

## Heavy Metal Toxicity

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### INTRODUCTION

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There are 35 metals that concern us because of occupational or residential exposure; 23 of these are the heavy elements or "heavy metals": antimony, arsenic, bismuth, cadmium, cerium, chromium, cobalt, copper, gallium, gold, iron, lead, manganese, mercury, nickel, platinum, silver, tellurium, thallium, tin, uranium, vanadium, and zinc (Glanze 1996). Interestingly, small amounts of these elements are common in our environment and diet and are actually necessary for good health, but large amounts of any of them may cause acute or chronic toxicity (poisoning). Heavy metal toxicity can result in damaged or reduced mental and central nervous function, lower energy levels, and damage to blood composition, lungs, kidneys, liver, and other vital organs. Long-term exposure may result in slowly progressing physical, muscular, and neurological degenerative processes that mimic Alzheimer's disease, Parkinson's disease, muscular dystrophy, and multiple sclerosis. Allergies are not uncommon and repeated long-term contact with some metals or their compounds may even cause cancer (International Occupational Safety and Health Information Centre 1999).

For some heavy metals, toxic levels can be just above the background concentrations naturally found in nature. Therefore, it is important for us to inform ourselves about the heavy metals and to take protective measures against excessive exposure. In most parts of the United States, heavy metal toxicity is an uncommon medical condition; however, it is a clinically significant condition when it does occur. If unrecognized or inappropriately treated, toxicity can result in significant illness and reduced quality of life (Ferner 2001). For persons who suspect that they or someone in their household might have heavy metal toxicity, testing is essential. Appropriate conventional and natural medical procedures may need to be pursued (Dupler 2001).

The association of symptoms indicative of acute toxicity is not difficult to recognize because the symptoms are usually severe, rapid in onset, and associated with a known exposure or ingestion (Ferner 2001): cramping, nausea, and vomiting; pain; sweating; headaches; difficulty breathing; impaired cognitive, motor, and language skills; mania; and convulsions. The symptoms of toxicity resulting from chronic exposure (impaired cognitive, motor, and language skills; learning difficulties; nervousness and emotional instability; and insomnia, nausea, lethargy, and feeling ill) are also easily recognized; however, they are much more difficult to associate with their cause. Symptoms of chronic exposure are very similar to symptoms of other health conditions and often develop slowly over months or even years. Sometimes the symptoms of chronic exposure actually abate from time to time, leading the person to postpone seeking treatment, thinking the symptoms are related to something else.

### Definition of a Heavy Metal

"Heavy metals" are chemical elements with a specific gravity that is at least 5 times the specific gravity of water. The specific gravity of water is 1 at 4°C (39°F). Simply stated, specific gravity is a measure of density of a given amount of a solid substance when it is compared to an equal amount of water. Some well-known toxic metallic elements with a specific gravity that is 5 or more times that of water are arsenic, 5.7; cadmium, 8.65; iron, 7.9; lead, 11.34; and mercury, 13.546 (Lide 1992).

## Beneficial Heavy Metals

In small quantities, certain heavy metals are nutritionally essential for a healthy life. Some of these are referred to as the trace elements (e.g., iron, copper, manganese, and zinc). These elements, or some form of them, are commonly found naturally in foodstuffs, in fruits and vegetables, and in commercially available multivitamin products (International Occupational Safety and Health Information Centre 1999). Diagnostic medical applications include direct injection of gallium during radiological procedures, dosing with chromium in parenteral nutrition mixtures, and the use of lead as a radiation shield around x-ray equipment (Roberts 1999). Heavy metals are also common in industrial applications such as in the manufacture of pesticides, batteries, alloys, electroplated metal parts, textile dyes, steel, and so forth. (International Occupational Safety and Health Information Centre 1999). Many of these products are in our homes and actually add to our quality of life when properly used.

## Toxic Heavy Metals

Heavy metals become toxic when they are not metabolized by the body and accumulate in the soft tissues. Heavy metals may enter the human body through food, water, air, or absorption through the skin when they come in contact with humans in agriculture and in manufacturing, pharmaceutical, industrial, or residential settings. Industrial exposure accounts for a common route of exposure for adults. Ingestion is the most common route of exposure in children (Roberts 1999). Children may develop toxic levels from the normal hand-to-mouth activity of small children who come in contact with contaminated soil or by actually eating objects that are not food (dirt or paint chips) (Dupler 2001). Less common routes of exposure are during a radiological procedure, from inappropriate dosing or monitoring during intravenous (parenteral) nutrition, from a broken thermometer (Smith et al. 1997), or from a suicide or homicide attempt (Lupton et al. 1985).

As a rule, acute poisoning is more likely to result from inhalation or skin contact of dust, fumes or vapors, or materials in the workplace. However, lesser levels of contamination may occur in residential settings, particularly in older homes with lead paint or old plumbing (International Occupational Safety and Health Information Centre 1999). The Agency for Toxic Substances and Disease Registry (ATSDR) in Atlanta, Georgia, (a part of the U.S. Department of Health and Human Services) was established by congressional mandate to perform specific functions concerning adverse human health effects and diminished quality of life associated with exposure to hazardous substances. The ATSDR is responsible for assessment of waste sites and providing health information concerning hazardous substances, response to emergency release situations, and education and training concerning hazardous substances (ATSDR Mission Statement, November 7, 2001). In cooperation with the U.S. Environmental Protection Agency, the ATSDR has compiled a Priority List for 2001 called the "Top 20 Hazardous Substances." The heavy metals arsenic (1), lead (2), mercury (3), and cadmium (7) appear on this list.

**Note:** The ATSDR provides comprehensive protocols called *Medical Management Guidelines for Acute Chemical Exposures in Volume III of the Managing Hazardous Material Incidents Series*. These protocols have a Chemical Abstracts Service (CAS) number and give a description of toxic substances; routes of exposure; health effects; prehospital, triage, and emergency medical department care; antidotes and treatment; disposition and follow-up; and reporting instructions. The series may be viewed or downloaded from the ATSDR web site at no cost.

## COMMONLY ENCOUNTERED TOXIC HEAVY METALS

- Arsenic
- Lead
- Mercury
- Cadmium
- Iron
- Aluminum

As noted earlier, there are 35 metals of concern, with 23 of them called the heavy metals. Toxicity can result from any of these metals. This protocol will address the metals that are most likely encountered in our daily environment. Briefly covered will be four metals that are included in the ATSDR's "Top 20 Hazardous Substances" list. Iron and aluminum will also be discussed even though they do not appear on the ATSDR's list.

## Arsenic

Arsenic is the most common cause of acute heavy metal poisoning in adults and is number 1 on the ATSDR's "Top 20 List." Arsenic is released into the environment by the smelting process of copper, zinc, and lead, as well as by the manufacturing of chemicals and glasses. Arsine gas is a common byproduct produced by the manufacturing of pesticides that contain arsenic. Arsenic may be also be found in water supplies worldwide, leading to exposure of shellfish, cod, and haddock. Other sources are paints, rat poisoning, fungicides, and wood preservatives. Target organs are the blood, kidneys, and central nervous, digestive, and skin systems (Roberts 1999; ATSDR ToxFAQs for Arsenic).

## **Lead**

Lead is number 2 on the ATSDR's "Top 20 List." Lead accounts for most of the cases of pediatric heavy metal poisoning (Roberts 1999). It is a very soft metal and was used in pipes, drains, and soldering materials for many years. Millions of homes built before 1940 still contain lead (e.g., in painted surfaces), leading to chronic exposure from weathering, flaking, chalking, and dust. Every year, industry produces about 2.5 million tons of lead throughout the world. Most of this lead is used for batteries. The remainder is used for cable coverings, plumbing, ammunition, and fuel additives. Other uses are as paint pigments and in PVC plastics, x-ray shielding, crystal glass production, and pesticides. Target organs are the bones, brain, blood, kidneys, and thyroid gland (International Occupational Safety and Health Information Centre 1999; ATSDR ToxFAQs for Lead).

## **Mercury**

Number 3 on ATSDR's "Top 20 List" is mercury. Mercury is generated naturally in the environment from the degassing of the earth's crust, from volcanic emissions. It exists in three forms: elemental mercury and organic and inorganic mercury. Mining operations, chloralkali plants, and paper industries are significant producers of mercury (Goyer 1996). Atmospheric mercury is dispersed across the globe by winds and returns to the earth in rainfall, accumulating in aquatic food chains and fish in lakes (Clarkson 1990). Mercury compounds were added to paint as a fungicide until 1990. These compounds are now banned; however, old paint supplies and surfaces painted with these old supplies still exist. Mercury continues to be used in thermometers, thermostats, and dental amalgam. (Many researchers suspect dental amalgam as being a possible source of mercury toxicity [Omura et al. 1996; O'Brien 2001].) Medicines, such as mercurochrome and merthiolate, are still available. Algaecides and childhood vaccines are also potential sources. Inhalation is the most frequent cause of exposure to mercury. The organic form is readily absorbed in the gastrointestinal tract (90-100%); lesser but still significant amounts of inorganic mercury are absorbed in the gastrointestinal tract (7-15%). Target organs are the brain and kidneys (Roberts 1999; ATSDR ToxFAQs for Mercury).

## **Cadmium**

Cadmium is a byproduct of the mining and smelting of lead and zinc and is number 7 on ATSDR's "Top 20 list." It is used in nickel-cadmium batteries, PVC plastics, and paint pigments. It can be found in soils because insecticides, fungicides, sludge, and commercial fertilizers that use cadmium are used in agriculture. Cadmium may be found in reservoirs containing shellfish. Cigarettes also contain cadmium. Lesser-known sources of exposure are dental alloys, electroplating, motor oil, and exhaust. Inhalation accounts for 15-50% of absorption through the respiratory system; 2-7% of ingested cadmium is absorbed in the gastrointestinal system. Target organs are the liver, placenta, kidneys, lungs, brain, and bones (Roberts 1999; ATSDR ToxFAQs for Cadmium).

## **Iron**

Discussion of iron toxicity in this protocol is limited to ingested or environmental exposure. Iron overload disease (hemochromatosis), an inherited disorder, is discussed in a separate protocol. Iron does not appear on the ATSDR's "Top 20 List," but it is a heavy metal of concern, particularly because ingesting dietary iron supplements may acutely poison young children (e.g., as few as five to nine 30-mg iron tablets for a 30-lb child).

Ingestion accounts for most of the toxic effects of iron because iron is absorbed rapidly in the gastrointestinal tract. The corrosive nature of iron seems to further increase the absorption. Most overdoses appear to be the result of children mistaking red-coated ferrous sulfate tablets or adult multivitamin preparations for candy. (Fatalities from overdoses have decreased significantly with the introduction of child-proof packaging. In recent years, blister packaging and the requirement that containers with 250 mg or more of iron have child-proof bottle caps have helped reduce accidental ingestion and overdose of iron tablets by children.) Other sources of iron are drinking water, iron pipes, and cookware. Target organs are the liver, cardiovascular system, and kidneys (Roberts 1999).

## **Aluminum**

Although aluminum is not a heavy metal (specific gravity of 2.55-2.80), it makes up about 8% of the surface of the earth and is the third most abundant element (ATSDR ToxFAQs for Aluminum). It is readily available for human ingestion through the use of food additives, antacids, buffered aspirin, astringents, nasal sprays, and antiperspirants; from drinking water; from automobile exhaust and tobacco smoke; and from using aluminum foil, aluminum cookware, cans, ceramics, and fireworks (ATSDR ToxFAQs for Aluminum).

Studies began to emerge about 20 years ago suggesting that aluminum might have a possible connection with developing Alzheimer's disease when researchers found what they considered to be significant amounts of aluminum in the brain tissue of Alzheimer's patients. Although aluminum was also found in the brain tissue of people who did not have Alzheimer's disease, recommendations to avoid sources of aluminum received widespread public attention. As a result, many organizations and individuals reached a level of concern that prompted them to dispose of all their aluminum cookware and storage containers and to become wary of other possible sources of aluminum, such as soda cans, personal care products, and even their drinking water.

(Anon. 1993).

However, the World Health Organization (WHO 1998) concluded that, although there were studies that demonstrate a positive relationship between aluminum in drinking water and Alzheimer's disease, the WHO had reservations about a causal relationship because the studies did not account for total aluminum intake from all possible sources. Although there is no conclusive evidence for or against aluminum as a primary cause for Alzheimer's disease, most researchers agree that it is an important factor in the dementia component and most certainly deserves continuing research efforts. Therefore, at this time, reducing exposure to aluminum is a personal decision. Workers in the automobile manufacturing industry also have concerns about long-term exposure to aluminum (contained in metal working fluids) in the workplace and the development of degenerative muscular conditions and cancer (Brown 1998; Bardin et al. 2000). The ATSDR has compiled a ToxFAQs for Aluminum to answer the most frequently asked health questions about aluminum. Target organs for aluminum are the central nervous system, kidney, and digestive system.

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# Heavy Metal Toxicity

## SYMPTOMS OF EXPOSURE AND TOXICITY

- Arsenic
- Lead
- Mercury
- Cadmium
- Aluminum

Exposure to toxic heavy metals is generally classified as acute, 14 days or less; intermediate, 15-354 days; and chronic, more than 365 days (ATSDR). Additionally, acute toxicity is usually from a sudden or unexpected exposure to a high level of the heavy metal (e.g., from careless handling, inadequate safety precautions, or an accidental spill or release of toxic material often in a laboratory, industrial, or transportation setting). Chronic toxicity results from repeated or continuous exposure, leading to an accumulation of the toxic substance in the body. Chronic exposure may result from contaminated food, air, water, or dust; living near a hazardous waste site; spending time in areas with deteriorating lead paint; maternal transfer in the womb; or from participating in hobbies that use lead paint or solder. Chronic exposure may occur in either the home or workplace. Symptoms of chronic toxicity are often similar to many common conditions and may not be readily recognized. Routes of exposure include inhalation, skin or eye contact, and ingestion (ATSDR MMGs and ToxFAQs; Anon. 1993; WHO 1998; International Occupational Safety and Health Information Centre 1999; Roberts 1999; Dupler 2001; Ferner 2001).

### Arsenic

Exposure to arsenic occurs mostly in the workplace, near hazardous waste sites, or in areas with high natural levels. Symptoms of acute arsenic poisoning are sore throat from breathing, red skin at contact point, or severe abdominal pain, vomiting, and diarrhea, often within 1 hour after ingestion. Other symptoms are anorexia, fever, mucosal irritation, and arrhythmia. Cardiovascular changes are often subtle in the early stages but can progress to cardiovascular collapse.

Chronic or lower levels of exposure can lead to progressive peripheral and central nervous changes, such as sensory changes, numbness and tingling, and muscle tenderness. A symptom typically described is a burning sensation ("needles and pins") in hands and feet. Neuropathy (inflammation and wasting of the nerves) is usually gradual and occurs over several years. There may also be excessive darkening of the skin (hyperpigmentation) in areas that are not exposed to sunlight, excessive formation of skin on the palms and soles (hyperkeratosis), or white bands of arsenic deposits across the bed of the fingernails (usually 4-6 weeks after exposure). Birth defects, liver injury, and malignancy are possible. (Arsenic has also been used in homicides and suicides.)

### Lead

Acute exposure to lead is also more likely to occur in the workplace, particularly in manufacturing processes that include the use of lead (e.g., where batteries are manufactured or lead is recycled). Even printing ink, gasoline, and fertilizer contain lead. Symptoms include abdominal pain, convulsions, hypertension, renal dysfunction, loss of appetite, fatigue, and sleeplessness. Other symptoms are hallucinations, headache, numbness, arthritis, and vertigo.

Chronic exposure to lead may result in birth defects, mental retardation, autism, psychosis, allergies, dyslexia, hyperactivity, weight loss, shaky hands, muscular weakness, and paralysis (beginning in the forearms). Children are particularly sensitive to lead (absorbing as much as 50% of the ingested dose) and are prone to ingesting lead because they chew on painted surfaces and eat products not intended for human consumption (e.g., hobby paints, cosmetics, hair colorings with lead-based pigments, and even playground dirt). In addition to the symptoms found in acute lead exposure, symptoms of chronic lead exposure could be allergies, arthritis, autism, colic, hyperactivity, mood swings, nausea, numbness, lack of concentration, seizures, and weight loss.

### Mercury

Acute mercury exposure may occur in the mining industry and in the manufacturing of fungicides, thermometers, and thermostats. Liquid mercury is particularly attractive to children because of its beautiful silver color and unique behavior when spilled. Children are more likely to incur acute exposure in the home from ingesting mercury from a broken thermometer or drinking medicine that contains mercury. Because mercury vapors concentrate at floor level, crawling children are subject to a significant hazard when the mercury is sprinkled throughout the house during religious ceremonies or when there is an accidental spill (Zayas et al. 1996). Mercury spills are difficult to clean up, and mercury may remain undetected in carpeting for some time. Symptoms of acute exposure are cough, sore throat, and shortness of breath; metallic taste in the mouth, abdominal pain, nausea, vomiting and diarrhea; headaches, weakness, visual disturbances, tachycardia, and hypertension.

Chronic exposure to mercury may result in permanent damage to the central nervous system (Ewan et al. 1996) and kidneys. Mercury can also cross the placenta from the mother's body to the fetus (levels in the fetus are often double those in the mother) and accumulate, resulting in mental retardation, brain damage, cerebral palsy, blindness, seizures, and inability to speak.

Dental amalgam is also suspected as being a possible source of mercury toxicity from chronic exposure. Some physicians suggest that amalgam fillings could be part of the explanation for the explosion of learning problems and autism in children since World War II, a time period corresponding with the introduction and widespread use of mercury amalgam (O'Brien 2001). Studies in both animals and humans have confirmed the presence of mercury from amalgam fillings in tissue specimens, blood, amniotic fluid, or urine (Vimy et al. 1990; Willershausen-Zonnchen et al. 1992; Gebel et al. 1996; Omura et al. 1996; Sallsten et al. 1996; Isacson et al. 1997). However, according to Dr. Robert M. Anderton of the American Dental Association, "There is no sound scientific evidence supporting a link between amalgam fillings and systemic diseases or chronic illness" (Anderton 2001).

The ADA does acknowledge that amalgam contains mercury and reacts with other substances. However, to date the ADA concludes that amalgam continues to be a safe material. Researchers reported finding "no significant association of Alzheimer's disease with the number, surface area, or history of having dental amalgam restoration" and "no statistical significant differences in brain mercury levels between subjects with Alzheimer's disease and control subjects" (Saxe et al. 1999).

Interestingly, the metallic mercury used by dentists to manufacture dental amalgam is shipped as a hazardous material to dental offices. Although the ADA does not advise removing existing amalgam fillings from teeth, it does support ongoing research to develop new materials that will prove to be as safe as dental amalgam (Anderton 2001). Symptoms in adults and children could include tremors, anxiety, forgetfulness, emotional instability, insomnia, fatigue, weakness, anorexia, cognitive and motor dysfunction, and kidney damage. People who consume more than two fish meals a week are showing very high serum levels of mercury.

## **Cadmium**

Acute exposure to cadmium generally occurs in the workplace, particularly in the manufacturing processes of batteries and color pigments used in paint and plastics, as well as in electroplating and galvanizing processes. Symptoms of acute cadmium exposure are nausea, vomiting, abdominal pain, and breathing difficulty.

Chronic exposure to cadmium can result in chronic obstructive lung disease, renal disease, and fragile bones. Protect children by carefully storing products containing cadmium, especially nickel-cadmium batteries. Symptoms of chronic exposure could include alopecia, anemia, arthritis, learning disorders, migraines, growth impairment, emphysema, osteoporosis, loss of taste and smell, poor appetite, and cardiovascular disease.

## **Aluminum**

Although aluminum is not a heavy metal, environmental exposure is frequent, leading to concerns about accumulative effects and a possible connection with Alzheimer's disease (Anon. 1993). Acute exposure is more likely in the workplace (e.g., unintentional breathing of aluminum-laden dust from manufacturing or metal finishing processes).

Chronic exposure may occur in the workplace from accumulated exposures to low levels of airborne aluminum dust and handling aluminum parts during assembly processes over many years. In the home, we are in constant contact with aluminum in foods and in water; from cookware and soft drink cans; from consuming items with high levels of aluminum (e.g., antacids, buffered aspirin, or treated drinking water; or even by using nasal sprays, toothpaste, and antiperspirants) (Anon. 1993; ATSDR ToxFAQs for Aluminum). Citric acid (e.g., in orange juice) may increase aluminum levels by its leaching activity.

Interestingly, aluminum-based coagulants are used in the purification of water. However, the beneficial effects of using aluminum in water treatment have been balanced against the potential health concerns. Water purification facilities follow a number of approaches to minimize the level in "finished" water (WHO 1998). Symptoms of aluminum toxicity include memory loss, learning difficulty, loss of coordination, disorientation, mental confusion, colic, heartburn, flatulence, and headaches.

## **LABORATORY TESTING AND DIAGNOSIS FOR THE PRESENCE OF HEAVY METALS**

- Arsenic
- Lead
- Mercury
- Cadmium
- Aluminum

The diagnosis of heavy metal toxicity requires observation of presenting symptoms, obtaining a thorough history of potential exposure, and the results of laboratory tests. Laboratory tests routinely used for seriously exposed persons include blood tests, liver and renal function tests, urinalysis, fecal tests, x-rays, and hair and fingernail analysis. Many of these tests are not routinely performed in a doctor's office. However, your physician can take blood samples and send them to the appropriate testing laboratory. Chest x-rays are recommended for persons with respiratory symptoms, and abdominal x-rays can detect ingested metals (refer to the ATSDR ToxFAQs for specific information).

## **Arsenic**

Arsenic levels can be measured in blood, urine, hair, and fingernails. Because arsenic clears fairly rapidly from the blood, blood tests are not always useful (Dupler 2001). Therefore, urine tests are the most reliable for arsenic exposure within the past few days; hair and fingernail testing are used to measure exposure over the past several months (ATSDR ToxFAQs for Arsenic). Abdominal x-rays can reveal metallic fragments (Ferner 2001). Note: Hair treatments, including hair dyes, can contaminate hair samples. When testing for any heavy metal, the most accurate results are obtained from hair that has not been chemically treated for at least 2 months.

## **Lead**

When there are presenting symptoms of lead toxicity, blood testing is done. Blood lead levels in children higher than 10 mcg/dL are considered to be of concern (Ferner 2001; ATSDR ToxFAQs for Lead). Symptoms in adults may not appear until blood lead levels exceed 80 mcg/dL (Dupler 2001). However, medical treatment is usually necessary in children who have levels of 45 mcg/dL. Significantly lower levels of 30 mcg/dL in children can cause mental retardation or cognitive and behavioral problems (ATSDR ToxFAQs for Lead). A complete blood count (CBC) is also done to check for abnormalities on red blood cells (basophilic stippling). In children, long-bone x-rays may reveal bands called "lead lines" that indicate failure of the bone to rebuild. These bands are not actual lead concentrations, but are bone abnormalities. Adults do not have lead lines. X-rays of the abdomen can reveal swallowed objects, such as paint chips, fishing sinkers, curtain weights, or bullets (Ferner 2001). A less common test is measurement of lead in teeth (ATSDR ToxFAQs for Lead). All children with brain-related symptoms should be considered for lead toxicity (Ferner 2001).

## **Mercury**

A 24-hour urine specimen is collected for measurement of mercury levels. Chest x-rays can reveal a collection of mercury from exposure to elemental mercury or a pulmonary embolism containing mercury (Ferner 2001). Abdominal x-rays can reveal swallowed mercury as it moves through the gastrointestinal tract. Blood and urine samples are used to determine recent exposure, as well as exposure to elemental mercury and inorganic forms of mercury. Scalp hair is used in testing for exposure to methylmercury. Liver and kidney function tests are also important in severely exposed persons. Blood mercury levels should not exceed 50 mcg/L (see the ATSDR Medical Management Guidelines).

## **Cadmium**

Laboratory testing procedures for cadmium toxicity include collection of a 24-hour urine specimen, CBC, and hair and fingernail clippings. Blood levels show recent exposure; urine levels show both recent and earlier exposure (ATSDR). Blood levels of cadmium above 5 mcg/dL and creatinine levels in urine above 10 mcg/dL suggest cadmium toxicity (Dupler 2001). Note: The ATSDR is unsure of the reliability of tests for cadmium levels.

## **Aluminum**

Testing procedures measure aluminum levels in blood, urine, hair and fingernails, and feces (ATSDR ToxFAQs for Aluminum). According to a spokesperson at the ATSDR in spring 2002, levels of aluminum that are recognized as average are less than 0.01 mg/L. However, blood testing might underestimate the total body level of aluminum; postmortem brain, lung, and bone measurements reveal much higher levels of aluminum than blood tests.

# **SIGNIFICANCE OF INDIVIDUALIZED TREATMENT REGIMENS**

It is very important to note that treatment regimens vary significantly and are tailored to each specific individual's medical condition and the circumstance of their exposure. Providing a complete history of the person, including their occupation, hobbies, recreational activities, and environment, is critical in diagnosing heavy metal toxicity. A possible history of ingestion often facilitates a diagnosis, particularly in children. Findings from physical examinations vary with the age of the person, health status of the person, amount or form of the substance, and time since exposure (absorption rate) (Ferner 2001).

Allopathic (conventional) and alternative medicine practitioners (and naturopathic practitioners to a lesser extent) treat heavy metal toxicity. Once toxicity is confirmed, all cases (even suspected) of heavy metal toxicity should be brought to the attention of a

professional who is experienced in diagnosing and treating poisoning. Often professionals consult with regional poison control centers or medical toxicologists for added expertise. Emergency room personnel and first responders are trained in recognizing symptoms and in proper handling, decontamination, and treatment techniques in acute exposure cases (see the ATSDR Medical Management Guidelines).

Conventional and alternative medical treatment includes chelation therapy, supportive care (intravenous fluids, cardiac stabilization, exchange transfusion, dialysis), and decontamination (charcoal, cathartics, emesis, gastric lavage, surgery). These procedures typically require hospitalization or treatment in a health care or clinical setting (Dr. Joseph F. Smith Medical Library 2001). Follow-up is required with laboratory testing until reference levels are within and remain in the normal range, particularly when the exposure was acute or if the person continues to have symptoms after treatment (ATSDR Medical Management Guidelines; Wentz 2000). Additionally, if there is a suspected homicidal or suicidal association, proper medical and legal resources should be involved (Ferner 2001). Medical personnel should report exposures to the appropriate agency to prevent additional public health risks either in the workplace or in the home (ATSDR Medical Management Guidelines; Anon. 1993; WHO 1998; International Occupational Safety and Health Information Centre 1999; Roberts 1999; Dupler 2001; Ferner 2001; USNML/NIH 2001a; 2001b; 2001c; 2001d).

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# Heavy Metal Toxicity

## THERAPEUTIC OVERVIEW

- Chelation Therapy
- Chelating Agents

Therapies to remove heavy metals from humans include chelation and decontamination procedures, as well as supportive measures, often used in combination. The therapies can be very complex and highly individualized, tailored to the specific needs of each individual and requiring the expertise of trained and experienced professionals, sometimes a team of professionals. Self-diagnosis and treatment is not appropriate.

### Chelation Therapy

Chelation is a chemical process that has applications in many areas, including medical treatment, environmental site rehabilitation, water purification, and so forth. In the medical environment, chelation is used to treat cardiovascular disease, heavy metal toxicity, and to remove metals that accumulate in body tissues because of genetic disorders (hemochromatosis). This protocol will address the use of chelation therapy for the removal of heavy metals as a result of ingested or environmental exposure.

Chelation therapy, simply defined, is the process by which a molecule encircles and binds (attaches) to the metal and removes it from tissue (Dr. Joseph F. Smith Medical Library 2001). Depending on the drug used, chelating agents specific to the heavy metal involved are given orally, intramuscularly, or intravenously. Once the bound metal leaves the tissue, it enters the bloodstream, is filtered from the blood in the kidneys, and then is eliminated in the urine (Dupler 2001). The decision to chelate should be made only by professionals with experience using chelation therapy, preferably in consultation with a poison control center or a medical toxicologist.

Typically, a patient receives a programmed series of intravenous infusions, intramuscular injections, or oral administration of a chelating agent (possibly a combination of the three). The therapy is often lengthy (from a few hours in an emergency room to several days of in-patient treatment in a hospital). Sometimes repeated courses of treatment are required (Wentz 2000). Chelation may be uncomfortable because of the side effects of the medicine itself or from the route of administration (e.g., pain in the area surrounding an injection site) (Ferner 2001). Frequent follow-up testing is required to determine the amount of the metal that is being removed. Sometimes, as in the case of lead, testing may show a rapid decline initially, but then a leveling off occurs over time. In the case of lead, this leveling off is caused by lead that continues to enter the blood from the bones where it has been stored (the "rebound effect"). The leveling off effect is used as a guide for determining how long chelation therapy should be continued (Wentz 2000). As time passes following exposure, chelation therapy is less effective in reducing the severity of poisoning and the risk of serious delayed effects (see the ATSDR Medical Management Guidelines). It cannot reverse neurological damage that has already been sustained.

Acutely poisoned symptomatic persons or persons with a clear history of exposure to a toxic heavy metal may require chelation therapy to start before confirmation can be obtained from a laboratory (see the ATSDR Medical Management Guidelines). However, asymptomatic patients are not usually treated with chelation therapy until after test results reveal levels that require treatment. Interestingly, Goyer (1996) points out that there is growing interest in removing toxic metals from asymptomatic persons who are known to have received low-levels of environmental exposure to heavy metals.

This interest has been generated because of the toxic effects (or damage) that may occur at levels that were previously thought to be safe. According to Goyer, "It is clear that the margin between the levels of exposure for persons living in the industrialized nations of the world and levels of exposure currently recognized as producing the lowest adverse effect is small." Goyer listed low-level exposure to lead as possibly causing impaired cognitive and behavioral development in children, accumulation of cadmium being associated with renal tube dysfunction, and allegations that mercury vapor from dental amalgam may be a possible cause of chronic health problems (Goyer 1996). Mercury vapor is released from amalgam in new fillings, when old amalgam fillings are replaced (Omura et al. 1996), and even when amalgam is scraped during cleaning.

Chelation is effective in treating arsenic, lead, iron, mercury, and aluminum poisoning. However, chelation is not considered to be particularly effective in treating cadmium poisoning, although it may be used to prevent further absorption in the gastrointestinal tract. To date there is no effective treatment for cadmium poisoning (ATSDR ToxFAQs for Cadmium 1999; Wentz 2000; Dr. Joseph F. Smith Medical Library 2001).

### Chelating Agents

An agent frequently used in chelation therapy is dimercaprol (also known as BAL or British Anti-Lewisite). Oral chelating agents

used as alternatives to BAL are 2,3-dimercaptosuccinic acid (DMSA), dimercaptopropanesulfonate (DMPS), and D-penicillamine (ATSDR MMG). Another agent, deferoxamine, is often used to chelate iron. Ethylenediaminetetraacetic acid (ETDA) also has an affinity for lead and was one of the first chelators developed.

BAL (Dimercaprol). BAL (British Anti-Lewisite) is a chelating agent administered by injection in the treatment of acute poisoning by certain heavy metals (e.g., arsenic, lead, mercury, gold, bismuth, and antimony). Contraindications to using BAL are preexisting kidney disease, pregnancy, hypertension, and current use of medicinal iron. BAL has significant side effects that are frequent and include pain at the injection site; hypertension and tachycardia; abdominal pain, nausea, and vomiting; headaches; burning sensation of the lips, excessive salivation, rhinorrhea, and tearing; fever; muscle pain, muscle spasms, and a feeling of chest constriction; and profuse sweating. It is considered to be the most toxic of the chelating agents (Wentz 2000). However, side effects can be medically managed and are seldom severe enough to cause treatment to be ended (Micromedex 1999).

DMSA (Dimercaptosuccinic Acid). DMSA is an oral chelating agent and an analogue of (similar to) BAL. DMSA is used in conjunction with or as an alternative to BAL for lead and mercury toxicity. DMSA is less toxic than BAL, and it is sometimes substituted for BAL when the patient's condition improves. It is also used when intolerance to BAL develops. Although DMSA is similar to BAL, it has fewer and milder side effects (e.g., nausea, vomiting, and diarrhea; rhinitis and cough; and rash) (see the ATSDR Medical Management Guidelines). An interesting study on thiol chelating substances showed that DMSA was more effective than DMPS and SAME (S-adenosylmethionine) in protecting mice from acute hepatic or renal toxicity caused by arsenic, and that all three substances were nontoxic to the liver or kidneys of mice (Tripathi et al. 1998). Contraindications to using DMSA are preexisting kidney or liver disease and pregnancy. Hydration is essential. DMSA is not used in conjunction with ETDA or D-penicillamine (USNML/NIH 2001b).

DMPS (Dimercaptopropanesulfonate). DMPS is another analogue of BAL. It has been shown to be less effective and to have more side effects than DMSA (Aaseth et al. 1995). DMPS is the drug of choice in Europe and Asia; however, the FDA has not approved DMPS for chelating purposes in the United States. It does, however, appear on the FDA list of drugs that appear to be safe. In the United States, DMPS is distributed to pharmacists in bulk form for compounding and dispensing in oral and injection forms (FDA 1999; Marcus 2001).

D-penicillamine. D-penicillamine is an oral chelating agent used to treat heavy metal toxicity, particularly arsenic and mercury. Side effects are gastrointestinal intolerance, nausea and vomiting, and itchy skin (wheals). Contraindications are allergy to penicillin, possible interaction with other drugs (immunosuppressants, digoxin), severe blood disorders, kidney insufficiency, and pregnancy (USNML/NIH 2001d).

Deferoxamine. Deferoxamine is used to chelate iron, especially in acute iron poisoning in small children. It is also used to chelate aluminum. Deferoxamine is administered by injection or intravenously. Common side effects are blurred vision, wheezing, rapid heartbeat, seizures, itching, skin rash, bluish skin, and redness and pain at the injection site. Gastrointestinal discomfort, fever, cramping, and bruising are less common. Contraindications are allergies to certain foods or dyes, other medicines currently being taken, pregnancy or breast feeding, and kidney disease (USNML/NIH 2001a).

EDTA (Ethylenediaminetetraacetic Acid, Edetate Disodium). EDTA is one of the oldest chelating agents, coming into prominence in the 1950s. EDTA has an affinity for lead. It is often used as a second-line of treatment in combination with BAL and given by IV infusion. Common side effects are gastrointestinal upset and headache. More serious side effects can include seizures, numbness or tingling in the hands and feet, irregular heartbeat, skin rashes, fever or chills, and blood in the urine (Ferner 2001). EDTA is contraindicated in pregnancy and if there is kidney disease. It can also interact with insulin and heart medicines (USNML/NIH 2001c).

The following table summarizes chelating agents, the heavy metals they are used to treat, their route of administration, and their brand name.

Chelating Agent	Toxin	Route**	Drug
Dimercaprol (BAL)	Arsenic	i.m.	Dimercaptol
	Lead		Injection B.P.
	Mercury (inorganic)*		BAL in Oil
Dimercaptosuccinic acid (DMSA) (Succimer)	Arsenic	p.o.	Chemet
	Lead		
	Mercury		
Dimercaptopropane- sulfonate (DMPS)	Arsenic	p.o. i.m.	Bulk form (for compounding by pharmacists)

D-pencillamine	Arsenic Mercury Lead	p.o.	Metalcaptase Pencillamine Cuprimine Depen
Ethylenediaminetetra- acetic acid (EDTA) (Edetate disodium)	Lead	IV	Chealamide Versenate
<i>*Not methylmercury poisoning.</i>			
<i>**Under supervision of a physician: i.m., intramuscular; p.o., peroral or by mouth; IV, intravenous.</i>			
<i>Source: Data from Beers et al. 1999; Micromedex 1999; Roberts 1999; Wentz 2000; Anon. 2001; Ferner 2001; Marcus 2001; USNML/NIH Drug Information 2001a; 2001b; 2001c; 2001d.</i>			

## GASTROINTESTINAL DECONTAMINATION

- Gastric Lavage
- Whole Bowel Irrigation
- Emesis
- Charcoal
- Cathartics
- Supportive Measures

In addition to chelation therapy, decontamination procedures are often required: gastric lavage, whole bowel irrigation, emesis, charcoal, or cathartics.

### ***Gastric Lavage***

Gastric lavage is washing out of the stomach with sterile water or a salt solution to remove swallowed irritants or poisons (Dr. Joseph F. Smith Medical Library 2001). Gastric lavage is accomplished by placing a plastic tube into the stomach via the mouth and esophagus. Normal saline, water, or a combination is introduced into the stomach via the tube. Gastric lavage is not indicated if the substance ingested is an alkaline corrosive. It is done in a health care environment or hospital and is most effective within the first hour of ingestion. Gastric lavage is not effective in removing large tablets or large clumps of tablets or other material (Klein-Schwartz et al. 2000), but it is indicated for arsenic (Ferner 2001). Insertion of the tube may injure the esophagus. Gastric lavage is more effective in adults than in children because a larger tube can be used (Klein-Schwartz et al. 2000; James 2001).

### ***Whole Bowel Irrigation***

Bowel irrigation is emptying of the bowel with large volumes of solutions such as Golytely, Colyte, sterile water, or some other fluid to remove swallowed irritants or poisons from the bowel (e.g., arsenic and lead) (Ferner 2001; James 2001). The fluid may be administered orally or by gastric tube until the bowel fluid has the same appearance as the solution administered (Klein-Schwartz et al. 2000; James 2001). Whole bowel irrigation is indicated if some time has elapsed since ingestion of the toxin and if the toxin will not be effectively bound by charcoal. It can take several hours and has the side effects of nausea and vomiting, diarrhea, and cramping. Whole bowel irrigation is not indicated if mental status is impaired or bowel sounds are decreased (Anon. 2001).

### ***Emesis***

Emesis is forceful emptying (vomiting) of the stomach and is most effective for recent oral ingestion of noncorrosive substances. Ipecac Syrup USP is considered to be an essential emesis agent in many homes with young children and for years has been the cornerstone of poison management (Anon. 2001). If instructed by a physician, Ipecac may be given in the home prior to the arrival of emergency personnel or treatment in an emergency department, often preventing significant absorption from stomach contents (Klein-Schwartz et al. 2000). However, use of Ipecac is only effective when administered within the first 5-20 minutes after ingestion of a toxin. After a toxin has left the stomach, inducing emesis with Ipecac is useless. Administering it after the first few minutes may actually delay beginning further medical treatment (Anon. 2001). Ipecac may take 20 minutes to produce forceful vomiting (James 2001), and the vomiting may last for some time (2-4 hours). Emesis should not be induced if the patient is having difficulty maintaining consciousness, the toxin is caustic or might cause choking (e.g., a clump of pills), or if the person has gastrointestinal bleeding (Anon. 2001). When appropriate, emesis is induced in cases of acute arsenic or mercury poisoning (Dr. Joseph F. Smith Medical Library 2001).

Contact a physician, emergency department, or poison center before using emesis..

## **Charcoal**

Charcoal is administered in single- or multiple-dose regimens, either intravenously or orally. Single doses are most effective if administered within the first hour after ingestion. Multiple-dose regimens are often used in complicated cases and in children because the smaller doses (half of a single dose) appear to be better tolerated than the larger single dose (Anon. 2001). Charcoal should not be administered for caustic or corrosive materials, and bowel sounds must be present. Its usefulness is limited in certain pesticides and compounds that are poorly water soluble (e.g., iron and elemental metals) (Anon. 2001). Gastrointestinal decontamination with activated charcoal is indicated to aid in removal of mercury (Ferner 2001).

## **Cathartics**

Cathartics are used to aid moving toxic material through the gastrointestinal tract, to remove and reduce concentrations, or to decrease absorption of toxic materials (Anon. 2001; James 2001). A cathartic agent increases intestinal action, increases the bulk of feces, makes feces soft, or adds water to the wall of the intestines, the term implying fluid bowel materials (Glanze 1996). Cathartics are often used in conjunction with charcoal in adults, particularly to prevent impaction or formation of charcoal "briquettes." Cathartics are not recommended for children under 1 year and should be used with caution in children under 3 years of age. Cathartics can produce significant diarrhea and electrolyte imbalance. They are not indicated if bowel sounds are absent (Anon. 2001).

## **Supportive Measures**

IV fluids, dialysis, and drugs to treat complications resulting from heavy metal toxicity and treatments, such as shock, anemia, kidney failure, breathing difficulties, cardiac irregularities, infections, and so forth, may be required. Close monitoring of symptoms by medical personnel and immediate response to them are also required (Anon. 2001; Dr. Joseph F. Smith Medical Library 2001; James 2001; ATSDR Medical Management Guidelines).

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## TREATMENT REGIMES FOR SELECTED HEAVY METALS

- Arsenic
- Mercury
- Iron
- Lead
- Aluminum
- Cadmium

### Arsenic

Chelation therapy shortens the distribution of arsenic in the blood and reduces the body burden. It can reduce the risks of serious delayed effects, but chelation does not reverse damage from the delayed effects of acute arsenic poisoning (see the ATSDR Medical Management Guidelines). BAL, DMSA, and D-penicillamine are the primary drugs used to remove arsenic. Chelation therapy with BAL by injection is the primary form of treatment for acute arsenic toxicity. The oral chelating agent DMSA is also an effective treatment choice.

Supportive care with abundant fluids to increase elimination of arsenic may be required. Exchange transfusion and hemodialysis may also be necessary in the event of kidney failure. However, these treatments are supportive and do not remove arsenic (Roberts 1999). Decontamination of the gastrointestinal system with gastric lavage aids in reducing continued absorption of arsenic. Whole bowel irrigation may also be necessary. Use supportive measures, such as correcting heart rhythm irregularities and hypotension (Ferner 2001).

### Mercury

Chelation therapy is the usual treatment method for mercury poisoning, using BAL, DMSA, or D-penicillamine (Ferner 2001). BAL is widely used for inorganic mercury poisoning (Roberts 1999), with D-penicillamine used as an alternative. Other treatments are activated charcoal for gastrointestinal decontamination unless there is evidence of corrosive damage in the gastrointestinal tract (Ferner 2001), gastric and whole bowel lavage, and supportive measures. However, charcoal is not usually given when elemental mercury is ingested because elemental mercury is poorly absorbed in the gastrointestinal tract (see the ATSDR Medical Management Guidelines; see Life Extension Magazine, May 2001, page 48, for a detoxification protocol to be used in conjunction with the removal of mercury amalgams).

### Iron

Chelation with deferoxamine is commonly used with blood serum levels greater than 500 mg/dL. (This level is only a guide. Much lower levels are known to produce cardiovascular difficulties, and some persons with higher levels exhibit no symptoms.) Deferoxamine is a drug that binds to absorbed iron very well and is eliminated in urine. Deferoxamine may be administered by injection or by intravenous administration; however, IV administration is less painful and more efficient. Supportive care with special attention to fluid balance and cardiovascular stabilization are essential in iron poisoning (Roberts 1999).

Blood levels are used as a guide to therapy, but the estimated ingested amount is often used to determine the initial course of action. If the person is symptomatic, however, or if the amount ingested exceeds 20 mg/kg (or as few as 5-9 30-mg tablets for a 30-pound child), gastrointestinal decontamination is recommended. Inducing emesis is an option within the first hour after ingestion. Gastric lavage may also remove fragments of tablets (Roberts 1999). Note: BAL chelation is contraindicated for iron toxicity, because BAL can combine with medicinal iron to become very toxic (see the ATSDR Medical Management Guidelines).

### Lead

Chelation therapy with DMSA for children with blood lead levels of greater than 45 mcg/dL was approved in 1991 by the FDA (Wentz 2000). A major advantage of DMSA is that it can be given orally, which leads to better compliance by the patient. DMSA is relatively safe and significantly reduces blood levels of iron (Fournier et al. 1988). BAL, D-penicillamine, and EDTA are also used (Wentz 2000). Whole bowel irrigation is used if x-rays indicate the presence of lead (Ferner 2001). Follow-up blood testing is required because stored lead in bones may continue to release from the bones when the lead exposure has been long-term (Wentz 2000).

### Aluminum

Although deferoxamine has not been approved by the FDA for aluminum chelation, deferoxamine has been used since 1980 as a

first-line of treatment in cases of aluminum toxicity. (Important: Remember that deferoxamine is used to chelate iron. Therefore, during chelation treatment for aluminum, iron would also be chelated.) EDTA may also be used (Wentz 2000).

## **Cadmium**

There is no known medical chelating method that is effective for the treatment of cadmium toxicity; however, DMSA may be used in cases of acute oral cadmium poisoning to help prevent additional absorption of cadmium in the gastrointestinal tract (Wentz 2000). Prevention or elimination of exposure is all that is available at this time for cadmium toxicity (ATSDR ToxFAQs for Cadmium).

## **PREVENTING HEAVY METAL POISONING**

Occupational exposure can be reduced by engineering solutions that address the manufacturing process, collecting and removing fumes, reducing dusts, and substituting other materials when possible. For example, in recent years, the pottery industry has replaced certain lead compounds in their products that are used as dishes or food containers. In most countries, laws have been passed to protect workers, setting limits of exposure, requiring monitoring in the workplace and medical surveillance of workers, and making recommendations (International Occupational Safety and Health Information Centre 1999):

- No smoking, eating, or drinking in work areas.
- Provide appropriate protective clothing that will remain at the facility.
- Provide showering facilities as needed.
- Work clothes and street clothes will not be kept in the same area.

Three agencies in the United States that provide information and guidance are the Occupational Safety and Health Administration (OSHA), the National Institute for Occupational Safety and Health (NIOSH), and the Agency for Toxic Substances and Disease Registry (ATSDR). Local health departments, regional poison control centers, and clinics that specialize in occupational and environmental health conditions can also provide valuable resources and guidance.

In the home, practical measures include raising your awareness of possible sources of exposure and reducing the threat of exposure. Think carefully about the necessity of having products containing toxic metals around the house or in the garage (e.g., fertilizers, fungicides, insect or rodent poisons, lead-based paint, refinishing chemicals, household cleaning agents, hobby supplies, photographic chemicals, batteries, etc.). Use alternatives when possible. When these products are necessary, store them carefully and dispose of them properly. Medicines and personal health care products should be stored so that they are in a location well out of the creative and imaginative reach of children. Emphasize safety rules with children. If appropriate, before leaving the workplace, follow decontamination procedures to avoid bringing toxic materials into your house on your clothing and shoes or on your skin and hair. Consider cumulative exposures, such as from cookware, storage containers, medicines, water, foodstuffs, and the environment (National Medical Library 2001).

1. Use the least harmful product possible.
2. Buy only as much as you need.
3. Read labels. Know the potential hazards of what you are buying.
4. Store products in their original container. Read the label every time you use a product. Refer to the label in case of an accidental spill or ingestion. Never store household chemicals in a food container, even if the container has been relabeled.
5. Support and use established disposal programs and facilities in your area.
6. Become familiar with the symptoms of and first aid procedures for ingestion of substances containing toxic metals.

## **NATURAL THERAPIES TO PROMOTE CHELATION, DETOXIFICATION, AND PROTECTION**

- Antioxidants
- Detoxifying Agents
- Dietary Fiber
- Protective Agents

There is no substitute for prompt professional medical attention in cases of heavy metal toxicity. However, there are a number of things of a dietary nature that you can do that are beneficial, protective, and supportive of good health and the body's own natural chelation mechanisms. Many herbs and supplements have natural chelating characteristics and properties that help to detoxify the body. Important supplements to consider are antioxidants, herbs, minerals, essential amino acids, phytoextracts, detoxifying agents, protective agents, and fiber (see also the Immune Enhancement protocol).

## Antioxidants

- Vitamin C
- Vitamin E
- Vitamin A
- Alpha-Lipoic Acid
- Glutathione
- Lactoferrin
- Selenium and Zinc
- Herbs
- Cilantro
- Garlic
- Green Tea
- Minerals
- Essential Amino Acids
- Cysteine and N-Acetyl Cysteine
- Glycine

Vitamins C, E, and A; alpha-lipoic acid; glutathione; lactoferrin; and selenium and zinc are important antioxidants that aid our overall health by increasing our protection from oxidative stress.

### ***Vitamin C***

Vitamin C has long been recognized as having positive effects for the prevention of heart disease and some forms of cancer, improving immune function, maintaining healthy skin and blood vessels, accelerating healing, and reducing allergic reactions. A steady supply of vitamin C is vital to overall good health. Because the human body cannot manufacture or store vitamin C, our requirements must be met from dietary sources, such as citrus fruit, vegetables, and supplements. Vitamin C is particularly beneficial for antioxidant protection for the lungs. It has been shown to protect the airways from inhaled (environmental) oxidants (Ghio et al. 1998). Additionally, researchers have shown that vitamin C can help reduce the harmful effects of lead, aluminum, copper, silica, and radiation (Dhir et al. 1990, 1993; West et al. 1994; Ghio et al. 1998; Vij et al. 1998; Cai et al. 2001).

### ***Vitamin E***

Some of the benefits of vitamin E include synergy with vitamin A; reducing cellular aging; reducing the risk of Alzheimer's disease; protecting the nervous system; preventing abnormal blood clotting; lowering the risk of heart disease (Pryor 2000); protecting immune function; lowering the risk of certain cancers; and protecting the lungs from toxins and pollutants (West et al. 1994).

As early as 1981, studies using three different feeding experiments revealed that when animals received silver, copper, cobalt, tellurium, cadmium, and zinc, the animals frequently developed lesions that were characteristic of selenium and vitamin E deficiency, such as necrosis (local destruction of tissue because of disease or injury) of cardiac and skeletal muscle and the smooth muscle of the intestine and gizzard. In studies by Van Vleet et al. (1981), vitamin E (and selenium) gave complete protection from muscle lesions produced by copper, cobalt, tellurium, cadmium, and zinc. Vitamin E also produced protection against lesions caused by silver. (There was partial protection using selenium.) Ten years later, in another study in animals, Tandon et al. (1992) found that cadmium caused kidney, liver, and blood biochemical markers to be changed negatively. When these researchers coadministered vitamin E, the cadmium-induced biochemical alterations were reduced and accumulation of cadmium in the kidneys, liver, and blood was also reduced. Tandon et al. (1992) concluded that the antioxidant properties of vitamin E seemed to be responsible for protection from cadmium toxicity.

A recent study reported by Milchak et al. (2002) examined lipid peroxidation (oxidative damage) and cell death on liver cells caused by iron (ferrous sulfate) in animals. Milchak et al. (2002) found that vitamin E reduced lipid peroxidation by 39% and increased cell viability by 12%. However, the greatest protective effect against iron-induced lipid peroxidation occurred when vitamin E, glutathione (GSH), and N-acetyl-cysteine (NAC) were combined. The combination reduced lipid peroxidation by 94% in iron-treated cells.

### ***Vitamin A***

Vitamin A (retinol) is essential for normal cell growth and protection from various diseases. Vitamin A has also been shown to help inhibit cancer cell proliferation (particularly against leukemia) and to aid in a return to normal cell growth patterns. Recent research into vitamin A has shown that it has protective effects against tumor growth as well (Villamor et al. 2000). Beta-carotene is a potent source of vitamin A (via the liver) and is another important antioxidant. However, continuous, high doses of vitamin A or beta-carotene are not recommended. Pregnant women should not take vitamin A.

### **Alpha-Lipoic Acid**

Alpha-lipoic acid is a potent free radical scavenger that has an ability to detoxify metals and regenerate other antioxidants, such as vitamins C and E, coenzyme Q10, and glutathione. Alpha-lipoic acid has also been used in the treatment of diabetes, heart disease, and other oxidant-related diseases. In a study by Gurer et al. (1999), lipoic acid improved the thiol capacity of cells by increasing glutathione levels and reducing malondialdehyde levels in lead-exposed cells.

**Note:** *Thiols participate in detoxification activity in the body. Malondialdehyde occurs in the bloodstream as a product of lipid peroxidation. It also occurs naturally in a variety of foods, depending on source and method of preparation.*

Another study used two different lipoic acid protocols on exposure to mercury and neurotoxicity, and the results showed ameliorating effects. Anuradha et al. (1999) concluded that "the ameliorating effect of lipoic acid and its therapeutic efficacy during various modes of therapy on the antioxidant status were established in the nervous tissues." Other toxic substances such as cyanide, glutamate, or iron ions have been shown to be neurotoxic. Prolonged pretreatment with lipoic acid provided protection for the cells (Muller et al. 1995). Alpha-lipoic acid also appears to have positive effects for cadmium toxicity, providing a protective effect for cadmium-induced cell dysfunction and membrane damage in hepatocytes (the most basic liver cells that perform all functions of the liver) (Muller et al. 1989; 1990).

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# Heavy Metal Toxicity

## **Glutathione**

Glutathione is a tripeptide (chain of amino acids) that functions as a modulator of cellular homeostasis (the orderly status of cell life), including detoxification of oxyradicals and carcinogens. If glutathione is depleted, an organism can be predisposed to incur stress from pollutants (Ringwood et al. 2000). Glutathione and glutathione-related enzymes are important antioxidants. These enzymes appear to play an important role in detoxifying carcinogens (Chouchane et al. 2001; Lorico et al. 2002; Maiti et al. 2001).

Glutathione status has also been shown to have an impact on the ability of the body to handle heavy metals such as cadmium, lead (Daggett et al. 1998; Wright et al. 1998), iron, and mercury. The pro-oxidative effects of heavy metals are compounded by the fact that they also inhibit antioxidative enzymes and deplete intracellular glutathione. Heavy metals also have the potential to disrupt the metabolism and biological activities of many proteins because of their high affinity for free sulfhydryl groups. When glutathione status is elevated or increased by supplementation and there is exposure to cadmium, lead, iron, or mercury (either independently or along with nutrients such as zinc or selenium), the tissues that were exposed were able to stop damage by the lipid peroxides that were created by exposure to the metals (Shukla et al. 1988; Turan et al. 1992; Sidhu et al. 1993; Tang et al. 1998; Tjalkens et al. 1998; Shaikh et al. 1999a). Interestingly, in a study in rats, Wright et al. (1998) concluded that their results indicated increases in renal glutathione (glutathione S-transferase or GST) "occur at levels of lead that are environmentally significant and that these changes precede cellular damage." Wright et al. (1998) suggested that GST "may serve as a tissue biomarker of lead exposure."

Additionally, glutathione appears to play a major role in arsenic toxicity (Maiti et al. 2001; Chouchane et al. 2001; Lorico et al. 2002). It is the most abundant cellular thiol in the body (Chouchane et al. 2001). Arsenic toxicity appears to be a result of the ability of arsenite to bind to protein thiols, causing the thiols to be unavailable for detoxification activity. Couchane et al. (2001) examined the effect of arsenic on the activity of a variety of glutathione enzymes but concluded that many more studies are needed to understand the relationship between glutathione-related enzymes and the products of arsenic metabolism in the role of arsenic toxicity and carcinogenesis. However, Lorico et al. (2002) stated: "These observations further demonstrate that glutathione is an important component of MRP1-mediated cellular resistance to arsenite and antimony."

Glutathione is also closely tied to immunity, protecting the cells and assisting the liver in detoxifying harmful compounds and toxins. When taking glutathione, vitamin C is also recommended because vitamin C assists glutathione in maintaining its powerful free radical-suppressing effects.

## **Lactoferrin**

Lactoferrin, a natural component of cow and human milk, is a subfraction of whey with well-documented antiviral, antimicrobial, anticancer, and immune modulating and enhancing effects. However, lactoferrin's best-known role is as an iron-binding protein. Lactoferrin acts as an antioxidant, scavenging free iron and helping to prevent uncontrolled iron-based free radical reactions. Interestingly, although lactoferrin is both an iron scavenger and donor (depending on the cellular environment), it has been found to scavenge or donate iron appropriately depending on what the body needs at any given time. At normal physiological pH, lactoferrin binds tightly to iron, diminishing oxidative stress to tissues (Brink 2000). Stella et al. (1995) examined the role of whey proteins, multifermented whey proteins, and lactoferrin in oxidative stress and made this bold statement: "We can conclude that whey protein, lactoferrin and multifermented whey are good candidates as dietary inhibitors of oxidative stress and should be considered as potential medicinal foods in various pathologies as HIV infection and cancer."

## **Selenium and Zinc**

Deficiency of selenium and zinc, important antioxidant micronutrients, contributes to compromised immunity (Girodon et al. 1999) and lowered defense against free radicals (Porter et al. 1999; Schumacher 1999). Selenium and zinc act as cofactors of antioxidant enzymes to protect against oxygen free radicals produced during oxidative stress (Leung 1998). Selenium is often found to be deficient in persons who have experienced physical trauma. Porter et al. (1999) concluded that patients who experienced severe trauma had fewer infections and less organ dysfunction when they received selenium supplementation. Interestingly, studies on the protective benefits of selenium have implications in the management of persons receiving chemotherapy, enhancing mediation of oxygen free-radical damage to normal tissue, and decreasing side effects such as nausea, emesis, vertigo, unsteady gait, and seizures caused by the chemicals and drugs used in chemotherapy (Pakdaman 1998). This is possibly a characteristic of persons with brain tumors who frequently have low blood levels of selenium (Pakdaman 1998; Schumacher 1999).

## **Herbs**

Herbs and herbal extracts have been used for decades and studied for years, particularly in Europe and China (Huang 1993). Many drugs commonly used in modern-day medicine have been derived either directly or indirectly from herbal origin. Herbs are often complexed (combined) to assist in blood purification and detoxification (e.g., dandelion root, yellow dock root, sarsparilla root, echinacea, licorice root, etc.) (see the Gulf War Syndrome Protocol for additional information on detoxification with herbs).

## **Cilantro**

*Coriandrum sativum* is a European herb in the parsley family. The leaves are cilantro (also Chinese parsley) and the fruit is coriander. Cilantro leaves are commonly used as a seasoning herb. However, dried coriander seeds have an entirely different flavor than the leaves and are used as a spice. Coriander stimulates appetite, helps increase secretion of gastric juices, and aids the digestive system. The essential oils of cilantro are considered to have antifungal and antibacterial properties (Omura et al. 1995; 1996).

In studies at the Heart Disease Foundation (New York), Omura et al. (1995; 1996) found that antibiotics used to treat infection were not effective in the presence of heavy metals such as mercury and lead. These metals appeared to coexist with infections such as *Chlamydia trachomatis* and Herpes simplex, as well as with cytomegalovirus and other microorganisms, including viruses responsible for cancer. Even with rigorous treatment and taking precautions to guard against reinfection, patients often had a recurrence of infection within several months after treatment was completed. However, quite by chance (after eating soup containing cilantro) and as the result of his own experience following a cardiac thallium study, Omura found that cilantro successfully eliminated mercury deposits (mercury resulted as a decay product of thallium). Omura et al. (1995) then gave subjects a course of either antibiotics or antiviral drugs along with cilantro. The amount of cilantro varied by individual because some subjects did not like either cooked or raw cilantro, but the researchers found that cilantro worked synergistically with antibiotic drugs and rapidly reduced symptoms and infection. They also found that cilantro accelerated the elimination of mercury, lead, and aluminum through the urine. They hypothesized that certain infectious organisms somehow use mercury or lead to protect themselves from antibiotics or that deposits of heavy metals somehow make antibiotics ineffective.

The next year, the same researchers (1996) investigated the potential health hazard of mercury in dental amalgam. In this case study, they monitored a patient who was having amalgam fillings removed. Even though considerable care was used so that the patient would not swallow minute particles of amalgam during the removal process (drilling), significant deposits of mercury were still found in the patient's lungs, kidneys, liver, and heart. These deposits were not present prior to the amalgam removal. However, the mercury deposits were eliminated by taking oral cilantro four times a day. Omura et al. (1996) initiated cilantro detoxification treatment before the removal procedure and continued it for about 2-3 weeks afterward.

## **Garlic**

Garlic has been valued for centuries for its medicinal properties. Research has shown that garlic can protect us from various pollutants and heavy metals (Cha 1987). Garlic is also important for its ability to prevent certain kinds of cancer, prompting the National Cancer Institute to develop a \$20.5 million program to study plant-derived compounds in common foods that may have cancer-prevention effects. Some scientists speculate that garlic may protect against cancer by its ability to help the body to inactivate and eliminate cancer-causing substances without damage. Depending on personal requirements or preferences, garlic supplements are available in a wide range of potencies. The aged form of garlic (Kyolic) is organically grown and then harvested and aged to produce a mild, odor-free garlic extract.

## **Green Tea**

Green tea is a powerful antioxidant that may protect cells from mutation caused by cancer-causing agents and damage caused by free radicals. For years, studies conducted in Japan demonstrated that persons who consumed green tea had a lower incidence of several types of cancer (stomach, liver, pancreas, breast, lung, esophagus, and skin).

## **Minerals**

In addition to the vitally important function of maintaining healthy bones and helping to restore bone density if it has been lost, calcium is required for proper liver function. The kidneys assist in processing body waste; however, the liver is the organ that has the primary function of processing body waste. Additionally, through complex chemical processes, the liver is also responsible for providing building and maintenance materials for all other organs and tissues in the body, providing vital digestive enzymes, and storing glucose not immediately needed by cells (Clayman 1999). Adequate absorption of calcium can be compromised by an existing condition of the liver or the intestinal tract. To aid optimized liver function, ensure that adequate dietary calcium is provided.

## **Essential Amino Acids**

Amino acids are the basic chemical "building blocks" of life that are derived from dietary protein that is broken down into individual amino acids by the body. The body then reassembles the amino acids into new and vital structures that are essential to produce protein structures for genes, enzymes, hormones, body fluids, and neurotransmitters (Clayman 1989). A deficiency in essential amino acids can negatively affect protein synthesis. Exposure to pollution, chemicals and agricultural pesticides are environmental sources that contribute to a deficiency of amino acids. L-cysteine and the acetylated form, N-acetyl-cysteine (NAC), act as antioxidants and liver protectants. When taking L-cysteine or NAC, taking vitamin C will help maintain their powerful free radical-suppressing effects.

## **Cysteine and N-Acetyl Cysteine (NAC)**

L-cysteine is a conditionally essential amino acid, one of three sulfur-containing amino acids. The other two are taurine (produced from L-cysteine) and L-methionine. L-cysteine can be produced from L-methionine in the body by a complex multistep process. L-cysteine acts as an antioxidant and has a pivotal role in inducible, endogenous (internal) detoxification mechanisms in the body. Exposure to metals taxes our supply of cysteine (Quig 1998).

N-acetyl-cysteine (NAC) is the acetylated (or combined) form of L-cysteine, which is more efficiently absorbed and used. NAC works in the extracellular environment and is a precursor of intracellular cysteine and glutathione. NAC has been used as a liver protectant, as well as to break up pulmonary and bronchial mucus. From decades of experience, NAC has been shown to be a safe and effective prophylaxis (prevention agent) and therapy for a variety of conditions, even in very high doses, mostly involving glutathione depletion and alterations of the redox status (De Flora et al. 2001).

**Note:** Redox = red(uction) + ox(idation).

NAC has an impressive list of protective effects: antioxidant activity, decrease of the biologically effective dose of carcinogens, anti-inflammatory activity, immunological effects, inhibiting progression to malignancy, inhibiting metastasis, and protection from the adverse effects of chemopreventive and chemotherapeutic agents. Although their studies were primarily directed at chemoprevention treatment and complementary approaches in high-risk individuals (e.g., people who smoke or who are ex-smokers), according to De Flora et al. (2001), "There is overwhelming evidence that NAC has the ability to modulate a variety of DNA damage and cancer-related end-points."

## **Glycine**

Glycine is another conditionally essential amino acid found in plant and animal protein. Chemically, glycine is the most simple and most ubiquitous (seemingly present everywhere) of all of the amino acids. It combines with many toxic substances and converts them to harmless forms, which are then excreted from the body. Glycine has a calming effect on the brain. It may also be a growth hormone releaser. (Along with cysteine and glutamic acid, glycine is also a component of glutathione.) In a study of the Japanese drug, Stronger Neo-Minophagen C, a drug containing glycine, glycylrhizin, and cysteine, which is said to be protective against chronic cadmium toxicity, Shaikh et al. (1999b) concluded that the reported beneficial effects of Stronger Neo-Minophagen C were from glycine. Glycine appeared to reduce the oxidative stress of chronic cadmium toxicity. However, as of spring 2002, Stronger Neo-Minophagen C was not available in the United States ([www.fda.gov](http://www.fda.gov)).

## **Detoxifying Agents**

- Alfalfa
- Chlorella
- MSM
- Rutin

### **Alfalfa**

Although most people consider alfalfa to be a plant that is primarily grown for animal feeds, and it has been widely studied for that purpose, alfalfa (also called buffalo herb, buffalo grass, Chilean clover, lucerne, and purple medic) is an excellent source of protein for humans. Alfalfa is high in vitamins A, D, E, B6, and K; calcium, magnesium, chlorophyll, phosphorus, iron, potassium, trace minerals; and several digestive enzymes. Alfalfa is also a high-fiber substance (21% crude fiber, 42% dietary fiber). High-fiber diets are generally recommended for reducing cholesterol, improving diabetes, and protecting against colon cancer. As early as 1981, researchers found that--because of its high-fiber content--alfalfa has properties to bind to material in the colon and aid in its removal (Smith-Barbaro et al. 1981). More studies are required, however, to determine if alfalfa has an ability to induce activity in a complex cellular system to inactivate dietary chemical carcinogens in the liver and small intestine and remove them before they have a chance to cause harm to the body.

Alfalfa should not be taken by individuals with toxic or chronic iron overload.

### **Chlorella**

Chlorella is a single-cell, fresh water algae that is rich in protein, vitamins, minerals, chlorella growth factor, and other beneficial substances. It is about the size of a human erythrocyte (red blood cell) or about 2-8 microns in diameter. Chlorella is high in chlorophyll, giving it a rich green color. For many years, chlorella has been accepted as a detoxifier, and it is commonly used in

colon cleansing regimes. Chlorella appears to bind to heavy metals as well as other toxic substances in the bowel and help with the detoxification process. Chlorella also increases serum albumin levels that are necessary for optimum health.

Many reports have come from Japanese research studies that followed the nuclear catastrophe resulting from atomic bombs that were dropped on the cities of Hiroshima and Nagasaki in 1945. In a report to the General Meeting of the Pharmaceutical Society of Japan on an early study in animals, Ichimura (1973) reported that chlorella (8 grams daily) increased elimination of cadmium: threefold in feces and sevenfold in urine. Other researchers from Japan showed that chlorella helped detoxify uranium and lead (Horikoshi et al. 1979). Chlorella has detoxification potential for similar compounds, such as dioxin and polychlorinated biphenyls. (PCBs are chemical compounds used in plastics, insulation, and flame retardants, with potential to cause cancer and liver damage.) Other research indicates that chlorella is useful in detoxification of high levels of mercury in the body caused by removal of mercury amalgam. Some dentists recommend chlorella to patients who are having mercury amalgams replaced (as well as to themselves and staff who can incur accidental exposure from day-to-day exposure to amalgam filling procedures) (O'Brien 2001).

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# Heavy Metal Toxicity

## ***MSM (Methylsulfonylmethane)***

Methylsulfonylmethane or dimethyl sulfone (MSM) is a naturally occurring sulfur compound. Dimethylsulfoxide (DMSO) and dimethylsulfide (DMS) are closely related compounds. In its purified form, MSM has no odor and is a slightly bitter tasting, water-soluble, white, crystalline powder that contains 34% elemental sulfur (chemical formula of  $[\text{CH}_3]_2\text{SO}_2$ ). The origins of MSM begin with the phytoplankton in the ocean. DMS is produced through a complex process occurring in the ocean. DMS escapes as a gas and rises into the upper atmosphere. (Some atmospheric chemists suggest that MSM and its related compounds, DMSO and DMS, are the source of 85% of the sulfur compounds in all living organisms.) In the atmosphere, DMS is oxidized by ozone and ultraviolet light into its chemical cousins, DMSO and MSM. DMSO and MSM return to the earth in rain, where they are absorbed by the soil. Then plants rapidly take up the two compounds and concentrate them. Next, animals eat the plants, which completes the cycle (Prater 1999).

Therefore, as a result of the cycle that began with phytoplankton, MSM occurs naturally in the human body as a result of the food we eat. It is a normal component of fresh fruits, vegetables, seafood, and meat and can also be found in tea, coffee, and chocolate. MSM can be detected in the circulatory system (about 0.2 ppm in a normal adult male) and in human urine. Normal adult humans excrete from 4-11 mg of MSM each day in their urine. The concentration of MSM decreases with age in vertebrates. Therefore some research suggests there is a minimum concentration of MSM that must be maintained in the body to preserve normal function and structure (Prater 1999).

Chelation involves a sulfur donor (Esteves et al. 2000). Because MSM is a compound that contains sulfur, theoretically it could be beneficial as a part of a detoxification protocol for heavy metals (e.g., there is a sulfur component in glutathione, methionine, cysteine, and NAC). After administering cadmium to rats, cysteine and methionine were given in combination. Esteves et al. (2000) found that cadmium was removed from the circulatory system, preventing its deleterious effects. In addition to its detoxifying potential, MSM has potential for allergy response reduction, control of hyperactivity, constipation relief, cancer prevention, and inflammatory conditions, such as rheumatoid and degenerative arthritis (Prater 1999).

## ***Rutin***

Rutin is a phytoextract (plant extract) found in many plants, particularly buckwheat. Other rich sources of rutin are black tea and apple peel. Rutin is thought to have antioxidant, anti-inflammatory, anticarcinogenic, and cytoprotective activities (Deschner et al. 1993; Perez Guerrero et al. 1994; Kostyuk et al. 1996; Galvez et al. 1997; Cruz et al. 1998). Studies in animals demonstrated that rutin has anti-inflammatory potential in colitis, reducing tissue damage (Galvez et al. 1997; Cruz et al. 1998). Kostyuk et al. (1998) reported free-radical scavenging and iron-chelating ability that significantly protected against cellular damage.

## ***Dietary Fiber***

Choosing foods with high fiber content and supplementing the diet with additional fiber (e.g., psyllium, acacia, apple pectin, and oat and wheat bran) aid the body in ridding itself of toxins. When adding fiber to your diet, use small amounts at first so that your digestive system can adjust to the added fiber. If gas or bloating occurs, reduce the amount until tolerance is achieved.

## **Protective Agents**

- S-AdoMet
- Silybinin

## ***S-AdoMet***

S-AdoMet or S-adenosylmethionine (also known as SAM or AdoMet) has been called "the liver's super-nutrient." Nothing else comes close to S-AdoMet in providing a spectrum of health benefits for the liver. As a preventive agent, S-AdoMet is so powerful that it can reverse the destructive effects of chemicals and alcohol as they occur. It also has a central role in liver biochemistry. S-AdoMet performs two crucial functions: methylation and trans-sulfuration. One result of trans-sulfuration is a transformation into glutathione, the liver's most vital substance. Glutathione is crucial for liver function and is a natural antioxidant for the liver. Because the liver also contains the third highest amount of S-AdoMet in the body (after the adrenal and pineal glands) and because S-AdoMet is so important for liver function, S-AdoMet can be considered to be an essential nutrient for the liver.

The principal function of the liver is to break down damaging substances encountered by the body (drugs, alcohol, infections, or even our own body products). Therefore, poor liver function is invariably accompanied by glutathione depletion. In addition to its many other functions, S-AdoMet also plays a leading role in liver regeneration. Anyone concerned about the effects of drugs, toxic

chemicals, alcohol, and aging on the liver should consider taking SAME for its protective benefits.

Several studies were conducted to investigate the role of SAME in arsenic toxicity (Yamanaka et al. 1997; Tripathi et al. 1998; Goering et al. 1999). A study by Goering et al. (1999) demonstrated that arsenic interferes with DNA methyltransferases, causing the tumor suppressor genes to be inactivated. The study suggests that arsenic-induced malignant transformation is linked to DNA hypomethylation subsequent to depletion of SAME, potentially resulting in aberrant gene activation, including cancer genes. Note: In methylation, a compound is derived from ethanol in which hydroxyl hydrogen is replaced by a metal.

Gubrelay et al. (2001) conducted a study in mice to determine the role of SAME to increase removal of cadmium from target organs by diethylenetriamine penta acetic acid (DTPA). Their results indicated that there was significant removal of cadmium concentration from the blood in DTPA-plus-SAME-treated animals compared to either one of the substances alone. Gubrelay et al. (2001) also found that treatment with SAME alone was effective in correcting zinc and glutathione concentrations.

As early as 1985, research was being done in mice to investigate the beneficial effects of SAME on acute and chronic lead exposure (Paredes et al. 1985). The mice were treated with subcutaneous SAME for 20-22 days. In all test subjects, there was significant recovery of erythrocytic (red blood cell) ALA-D following SAME therapy. There was also decreased lead content in blood, liver, and kidneys, with near normal levels attained in 2 weeks. Glutathione (GSH) concentration in blood and liver that had been diminished also increased after SAME administration, reaching normal levels.

### **Silibinin**

Silibinin (also silybin) is the most biologically active ingredient in silymarin. Silymarin is an extract derived from the herb milk thistle (a member of the Compositae or daisy family). Silymarin and its main active ingredient, silibinin, help prevent toxic liver damage. Standardized milk thistle extract usually consists of a minimum of 35% silybin (by HPLC analysis).

A recent study by Skottova (1999) compared the effectiveness of silymarin with silibinin to inhibit copper-induced oxidation of low-density lipoproteins in vitro. Silymarin and silybinin were found to be equally effective in prolonging the initial "lag phase" (the slow stage of the oxidation process). As a result, Skottova concluded that "silybin is the most important compound of silymarin in protecting the LDL from oxidation."

There have been a few studies to investigate the activity of silibinin on heavy metals. This research supports the use of silibinin as an adjunct for liver, kidney, pancreas, and other organ support in any heavy metal detoxification program. The importance of silibinin for heavy metal detoxification is in its ability to aid liver function and regeneration (Pietrangelo et al. 1995; Wellington et al. 2001), elevate glutathione enzyme levels (Gonzalez-Correa et al. 2002), reduce oxidation (Pietrangelo et al. 1995; Skottova et al. 1999), and improve cellular thiol status (Tager et al. 2001).

However, if the liver has already been damaged by toxic substances, silymarin and silibinin can help speed up liver regeneration. Silymarin and silibinin actually accelerated the rate of protein synthesis in the liver, leading to faster cell regeneration (Sonnenbichler et al. 1986; Valenzuela et al. 1994). At the Max Planck Institute for Biochemistry in Germany, Sonnenbichler et al. (1999) discovered that silibinin also protected the kidneys from toxic injury and produced accelerated kidney regeneration after toxic damage (e.g., from agents such as chemotherapy drugs). Because the kidneys can be damaged by analgesics, chemotherapy drugs, and other toxic substances, the finding that silibinin has protective benefits and even stimulates regeneration has tremendous clinical interest.

## **CONCLUSION**

For most people, acute heavy metal toxicity will rarely be a concern or pose a problem. However, certain groups are at a higher risk:

- Those who live in homes that contain lead pipes and lead-based paint or in areas having high environmental levels of elemental mercury, iron, or aluminum
- Those who work in industries that manufacture batteries, pesticides, and fertilizers or who are members of their households
- Those who work in industries that are involved in metal finishing
- Those who handle chemicals in scientific or laboratory settings

Exposure to heavy metals can be considered acute from an accident or chronic from long-term exposure. Unrecognized or untreated toxicity will likely result in illness and reduced quality of life. Testing is essential if you suspect you or someone in your household might have heavy metal toxicity. If test results are positive, initiation of appropriate conventional and natural medical procedures described earlier in the protocol might be required. However, there are many proactive things you can do to provide yourself with natural chelating, detoxifying, anti-inflammatory, and antioxidant qualities and to aid your vital organs in performing at their best.

## SUMMARY

If you suspect you have heavy metal toxicity, consult your personal physician. If you have a specific medical condition or are taking prescription medicine, you must also consult your personal physician about possible contraindications for your condition or possible drug interactions before using any suggested product. More aggressive treatment approaches for chelation therapy require the supervision and monitoring by a qualified medical health professional.

Observe workplace safety rules and follow procedures to protect yourself in the workplace. When leaving the workplace, follow decontamination procedures to avoid wearing contaminated clothing that could potentially expose other persons, particularly children in the home. At home, raise your awareness of potential sources of exposure to toxic materials. Take measures to limit access to toxic products. Whenever possible, replace toxic products with less dangerous alternatives. Properly dispose of those that are no longer needed. Learn to recognize the symptoms of ingested toxic substances. Learn first aid procedures. Display emergency contact numbers by the telephone.

Strive to achieve proper, balanced nutrition by choosing fresh (organic when possible) fruits, vegetables, grains, lean meat, and cold-water fish.

Consider taking supplemental antioxidants, herbs, minerals, amino acids, phytoextracts, detoxifying agents, protective agents, and fiber as adjuncts to a healthy diet to enhance vital organ functioning and to aid in your body's natural detoxifying actions. The dosage recommendations listed below are for healthy persons.

1. Life Extension Mix provides a convenient source of vitamins, trace minerals, amino acids, and herb extracts. The recommended dose of Life Extension Mix is 3 tablets taken 3 times daily.
2. Life Extension Booster contains three forms of selenium, vitamin E, and other important nutrients. The suggested dose is 1 capsule daily with any meal.
3. Vitamin C is an antioxidant known for its immune and oxidative benefits. A prophylactic dose of 2.5-6 grams daily from all of the various forms of vitamin C (including dietary sources) is recommended. Vitamin C may cause gastric upset for some people. Taking vitamin C with meals may alleviate gastric upset, as might using an antacid, buffering agent, or a buffered form of vitamin C.
4. Vitamin E has known antioxidant, immune enhancement, and cardiovascular benefits. The suggested dose is one 400-IU capsule daily. For therapeutic use, a dose of 1-5 capsules taken with meals is suggested.
5. Vitamin A has important antioxidant properties and proven benefits for cancer and heart disease prevention. A daily dose of one to two 25,000-IU capsules is recommended.
6. Glutathione is one of the body's most powerful antioxidants. A daily dose of two to six 750-mg capsules daily is recommended.
7. Selenium is an essential micronutrient that is important in immune and antioxidant functions. A recommended daily dose is one 200-mcg capsule of selenium.
8. Zinc is another essential micronutrient that is important in immune and antioxidant functions. One 30-mg capsule of zinc daily is suggested.
9. Lactoferrin is known for its ability to have an affinity for iron. One 300-mg capsule of Lactoferrin daily is recommended as a dietary supplement.
10. Garlic has been used for centuries for medicinal purposes and has proven protective benefits from pollutants, heavy metals, and cancer-causing substances. A recommended dose is two 200-mg capsules taken with meals.
11. Consider using cilantro. Cilantro is readily available from high-quality produce sources or as oil that can be rubbed into the skin. Steep 1-15 drops in hot water 2 times daily (5 days on, 2 days off). During mercury chelation therapy, stop using cilantro after 2 weeks or on the day therapy begins during the third week.  
Keep cilantro out of the reach of children. If you have any discomfort after taking cilantro, discontinue using it orally and try using cilantro oil on your skin (1 drop on the wrist twice daily).
12. Green tea has been demonstrated to be a powerful antioxidant. For protective purposes, one 725-mg capsule daily is suggested. For therapeutic purposes, consider taking two capsules.
13. Calcium is an essential mineral for maintaining healthy bones as well as having properties that block the absorption of free radical-generating iron into the bloodstream. Depending on individual requirements, 1000 mg is a beginning dose of supplemental calcium. A daily dose of one to two 1000-mg capsules is suggested. For those who have a low calcium-content diet or who do not take other calcium supplements, consider taking more. Calcium absorption and utilization is enhanced by also taking vitamin D3. It is recommended that calcium be taken daily in divided doses.
14. L-cysteine, N-acetyl-cysteine, and glutathione are important antioxidants. When taking L-cysteine, N-acetyl-cysteine, or glutathione, it is recommended that vitamin C also be taken to help maintain their powerful free radical-suppressing effects. Take 2-6 capsules of the supplement L-Glutathione, L-Cysteine, & C daily.
15. Alfalfa sprouts are available as a food product in most health food stores and may be added to salads or blended into a juice. Dried herbs from alfalfa leaves and sprouts may be brewed into a tea--1 oz steeped in 1 pint of water for 20 minutes--2 cups daily. Dried powder capsules may also be taken at a dose of 4-6 capsules a day. Due to its high iron content, alfalfa should

not be taken by individuals with toxic or chronic iron overload.

16. Include citrus fruit and foods containing buckwheat flour in your diet as natural sources of rutin. A convenient source of supplemental rutin is 1/4 tsp of Rutin Powder taken 2-3 times daily with a beverage.
17. Consider taking MSM, alpha-lipoic acid, glycine, and chlorella for their natural detoxifying benefits. MSM has anti-inflammatory benefits. A daily dose of one to three 1000-mg capsules is suggested. MSM is most effectively utilized when taken with meals. Alpha-lipoic acid is a universal antioxidant and meets all antioxidant evaluation criteria. For healthy people, take one to two 250-mg capsules daily. Glycine is a chemically simple and abundant conditionally essential amino acid. It combines with many toxic substances and converts them to harmless forms, which are then excreted. One tsp. of glycine powder provides 2.8 grams of pure glycine (1 gram or more may be taken because glycine is nontoxic). Glycine powder is easily soluble in juice or water and is not unpleasant tasting.

**Note:** *Chlorella causes diarrhea in some persons. Start with a small dose (i.e., two 500-mg tablets daily) and consider adding cellulose enzyme.*

18. Include daily dietary fiber from natural sources such as carbohydrates, fruits, vegetables, whole grain products, wheat bran, and beans, when possible. Supplemental fiber from Fiber Food Caps is another good source of natural, soluble fiber. Take 6 capsules with each meal and at least 10 oz of water. If necessary, use smaller doses at first until your digestive system adjusts to the added fiber. If gas or bloating occurs, reduce the dose until tolerance is achieved.
19. On an empty stomach, take one to four 200-mg capsules of SAME daily with water. Take folic acid, B12, and B6 when taking SAME.

SAME should not be taken with antidepressants except under a physician's care.

20. Consider silibinin and silymarin for their liver protective benefits. A suggested dose of Silibinin Plus is one 326-mg capsule taken 2 times daily. An alternative is one 100-mg capsule of Silymarin taken 4 times daily. Silymarin contains milk thistle standardized at 80%.

### FOR MORE INFORMATION

American Board of Chelation Therapy, (312) 266-7246; American College of Advancement in Medicine, American College of Nutrition, (727) 446-6086; American Association of Naturopathic Physicians, (877)969-2267; National Institutes of Health, (301) 496-4000; Food and Drug Administration, (888) 463-6332; Agency for Toxic Substances and Disease Registry, (888) 422-8737.

### PRODUCT AVAILABILITY

Life Extension Mix, Life Extension Booster, selenium, zinc, Lactoferrin, vitamin E, Vitamin C Caps, Beta-Carotene, Liquid Emulsified Vitamin A, garlic, green tea, L-cysteine capsules, N-Acetyl-Cysteine Capsules, L-Glutathione, rutin powder, MSM, lipoic acid, glycine powder, fiber, SAME, Silibinin Plus, and silymarin are available from Life Extension by telephoning (800) 544-4440 or by ordering online.



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