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### 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
- glucoronidation
- 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 in order to neutralize the ROS and free radicals produced during Phase I transformation:

- bioflavonoids
- vitamin A
- vitamin C
- vitamin E
- CoQ10
- copper
- maganese
- pycnogenol
- selenium
- silymarin
- thiols (found in sulfurous veggies like Brussels sprouts, broccoli, cabbage, cauliflower, onions, garlic, leeks)

## PHASE I DETOXIFICATION SUPPORT

|  | NUTRIENTS AND COFACTORS<br>Riboflavin (vitamin B2)<br>Niacin (vitamin B3)<br>Pyridoxine (vitamin B6)<br>Folic Acid<br>Cobalamin (Vitamin B12)<br>Bioflavonoids<br>Glutathione<br>Branched chain amino acids (leucine,<br>isoleucine, and valine) |
|--|--|
| Nutrients To Support Both Phases:  |  |
| <ul> <li>silymarin (milk thistle)</li> <li>selenium</li> <li>copper</li> <li>zinc</li> <li>manganese</li> <li>vitamin C</li> <li>vitamin E/tocopherols</li> <li>beta-carotene</li> </ul> | <ul> <li>vitamin A</li> <li>bioflavonoids</li> <li>coenzyme Q10</li> <li>thiols/sulfur<br/>compounds found in<br/>garlic, onions, broccoli,<br/>cabbage, Brussels<br/>sprouts</li> </ul>   |
| NUTRIENTS AND COFACTORS<br>Glutamine<br>Glycine<br>Taurine<br>Cysteine<br>Methionine<br>N-acetylcysteine   |  |

## PHASE II DETOXIFICATION SUPPORT

### ALUMINUM

Aluminum (AI) 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, Al<sup>3+</sup>, 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 the provocation of Alzheimer's disease, breast cancer, osteoporosis, and autism spectrum disorder. Early symptoms of aluminum toxicity include flatulence, headaches, colic, dryness of the skin and mucous membranes, tendencies for colds, burning pain in the head relieved by food, heartburn, and an aversion to meat. Later symptoms include paralytic muscular conditions, loss of memory, and mental confusion.

#### 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. Aluminum can be absorbed transdermally, such as through the use of 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.

#### **Supplement Options**

If aluminum toxicity is suspected, consider increasing dietary intake of nutrients that support Phase I and Phase II hepatic detoxification.

#### **Chelation Options**

Deferoxamine, sold under the brand name Desferal, is an aluminum-chelating agent. Vitamin C is a non-toxic chelating agent for aluminum. Aluminum is principally eliminated through urine, therefore adequate kidney function is essential.

## 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, and stomach ulcers have been observed in humans, and lung cancer, liver disease, and infertility have been observed in animals with antimony toxicity.

#### 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. Foods stored in enamel vessels or cans may have higher levels of antimony. Cilantro is a plant that is known to accumulate higher levels of antimony than usual.

#### **Supplement Options**

Consider increasing dietary intake of nutrients that support Phase I and Phase II hepatic detoxification.

#### **Chelation Options**

Dimercaprol is an effective chelating agent for antimony. Absorption, distribution, and excretion of antimony are variable based on its oxidation state.

## 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 also interferes with the uptake of folic acid. Acute (short-term) 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 also to bladder, liver, and lung cancer. The EPA has classified inorganic arsenic as a human carcinogen.

#### How it Gets Absorbed

Arsenic can be inhaled, ingested, and transdermally absorbed. 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.

## ARSENIC (CONT.)

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 flours in gluten-free foods, practitioners should caution at-risk individuals on the use of gluten-free foods with rice flour-based ingredients.

#### **Supplement Options**

If arsenic toxicity is suspected, consider increasing dietary intake of nutrients that support Phase I and Phase II hepatic detoxification.

#### **Chelation Options**

Dimercaprol is an effective chelating agent for arsenic. Vitamin C and Alpha-Lipoic-Acid (ALA) are protective supplements to consider, as an important detrimental effect of arsenic is inactivation of lipoic acid, a vitamin cofactor needed for metabolism of pyruvate and alpha-ketoglutarate. Avoid eating fish and shellfish if you have high arsenic levels.

### 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, 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.

#### **Supplement Options**

If barium toxicity is detected, consider increasing dietary intake of nutrients that support Phase I and Phase II hepatic detoxification.

#### **Chelation Options**

Use agents such as glutathione, cilantro, alpha lipoic acid, N-Acetyl Cysteine, DMSA, modified citrus pectin, and sauna therapy to reduce excess barium detected on urine tests. Excretion occurs via the urinary or fecal route.

### 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. Beryllium is relatively water insoluble and adsorbs tightly to soil, therefore, it is not often a drinking water contaminant. It has been found in various foodstuffs, but bioaccumulation in the food chain is not significant.

#### **Supplement Options**

If beryllium toxicity is suspected, consider increasing dietary intake of nutrients that support Phase I and Phase II hepatic detoxification.

#### **Chelation Options**

In animal models, Tiron has been found to be a significantly more efficacious beryllium chelator than CaNa<sub>2</sub>EDTA.

### 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, shortterm 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 (BiOCI), 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.

#### **Supplement Options**

There do not appear to be nutrients displaced by bismuth, however, in cases of toxicity, monitoring fluids, renal function, and hepatic function are recommended.

#### **Chelation Options**

DMSA may be an appropriate chelation agent 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 known human carcinogen.

#### **Clinical Manifestations of Toxicity**

Symptoms of toxicity of cadmium 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.

#### **Supplement Options**

Consider cysteine and antioxidants to support endogenous metallothionein production, and glutathione. 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.

#### **Chelation Options**

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.

Selenium is another nutrient mineral that can decrease absorption of cadmium, or increase its excretion through up-regulation of glutathione peroxidase (GPx) activity. Iron competes with cadmium for access to intestinal metal uptake transporters, therefore, optimal iron intake can decrease absorption of cadmium from the GI tract.

### 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.

#### **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 water and plant life, 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.

#### **Supplement Options**

If cesium toxicity is detected, consider increasing dietary intake of nutrients that support Phase I and Phase II hepatic detoxification.

#### **Chelation Options**

Cesium is naturally excreted by the human body within weeks of exposure, usually. Consider EDTA as a chelation agent 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.

#### Sources of Gadolinium Exposure

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

#### **Supplement Options**

If gadolinium toxicity is detected, consider increasing dietary intake of nutrients that support Phase I and Phase II hepatic detoxification.

#### **Chelation Options**

Use agents such as glutathione, cilantro, alpha lipoic acid, N-Acetyl Cysteine, DMSA, modified citrus pectin, and sauna therapy to reduce excess gadolinium. Excretion occurs via the urinary, skin, or fecal route.

### 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, and, 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
- Chromic disease
- Hyperthyroidism
- Immobilization (bedridden, etc.)
- Kidney disease

- Lactation
- Menopause
- Physiologic stress
- Pregnancy
- Calcium deficiency

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.

### LEAD (CONT).

#### 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 commonly 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.

#### **Supplement Options**

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. In addition to supplementation, assessment of home/work factors should be performed to determine source/ route of exposure and to prevent further intoxication.

#### **Chelation Options**

Glutathione is a potent naturally occurring chelator of heavy metals. Compounds in algae, chlorella, and modified citrus pectin may reduce GI absorption of heavy metals, as well as blood lead levels. Poly( $\gamma$ -glutamic acid), produced by Bacillus species during fermentation in the colon, is found to be able to bind metal cations.

Cilantro has some limited chelation actions, mainly to prevent lead absorption into bone tissue, but conflicting findings on whether it increases renal excretion of lead. N-acetylcysteine (NAC) and alpha lipoic acid (ALA) are both reported to have metal chelating properties, particularly when levels of vitamins C and E are optimized.

### 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.

#### **Supplement Options**

If mercury toxicity is detected, consider increasing dietary intake of nutrients that support Phase I and Phase II hepatic detoxification.

#### **Chelation Options**

The mineral zinc can chelate small amounts of mercury. Other natural chelating agents are spirulina, alpha lipoic acid, N-acetyl cysteine (NAC), cilantro, glutathione, modified citrus pectin, and sauna therapy. Prescription chelators can also be used such as dimercaprol, DMPS, and DMSA. Excretion occurs via urine or stool.

### 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.

#### How it Gets Absorbed

Smokers have a higher nickel uptake through their lungs. Nickel can be absorbed transdermally, inhaled, and ingested.

#### Sources of Nickel Exposure

Nickel occurs in the environment only at very low levels. Sources of nickel include cigarette smoking, 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.

#### **Supplement Options**

If nickel toxicity is suspected, consider increasing dietary intake of nutrients that support Phase I and Phase II hepatic detoxification.

#### **Chelation Options**

Nickel has a tendency to accumulate in the kidneys, therefore adequate kidney function is essential for elimination. Disulfiram, sold under the brand name Antabuse, might decrease how much nickel the body absorbs, making nickel supplements less effective.

### 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 commonly used in catalytic converters in the automotive industry. Palladium is extensively used in jewelry, most commonly 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 through 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.

Palladium is sold in liquid form for medicinal purposes.

#### **Supplement Options**

If palladium toxicity is suspected, consider increasing dietary intake of nutrients that support Phase I and Phase II hepatic detoxification.

#### **Chelation Options**

CaNa<sub>2</sub>EDTA may be an effective chelating agent for palladium toxicity.

### PLATINUM

Platinum (Pt) serves no physiological role in the human body. Platinum has many uses. Its wearand 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.

#### **Supplement Options**

If platinum toxicity is detected, consider increasing dietary intake of nutrients that support Phase I and Phase II hepatic detoxification.

#### **Chelation Options**

Use agents such as glutathione, cilantro, alpha lipoic acid, N-Acetyl Cysteine, DMSA, modified citrus pectin, and sauna therapy to reduce excess tungsten. Excretion occurs via the urinary, skin, or fecal route.

### 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 water and plant life.

#### **Supplement Options**

If tellurium toxicity is detected, consider optimizing dietary intake of nutrients that support Phase I and Phase II hepatic detoxification.

#### **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 (TI) is an odorless, tasteless organic compound found naturally-occurring in the earth's crust, but which 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 commonly used in the semiconductor industry, and in more rare cases, in specialty glass manufacturing. Homegrown fruits and vegetables grown in soil that is contaminated by thallium are the most common source of exposure. This soil contamination occurs in areas near coal-burning and smelting factories, which release thallium into the air, and which 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.

### THALLIUM (CONT).

#### **Supplement Options**

Common provocation agents (EDTA and DMSA) do not work to increase renal excretion of thallium, and, therefore, provocation prior to a test may not affect excretion of thallium.

#### **Chelation Options**

Supplements and compounds found to increase excretion of thallium from the human body include, but are not limited to: activated charcoal, chlorella, Prussian blue, and certain forms of zeolite.

### 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 deposit 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.

#### **Supplement Options**

Thorium appears to respond well to provocation before testing urine samples.

#### **Chelation Options**

Intravenous chelation with CaNa2EDTA may be a successful intervention for thorium toxicity. Diethylenetriaminepentacetic acid (DTPA) may be an effective chelation agent for the removal of thorium, but may be more effective at chelating ionic thorium vs 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 organic tin compounds (i.e., dibutyltin, tributyltin, triphenyltin). These compounds are used to make plastics, food packages, plastic pipes, pesticides, paints, and pest repellents.

Tin meta 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 commonly absorbed via oral ingestion of contaminated sources.

#### Sources of Tin Exposure

The main exposure source of tin is eating foods contaminated with tin.

#### **Supplement Options**

Replacing zinc and copper if deficient is recommended in the presence of tin toxicity.

#### **Chelation Options**

Activated charcoal slurry is recommended after acute oral exposure (240 mL water/30g charcoal).

## 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.

#### Sources of Tungsten Exposure

Exposure to low levels of tungsten by breathing air, drinking water, or eating contaminated food are common sources of tungsten exposure.

#### **Supplement Options**

If tungsten toxicity is detected, consider increasing dietary intake of nutrients that support Phase I and Phase II hepatic detoxification.

#### **Chelation Options**

Use agents such as glutathione, cilantro, alpha lipoic acid, N-Acetyl Cysteine, DMSA, modified citrus pectin, and sauna therapy to reduce excess tungsten. Excretion occurs via the urinary, skin, or fecal route.

### 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. The majority of 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.

### URANIUM (CONT).

#### 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 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. Other sources of exposure to uranium include living near uranium mining, processing, and manufacturing facilities and living near areas where depleted uranium weapons are used.

In order 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.

#### **Supplement Options**

If uranium toxicity is detected, consider increasing dietary intake of nutrients that support Phase I and Phase II hepatic detoxification.

#### **Chelation Options**

Chelating agents that have been shown to be effective at treating uranium toxicity include catechol-3,6-bis (methyliminodiacetic acid) (CBMIDA), EDTA, DTPA (diethylenetriaminepentaacetic acid), and ethane-1-hydroxy-1,1-bisphosphonate (EHBP).



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