron can lead to greater absorption and toxicity of cadmium. Optimizing these nutrients may help to prevent absorption of cadmium from contaminated food and water sources.
- Vitamins C & E have strong antioxidant properties that attenuate damage caused by cadmium intoxication.
- Selenium is another nutrient mineral that can decrease absorption of cadmium or increase its excretion through up-regulation of glutathione peroxidase (GPx) activity (Zhai et al., 2015).
- Curcumin has been shown to decrease liver toxicity secondary to cadmium toxicity (Mehrandish et al., 2019; Tunali-Akbay et al., 2007).

Chelation Options
DMSA, DMPS, and calcium disodium EDTA have been used as chelating agents for cadmium toxicity.

Cesium

Cesium (Cs) has no human physiological role. Cesium is a naturally occurring element found combined with other elements in rocks, soil, and dust in low amounts. Naturally occurring cesium is not radioactive and is referred to as stable cesium. There is only one stable form of cesium naturally present in the environment, 133Cs (read as cesium one-thirty-three). Nuclear explosions or the breakdown of uranium in fuel elements can produce two radioactive forms of cesium, 134Cs and 137Cs. It takes about 2 years for 134Cs to radioactively decay and about 30 years for 137Cs; this is called the half-life (ATSDR, 2021).

Clinical Manifestations of Toxicity

Skin, respiratory, central nervous, and hematological abnormalities may occur in cesium toxicity. Specifically, symptoms may include ventricular arrhythmias, cardiotoxicity, headache, nausea, and epileptic seizures.

How it Gets Absorbed

Cesium can be absorbed via inhalation, ingestion, and dermal routes via contaminated sources.

Sources of Cesium Exposure

The main exposure source of cesium is contaminated food and drinking water, particularly near nuclear sites of disposal of radioactive waste. The Fukushima nuclear power plant leak in Japan caused cesium to be present in waters in the north Pacific Ocean, between Japan and the United States.

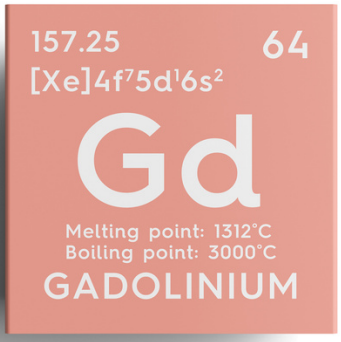
Dietary & Supplement Considerations

- Potassium iodide has been shown to offer protection systemically, and to the thyroid gland specifically, after exposure to radioactive cesium (Zhemkova et al., 1985).
- Zeolite has also been found to bind radioactive cesium (Mumpton, 1999).
- Activated charcoal has been shown to neutralize radioactive cesium in water (Hamasaki et al., 2014).
- Beet pulp was shown to decrease retention of radioactive cesium concentration in rats (Wolsieffer et al., 1969).

Chelation Options

EDTA and oral Prussian blue (also known as the brand name, Radiogardase) have been used as chelating agents for cesium toxicity.

Gadolinium



Gadolinium (Gd) serves no physiological role in the human body. Gadolinium is a rare earth metal typically used in microwave technology, color TV tubes, synthetic gemstones, compact discs, and computer memory. It is most often used in contrast dye for MRI testing. The gadolinium contrast agent is injected into the bloodstream where it becomes stored in the blood vessels and in abnormal tissue thus allowing the easy detection of problems found in the body.

Clinical Manifestations of Toxicity
The symptoms of gadolinium toxicity can present shortly after an MRI and can present as aching, burning, tingling, pins and needles, tight skin, lesions, hyperpigmentation, muscle twitching, worsening vision, tinnitus, swallowing and voice problems, hair loss, edema, and balance problems.

How it Gets Absorbed
Gadolinium can be injected directly into the system as part of a contrast dye for MRI testing. Excretion occurs via the urinary, skin, or fecal route.

Sources of Gadolinium Exposure
The most common route of exposure is via contrast dye used with an MRI.

Dietary & Supplement Considerations

- Zeolite, activated charcoal, fulvic acid, and humic acid have all been used as universal, natural chelating agents to help clear gadolinium.
- N-acetyl cysteine (NAC) has been shown to inhibit gadolinium associated cell death and endoplasmic reticulum stress when used prophylactically in vitro (Rogosnitzky & Branch, 2016).

Chelation Options
EDTA has been used as a chelating agent for gadolinium toxicity.

Lead

Lead (Pb) does not have a natural physiological function in the human body. Once absorbed, lead is exchanged between circulating blood, mineralized tissues (bone and teeth), and organs (liver, kidneys, brain, spleen, muscles, and the heart).

The half-life of lead in the blood is about 28 days, however, blood measures of lead are indicative of very recent exposure only. In adults, 94% of total body lead burden is found in the bones and teeth, and 78% of the total body lead burden is found in bones and teeth in children. Excretion of lead occurs through the kidneys; therefore, urine may be a better indicator of lead burden.

Clinical Manifestations of Toxicity

Conditions that may exacerbate bone-to-blood movement of lead include:

- Advanced age
- Broken bones
- Chronic disease
- Hyperthyroidism
- Immobilization
- Kidney disease
- Lactation
- Menopause
- Calcium deficiency
- Physiologic stress
- Pregnancy

The nervous system is the most impacted by lead exposure in children and some adults, but lead can impact every organ system. Lead has a particular affinity for sulfhydryl groups, which makes it very toxic to many enzyme systems, particularly those associated with heme biosynthesis, which leads to anemia and abnormalities with RBCs. Lead inhibits the body's ability to absorb calcium, iron, and zinc, which, over time, manifests in children and adults as learning disabilities, low IQ, aggression, violent behavior, depression, mood abnormalities, cognitive impairment, ADHD, hypertension, renal dysfunction, and reproductive dysfunction. Lead also commonly causes neuropathy in adults. Lead also impairs vitamin D synthesis. Lead lowers sperm counts in adult males and delays or inhibits conception in adult women. Lead readily crosses the placenta and causes birth defects in affected infants. Lower bone mineral density is also found in individuals affected by lead poisoning.

How it Gets Absorbed

Absorption of lead can occur through the gastrointestinal tract and through the respiratory tract, primarily. Absorption is inversely proportional to the exposure particle size. Smaller particles of lead are more easily absorbed. Lead ingested is absorbed at much higher rates (up to 80% in adults and up to 100% in children) when absorbed on an empty stomach.

Sources of Lead Exposure

Organic lead sources (e.g., gasoline, paint) are metabolized in the liver; inorganic lead sources (e.g., metal dust, pipes/plumbing, construction materials) are not metabolized in the liver. Exposure to lead can come most from the following sources: lead dust (from paint and lead pipes in older buildings), lead paint chips, inhaled from lead additives in fuel, residual lead in plumbing in older buildings.

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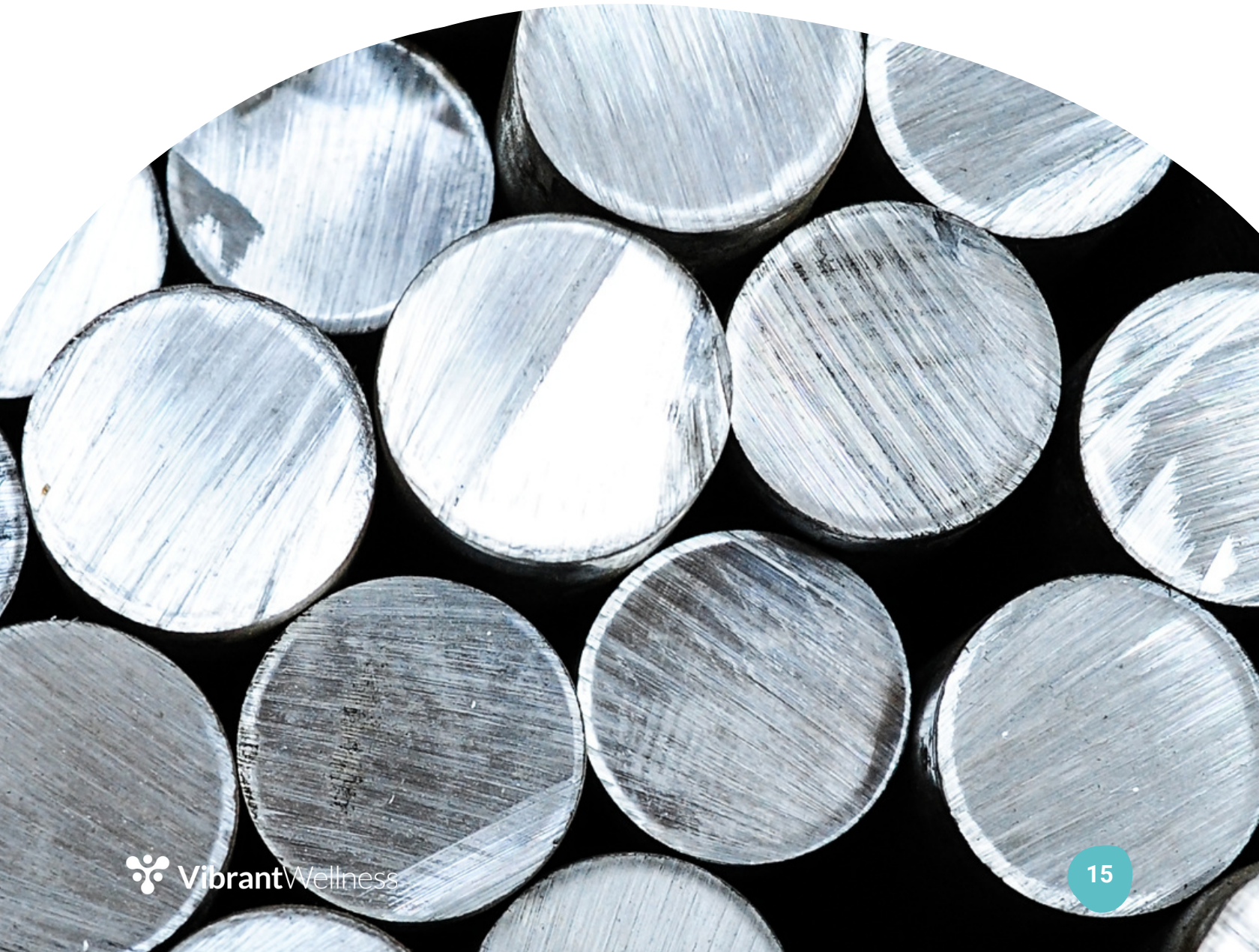
Dietary & Supplement Considerations

- Calcium, iron, and zinc are minerals depleted or poorly absorbed when lead toxicity is found. These minerals may need to be supplemented if found to be deficient.
- Garlic, onions, broccoli, cauliflower, cabbage, kale, Brussels sprouts, turnips, and kohlrabi can help clear lead from the liver via binding to sulfur compounds in these foods (Mehrandish et al., 2019).
- Vitamin C and silymarin in combination was shown to decrease lead in animal models (Mehrandish et al., 2019).
- Ginkgo biloba has been shown to decrease oxidative stress and lipid peroxidation associated with lead toxicity (Mehrandish et al., 2019; Tunali-Akbay et al., 2007).
- Curcumin has been shown to decrease liver toxicity secondary to lead toxicity (Mehrandish et al., 2019; Tunali-Akbay et al., 2007).
- Chlorella has been reported as a natural chelating agent for lead (Mehrandish et al., 2019).
- Cilantro has been shown to increase detoxification of lead (Trevor et al., 2010).

Chelation Options

Dimercaprol, calcium disodium EDTA, penicillamine, and DMSA have been used as chelating agents for lead toxicity.



Mercury

Mercury (Hg) serves no physiological role in the human body. It was used extensively by doctors in the 1800's and early 1900's to treat disease. Mercury toxicity has been implicated in several long-term chronic conditions such as autism, Alzheimers disease, chronic fatigue, multiple sclerosis, Parkinson's disease, and autoimmune thyroiditis.

Clinical Manifestations of Toxicity

All forms of mercury can affect the nervous system. Methylmercury and metallic mercury vapors can be more harmful than other forms because these forms are more likely to reach the brain. Effects of acute high levels of exposure to metallic mercury can result in nausea, vomiting, lung damage, diarrhea, increased blood pressure, skin rash, and eye irritation. Long-term effects can manifest as brain and/or kidney damage, damage to a developing fetus, changes in vision, tremors, hearing, memory problems, and irritability.

How it Gets Absorbed

Mercury can be breathed in through polluted air, absorbed through the oral cavity from amalgam fillings, injected into veins from mercury-containing vaccines, and absorbed through the digestive system from contaminated food, drugs, and supplements.

Sources of Mercury Exposure

Mercury is found in high levels in the atmosphere surrounding coal burning plants, incinerators, and other types of industry. It is a component of thimerosal, which is used only in multi-dose vials of the flu vaccine, but not single doses of the vaccine, certain other medications, and makes up at least 50% of an amalgam filling placed in a tooth.

Mercury is also found in significant levels in large fish such as tuna, swordfish, king mackerel, grouper, marlin, bluefish, shark, orange roughy, and tilefish. Pregnant women should avoid eating these types of fish more than once per week.

Dietary & Supplement Considerations

- The mineral zinc can chelate small amounts of mercury.
- Curcumin has been shown to decrease liver toxicity secondary to mercury toxicity (Mehrandish et al., 2019; Tunali-Akbay et al., 2007).
- Chlorella has been shown to increase the clearance of mercury (Rafati-Rahimzadeh et al., 2014).
- Cilantro has been shown to increase detoxification of mercury (Uchikawa et al., 2011).

Chelation Options

Dimercaprol and DMSA have been used as chelating agents for mercury toxicity.

Nickel

Nickel (Ni) is a hard, silver-colored substance used in many industries to make stainless steel and other metal alloys. Nickel is believed to have some physiological roles related to the functions of lipids, hormones, and membrane metabolism and, thus, it is considered an essential nutrient in trace amounts. Nickel is used to treat weak bones, to increase iron absorption, and prevent anemia.

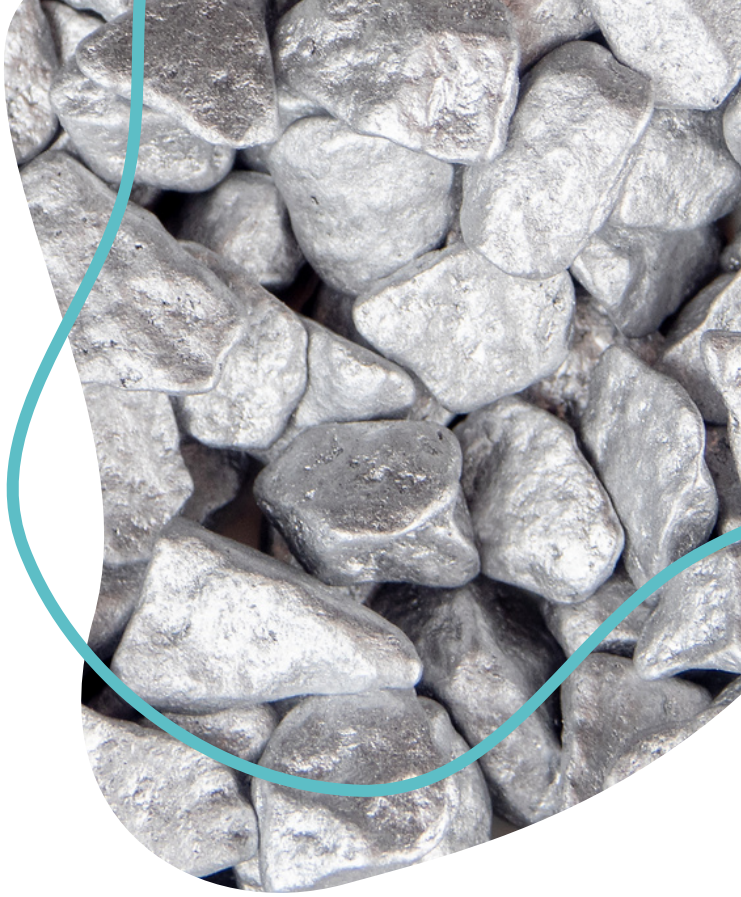
Clinical Manifestations of Toxicity
Exposure to nickel can cause skin irritation, harm the lungs, stomach and kidneys, and it can cause cancer. Possible symptoms of nickel toxicity include low blood pressure, malaise, muscle tremor, tetany and paralysis, nausea, vomiting, hemorrhages, heart attack, oral and/or intestinal cancer, and kidney dysfunction. Nickel tends to accumulate in the kidneys, therefore adequate kidney function is essential for elimination.

How it Gets Absorbed
Smokers have a higher nickel uptake through their lungs. Nickel can be absorbed dermally, inhaled, and ingested.

Sources of Nickel Exposure
Nickel occurs in the environment only at very low levels. Sources of nickel include cigarette smoke, nickel plating found on products such as batteries, wires, and electrical parts, hydrogenated vegetable oils, vegetable shortening, imitation whipped cream, chocolate, kelp, oysters, tea, and commercial peanut butter. Nickel is a common trace element in multivitamins.

Dietary & Supplement Considerations
- Consider vitamin C for antioxidant support for nickel toxicity-induced lipid peroxidation and oxidative stress (Das and Buchner, 2007).[EB1]

Chelation Options
Although data on chelation of nickel is limited and further research is needed, diethyldithiocarbamate (DDC), calcium disodium EDTA, and DMSA have been used as chelating agents for nickel toxicity. Also, interestingly, disulfiram, sold under the brand name Antabuse, has been used as an alternative treatment as it is metabolized into DDC in the body.



Palladium

Palladium (Pd) is a white, ductile metal resembling platinum and has no biological role.

Palladium is used in dentistry in the form of gold, silver, and copper alloys. Palladium is most used in catalytic converters in the automotive industry. Palladium is extensively used in jewelry, most found in white gold and platinum pieces.

Clinical Manifestations of Toxicity
Palladium may cause skin, eye, or respiratory tract irritation. Liquid palladium may cause burns to the skin and eyes. Palladium chloride is toxic and harmful if swallowed, inhaled, or absorbed in the skin; it causes bone marrow damage, liver damage, and kidney damage in laboratory animals.

How it Gets Absorbed
Palladium is regarded as having low toxicity, being poorly absorbed by the body when ingested. It is most likely to be inhaled or absorbed through dermal contact.

Sources of Palladium Exposure
Despite its widespread presence, palladium compounds are encountered relatively rarely by most people, yet they may be found in dental applications, jewelry, food and emissions from automobile catalytic converters.

Dietary & Supplement Considerations
Glutathione and NAC act as antioxidants against palladium toxicity and therefore have shown promise in the detoxification of palladium (Mukhtiar et al., 2018).

Chelation Options
DMPS, penicillamine, and calcium disodium EDTA may be effective chelating agents for palladium toxicity.

Platinum

Platinum (Pt) serves no physiological role in the human body. Platinum has many uses. Its wear and tarnish-resistance characteristics are well-suited for making fine jewelry. Platinum and its alloys are used in surgical tools, laboratory utensils, electrical resistance wires, and electrical contact points. The largest use (50%) of platinum is for jewelry, another 20% is used in industry: platinum is used in the chemical, electrical, glass, and aircraft industries, each accounting for about 10 tons of the metal per year. The glass industry uses platinum for optical fibers and liquid crystal display glass, especially for laptops.

Clinical Manifestations of Toxicity

Platinum as a metal is not very dangerous but platinum salts can cause several deleterious health effects, such as: altered DNA, cancer, hearing damage, allergic reactions on the skin and mucosa, and damage to organs such as intestines, kidneys, and bone marrow. Neurotoxicity can occur with platinum-based anti-cancer drugs.

How it Gets Absorbed

Platinum is emitted into the air through the exhausts of cars that use leaded gasoline. Consequently, platinum levels in air may be higher in certain locations, for instance in garages, in tunnels, and on terrains of trucking companies.

Sources of Platinum Exposure

Platinum exposure is most likely to occur by breathing in contaminated air (exhaust from leaded gasoline), absorption through the skin by working with platinum containing jewelry, and ingestion via platinum containing medicines used for chemotherapy. Excretion occurs via the urinary, skin, or fecal route.

Dietary & Supplement Considerations

- Vitamin E is one of the most well-studied natural antioxidants used, both preventatively and therapeutically, for the toxic effects associated with platinum medications; see below under Chelation Options. (Stankovic et al., 2020).
- Acetyl-L-carnitine has been used to treat the neurotoxic effect of platinum-based chemotherapy medications, namely paclitaxel or cisplatin, and is thought to possess antioxidant and neuroprotective properties while also offering mitochondrial and cell membrane support (De Grandis, 2007).
- NAC and glutathione; see below under Chelation Options.

Chelation Options

Although chelation is rarely discussed for platinum toxicity, there are supportive reports of addressing neurotoxicity associated with platinum-based chemotherapy using neuroprotective agents such as vitamin E, glutathione, amifostine, xaliproden, and venlafaxine (Avan et al., 2015).

Tellurium

Tellurium (Te) has no human physiological role. Tellurium is a metalloid that is found in the earth's crust, although its presence is rare. Tellurium is chemically related to selenium and sulfur. Tellurium is extracted as a byproduct of copper and lead production and is used industrially in iron, stainless steel, copper, and lead alloys and the semi-conductor and electronics industry.

Clinical Manifestations of Toxicity
Skin, respiratory, central nervous system, and hematological abnormalities may occur in tellurium toxicity. Symptoms may include sweating, dry mouth, garlic-like breath, metallic taste, drowsiness, anorexia, nausea, and dermatitis in humans, and central nervous system and red blood cell changes in animals with tellurium toxicity.

How it Gets Absorbed
Tellurium can be absorbed via inhalation, ingestion, and dermal routes via contaminated sources.

Sources of Tellurium Exposure
The main exposure source of tellurium is contaminated foods, such as vegetables, legumes, potatoes, cereals, meat, dairy, and water. It may also be found in coloring agents used for glass and ceramics.

Dietary and Supplement Considerations
Selenium has shown promising results when studied in animal models as a treatment for tellurium-induced neurotoxicity and oxidative stress (Khuwaja et al., 2020).

Chelation Options
Traditional chelation agents may increase the toxicity of tellurium and should be used with caution in the case of tellurium toxicity.

Thallium

Thallium (Tl) is an odorless, tasteless organic compound found naturally occurring in the earth's crust, but does not have a physiological function in the human body. Approximately half of the thallium absorbed from exposure leaves the human body within 3 days, but elevated thallium levels can be found in urine up to 2 months after exposure.

Clinical Manifestations of Toxicity

Organ systems affected by thallium poisoning include cardiovascular, hepatic, neurological, renal, and respiratory if large amounts are consumed over longer periods of time. If larger doses are consumed or absorbed acutely, temporary hair loss, vomiting, and diarrhea can also occur, and death may result. After inhalation exposure to thallium, neurological symptoms commonly include paresthesia, numbness of toes and fingers, "burning feet" phenomenon, and muscle cramps. Elevated acute oral consumption of thallium in supraphysiological doses has been shown to cause severe neuron axonal damage. Respiratory damage can also occur with acute elevated thallium inhalation. Acute high dose ingestion of thallium can cause gastroenteritis, diarrhea or constipation, vomiting, and abdominal pain. Elevated prolonged thallium exposure may contribute to myopathies. Thallium can also lead to damage to the liver and kidneys, however, doses required for this vary. Thallium can cross the placenta; however, human studies are sparse on toxicity in fetal development.

How it Gets Absorbed

Thallium exposure can come from food, water, and air; however, exposure from water and air are extremely small amounts not likely to cause harm to humans. Produce grown in contaminated soil and contaminated groundwater are the most common routes of exposure in humans.

Sources of Thallium Exposure

Thallium is most used in the semiconductor industry and, in more rare cases, specialty glass manufacturing. Homegrown fruits and vegetables grown in soil that is thallium contaminated are the most common source of exposure. Thus, soil contamination occurs in areas near coal-burning and smelting factories which release thallium into the air and which then falls into the surrounding soil and groundwater sources. Thallium is present in cigarette smoke, and smokers have approximately twice as much thallium in their bodies as those who do not smoke. Individuals who work in coal manufacturing and smelting facilities can inhale particulate thallium.

Dietary & Supplement Considerations

- Zinc sulfate is thought to be an effective treatment for thallium toxicity with dermatologic signs and symptoms like those seen in zinc deficiency (Kumar, 2022).
- Activated charcoal has been shown to bind thallium in vitro and may be more effective than Prussian blue in removing thallium (Kumar, 2022).

Chelation Options

Dimercaprol has been used with varying success as a chelating agent for thallium. Prussian blue has also been used to successfully treat thallium toxicity.

Thorium

Thorium (Th) is a naturally occurring radioactive element present in soil, rocks, and found in trace amounts in most animals. It is a known human carcinogen. It serves no physiological function in the human body. Thorium is used in the ceramics industry, gas lantern mantles, and is incorporated into metals used in the aerospace industry and in nuclear reactions. It can also be used as a fuel for generating nuclear energy.

Clinical Manifestations of Toxicity
Symptoms and side effects of thorium toxicity are most likely to manifest in the hematological, hepatic, and respiratory systems, as well as possible cancers. The most common symptoms of thorium toxicity are respiratory distress and pneumonia, pulmonary hypertension, and fibrosis.

Individuals who breathe thorium dust may develop lung disease. Thorium in the blood may lead to liver and hematological damage. Individuals with high exposure to thorium dust, cigarette smoke, and radon gas are found to have higher incidence of cancers of the lung, pancreas, and blood. Thorium may also be deposited in greater amounts in bone tissue.

How it Gets Absorbed
Small amounts of thorium are present in air, water, and soil, and it is impossible to completely avoid this element. Thorium can enter the body through the respiratory, gastrointestinal, and dermatological systems.

Sources of Thorium Exposure
Those most likely to accumulate higher levels of thorium include individuals who live or work near facilities where uranium, phosphate, or tin ore are processed due to the contamination of thorium in the air around those facilities; individuals who work in the uranium, thorium, tin, and phosphate mining, and gas mantle production industries; individuals living in homes built on soil containing high levels of thorium; and individuals who live or work near radioactive waste disposal sites.

Dietary & Supplement Considerations
Activated charcoal has been used to naturally bind thorium but its efficacy is unknown.

Chelation Options
Chelation with EDTA may be a successful intervention for thorium toxicity. Diethylenetriaminepentaacetic acid (DTPA) may be an effective chelation agent for the removal of thorium but may be more effective at chelating ionic thorium versus colloidal thorium (used in some radiographic contrasts before the 1950s).

Tin

Tin (Sn) has no human physiological role. Tin is used to line cans for food, beverages, and aerosols. Tin can combine with other chemicals to form compounds. Combinations with chemicals like chlorine, sulfur, or oxygen are called inorganic tin compounds (i.e., stannous chloride, stannous sulfide, stannic oxide). These are used in toothpaste, perfumes, soaps, food additives, and dyes. Tin also can combine with carbon to form organotin compounds (i.e., dibutyltin, tributyltin, triphenyltin). These compounds are used to make plastics, food packages, plastic pipes, pesticides, paints, and pest repellents. Tin metal and inorganic and organic tin compounds can be found in the air, water, and soil near places where they are naturally present in the rocks, or where they are mined, manufactured, or used. Organic tin compounds stick to soil sediment and particles in water. Organic tin compounds in water can build up in fish, other organisms, and plants.

Clinical Manifestations of Toxicity
Hematological and immunological abnormalities have been observed in tin toxicity in humans and animals. Tin toxicity may reduce zinc and copper stores.

How it Gets Absorbed
Tin is most absorbed via oral ingestion of contaminated sources.

Sources of Tin Exposure
The main exposure source of tin is eating foods contaminated with tin, particularly seafood from coastal waters contaminated with organotins and exposure to organotin-containing household products such as plastics and silicon-coated baking parchment paper.

Dietary & Supplement Considerations
- Replacing zinc if deficient is recommended in the presence of tin toxicity due to tin's apparent inhibition of zinc absorption (Valberg et al., 1984).
- Supplementation of copper and iron may help prevent and mitigate anemia secondary to tin toxicity as shown in animal models (de Groot, 1973).

Chelation Options
Although traditional chelating agents are rarely discussed for tin toxicity, activated charcoal slurry is recommended after acute oral exposure.

Tungsten

Tungsten (W) serves no physiological role in the human body. Tungsten is a naturally occurring element that is typically found in solid form in rocks and minerals. Tungsten can be used as a pure metal or mixed with other metals to form an alloy. The tungsten alloys are used in light bulb filaments, as part of X-ray tubes, as a catalyst to speed up chemical reactions, as a component of steel in high-speed tools, in turbine blades, in darts, and in golf club components.

Clinical Manifestations of Toxicity
Tungsten compounds have caused breathing problems and changed behavior in some animals given very large amounts of tungsten compounds. Children could be affected in the same ways as adults.

How it Gets Absorbed
Breathing contaminated air, drinking contaminated water, skin contact with compounds that contain tungsten, or eating food that contains tungsten are the most common ways tungsten toxicity occurs. Excretion occurs primarily via urine.

Sources of Tungsten Exposure
Contaminated air, drinking water, and food are common sources of low-level tungsten exposure. Tungsten carbide is the most common tungsten compound used and can be found in cutting, mining, and drilling tools, and wear-resistant applications.

Dietary & Supplement Considerations
Because exposure to tungsten in the general population is thought to be very low, there is a lack of evidence regarding dietary and supplement options for toxicity at the time of this writing. Consider air filtration in the home and workplace if living in an urban environment with more tungsten in the ambient air compared to rural environments.

Chelation Options
DMSA has been used as a chelating agent for tungsten toxicity.

Uranium

Uranium (U) is a naturally occurring radioactive element found on Earth. It is considered experimentally carcinogenic in animals and has some limited evidence of carcinogenicity in humans. Uranium does not have a physiological purpose in the human body. Radioactive decay of uranium takes a very long time (100,000s to billions of years, depending on the isotope), and, therefore, is why this element is still found in numerous rock deposits on Earth. The isotope 235U is useful as a fuel in power plants and weapons. In fuel manufacturing, natural uranium is separated into a fuel portion and the leftover portion. The fuel portion, with greater 235U, is called enriched uranium. The leftover portion with less 235U is called depleted uranium, or DU. Depleted uranium is the least radioactive isotope and enriched uranium the most radioactive.

Clinical Manifestations of Toxicity

Uranium that is absorbed is deposited throughout the body. Approximately 66% of absorbed uranium is deposited into the bones. The half-life of uranium in the bones is 70-200 days. The rest of the uranium not deposited into the bones leaves the body in about 1-2 weeks after ingestion. The kidneys are the most impacted organ system after depleted uranium exposure, both chronic and acute. Depleted uranium can also impact DNA and cause chromosomal abnormalities. The main manifestation of uranium exposure is cellular depletion of antioxidants and formation of reactive oxygen species (ROS), as well as increased oxidative stress. Depleted uranium is not considered radiotoxic, unlike natural uranium, which is a radioactive element. The adverse effects of natural and depleted uranium exposure are typically due to the element itself and not due to the radiation from uranium.

How it Gets Absorbed

Uranium can be ingested through the lungs, gastrointestinal tract, and absorbed through the skin. Most of the uranium that is inhaled through the lungs or ingested through the GI tract is not absorbed and leaves the body through the feces. Water-soluble sources of uranium being ingested may lead to kidney problems.

Sources of Uranium Exposure

Uranium is naturally occurring in rocks, soil, air, and water. The most likely sources of contamination or exposure to uranium in humans are soil and water. Soil-based crops such as potatoes, parsnips, turnips, and sweet potatoes contribute the highest amounts of uranium to the diet due to uranium's ability to 'stick' to these vegetables as they grow in the soil. Drinking water may contain elevated levels of uranium in areas where greater than normal deposits of uranium are present in the soil and may be particularly high in well water. Other sources of exposure to uranium include living near uranium mining, processing, and manufacturing facilities and areas where depleted uranium weapons are used.

Dietary & Supplement Considerations

- To reduce uranium exposure in areas with higher-than-normal uranium soil levels, washing vegetables thoroughly or removing outer skins of soil-based root vegetables before consumption is recommended.
- Testing drinking water sources for uranium levels may also be appropriate if elevated levels of uranium are found in blood or urine.
- Citrate and citric acid-rich foods such as citrus fruits (lemons, limes, oranges, and grapefruit) may offer prophylactic and therapeutic benefit against uranium toxicity as suggested by successful treatment of uranium toxicity and renal lesions from uranium toxicity using oral and IV sodium citrate in animal models (Lawrence et al., 2014).
- Avoid added sugar to limit fructose consumption as it has been shown to exacerbate uranium toxicity. This is especially important if increasing dietary sources of citrate as many citrate-rich products such as juice may have added sugar (Ortega et al., 1989).

Chelation Options

EDTA and deferoxamine have been used as chelating agents for uranium toxicity.

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