# Diagnosis and Treatment of Heavy Metal Toxicity

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When using an integrative approach to medicine, one is often presented with a patient who has numerous general symptoms. These typically include fatigue, muscle aches, cognitive impairment, neurological problems, mood disturbances, and other signs of metabolic and nutritional derangements. Patients have usually been to several physicians or specialists, with no unifying diagnosis.

Symptoms of heavy metal toxicity include anemia, fatigue, musculoskeletal complaints, mood disturbances, neurological problems, high blood pressure, kidney and liver dysfunction, gastrointestinal (GI) and endocrine problems, and immune system dysfunction. In other words, heavy metal toxicity causes a systemic, biochemical maladaptation of the system. It presents in various body systems, depending on where the biochemical imbalance or disruption occurs, or the area(s) of deposition of the metal (e.g., brain, pituitary, kidneys).

Heavy metals are eliminated through the urine, feces, and sweat glands. It is when the natural eliminatory routes are compromised, and our exposure is increased, that we begin to experience toxic effects.

Chronic exposure to heavy metals is becoming a serious health problem worldwide. There is con-tamination of the air, soil, and water, along with the general accumulation of toxic heavy metals in the body that occurs with age. It seems that as we age, in addition to accumulating heavy metal burdens, we are increasingly susceptible to their toxic effects.(1) These unfortunate trends mandate that we, as clinicians, consider toxicity in our patients' health assessments.

**Table I: Lab Testing for Heavy Metals**

| | RBC | Lymphocyte | Hair | Blood | Serum | Urine | Provoc | Other |
|---|---|---|---|---|---|---|---|---|
| **Aluminum** (Al) | | | **TT**(32) | | **TT**(33) | | **EDTA** | |
| **Arsenic** (Ar) | | | **TT**(34) | **T** | | **TT**(35) | **(TT) DMSA** | |
| **Cadmium** (Cd) | | | **TT**(36) | **P**(37) | | | **EDTA** | |
| **Copper** (Cu) | | | **T** | **T** | | | **Penicillamine** (38) | **(TT) RC SOD**(39) |
| **Mercury** (Hg) | **TT**(40,41) | | **TT**(42,43) | **Methyl Mercury** | | **P** | **(TT) DMSA DMPS** | |
| **Iron** (Fe) | | | **P** | | **T**(44) | | | **Ferritin** |
| **Lead** (Pb) | **TT**(45) | | **TTT**(46) | **T**(47) | **TT** | **TT**(48) | **(TT) EDTA DMSA**(49) | **(TTT) BM Biopsy**(50) |
| **Magnesium** (Mg) | **TT** (WBC>RBC) | | **P**(51) | **T** | **TT**(52) | **TTT** | **Mg Challange** for deficiency | |
| **Manganese** (Mn) | | **TT** | **T**(53) | **TT**(54) | **T** | **TT** | | **Fecal Hg** for exposre |
| **Selenium** (Se) | | | **TT**(55) | **TT**(57) | **TT**(57) | **T**(58) | | |
| **Zinc** (Zn) | **TT** | **TT** | **T** | **T** | **T** | | | **Zinc taste test**(59) |

**P - Poor T - Fair TT - good TTT - Excellent**

**Prevalence of Lead**

Lead has been around since the start of recorded civilization. Exposure to lead and other toxins have all increased since the industrial age. Air, water, soil, industry, and food are sources of heavy metal contamination. Land adjacent to foundries, gas stations, and highways are contaminated with lead. In a 1991 report for the USDA, gardens in

Maryland were found to contain lead levels as high as 5,000 ppm. The Environmental Protection Agency (EPA) considers soil with more than 500 ppm of lead to be hazardous.

Lead has been shown to cause learning disabilities and neurological problems in children. All pediatric patients are presently tested for blood lead levels. The Port Pirin Cohort study showed that the cognitive deficit associated with childhood lead exposure appears to be only partially reversible, even when the blood levels are decreased.(2) Recent evaluation of the NHANES III study, conducted by the National Center for Health Statistics, yielded several conclusions. Data suggest that subtle health effects, such as lower IQ scores in children, may extend to blood lead levels well below the 10 ug/dL threshold.(3) There was also evidence that this may extend to cognitive function in middle-aged and elderly men.(4)

"There is increasing evidence that the effects of lead toxicity span the gamut from sub-clinical to classical clinical effects." Lead affects the nervous system, cardiovascular system, the endocrine and immune systems, the heme-containing enzymes, and the reproductive functions.(5)

Furthermore, an association between environmental lead exposure and increased prevalence of dental caries was observed, although a causal link was not found.(6) Watson discovered that exposure to lead, in utero and after birth, results in a high rate of dental cavities in laboratory rats.(7)

It was also found that serum ascorbic acid level is an important independent correlate of blood lead level. If a causal relationship is confirmed, this may justify use of higher levels of ascorbic acid for the prevention of lead toxicity in the general population.(8) Lead paint and lead gasoline were only recently banned.

**Dangers of Mercury**

In 1940, Hunter and Russell found methyl mercury poisoning in factory workers producing a mercurial fungicide for cereal.(9) In 1956, Minamata disease was identified. It was found that nearly 150 tons of industrial methyl mercury was dumped into Minamata Bay, causing the syndrome.(10)

High accumulations of methyl mercury are sometimes found in fish. Data from Finland suggest that high intake of mercury from fresh-water fish is associated with increased incidence of acute myocardial infarction, death from coronary artery disease, and cerebral vascular disease. This result may be due to the promotion of lipid peroxidation from mercury in fish.(11)

Elemental mercury, from dental amalgams, is lipid soluble and crosses the blood-brain barrier. A direct link between mercury fillings and disease is yet to be proven. Central nervous system (CNS) toxicity, manifested by symptoms of mood and cognitive dysfunction, are found to be associated with an elevated body burden of mercury. This can be secondary to mercury vapor from dental amalgam fillings.(12)

Chewing releases increased intraoral Hg from amalgams. This has been reported as a major source of chronic mercury exposure.(13) Mercury released from amalgams can increase Hg resistance and antibiotic-resistant plasmids in the oral bacterial flora. This has implications for the effects of mercury, not only influencing the immune host response, but also effecting changes in bacterial virulence.(14) Bigazzi reviews the literature and finds strong associations between autoimmunity and heavy metals, particularly cadmium, gold, and mercury. Solid evidence indicates that mercury can induce autoimmune disease of the TH 2 cell type (Ab mediated) in humans and experimental animals.(15,16)

In addition, mercury inhibits the polymerization of tubulin, resulting in brain lesions resembling those found in Alzheimer’s disease.(17) Mercury can cause fatigue by several mechanisms: (a) by inhibiting conversion of T4 to T3, (b) by interfering with hormone metabolism, and (c) by depleting glutathione and lipoic acid.(18)

The FDA Public Health Service and American Academy of Pediatrics have issued a joint statement requesting that thimerosal, a mercury-containing preservation, be removed from vaccines. The thimerosal-containing vaccines are DTaP, DPT, hepatitis B, and HiB.(19)

**Other Toxic Heavy Metals**

Research is currently finding other heavy metals that may affect health adversely. For example, chromium is an essential mineral in glucose metabolism. However, the hexavalent form of chromium (Cr VI) is a potent inhalant toxicant in metallurgy and metal sculpture. Chronic genotoxicity manifests as gene mutation. At the cellular level, chromium leads to cellular apoptosis and neoplastic transformation.(20)

Antimony compounds are used in manufacturing in semiconductor industries. Research is finding that antimony can cause potent genotoxic and cytotoxic damage to cells. Evidence points to an increasing cancer risk from exposure to semi-conductive metals such as antimony. Antimony also affects the pulmonary and circulatory systems. Studies demonstrate that metals, such as antimony, thallium, and iridium, alter cellular defense mechanisms involved in the carcinogenic process.(21) Heavy metals (particularly arsenic and hexavalent chromium) are considered human carcinogens. They apparently alter the expression of specific, susceptible genes.(22)

Cadmium is a toxic metal used in industry. The mining process releases about 1.3 million lbs of cadmium into the air

every year. Cigarette smoke is another potent source of cadmium. One pack of cigarettes deposits about 4 mg of cadmium into the lungs of a smoker.

Arsenic toxicity involves the nervous, cardiovascular, GI, genitourinary (GU), hemapoietic, and dermatological systems. It impairs cellular respiration by inhibiting mitochondrial enzymes, substituting for phosphorous in ATP, inhibiting sulfhydryl-containing enzymes, and uncoupling oxidative phosphorylation.(23)

Sulfhydryl reactive metals promote the formation of lipid peroxidation and reactive hydroxyl radicals. They inhibit antioxidant processes, deplete glutathione, bind to proteins, and derange enzyme systems.

Aluminum has been shown to be a neurotoxin. It increases free-radical pathology, accelerates iron-induced lipid peroxidation, and produces cross-linking between molecules. This produces cellular damage, especially to neurons in the brain.

Recently, a protein, DMTI, has been identified. It is located in enterocytes and other cells. This molecule, referred to as a divalent metal ion transporter, displays a broad selectivity with transport capacity, decreasing in order from Fe++, Zn++, Mn++, Co++, Cu++, Ni++, Pb++. It is possible that this carrier contributes to the etiology of certain neurodegenerative diseases. It could promote generation of ROS by divalent cations, resulting in lipid peroxidation and damage to essential cellular elements. This mechanism of cell membrane transport, for a variety of cations, may have important chemical and toxicological implications.(25) For example, a high expression of DMT1 occurs in the substantia nigra. In Parkinson's disease, an increased accumulation of iron in neurons may contribute to increased cell death.

**Role of Minerals**

Minerals, such as magnesium, zinc, calcium, selenium, and manganese, function as co-factors in various enzyme systems of the body. The toxic heavy metals inhibit metabolic actions by displacing trace minerals, inhibiting enzyme systems, and attaching to proteins. Deficiencies of some minerals (e.g., zinc, calcium, iron, magnesium, manganese, and selenium) augment heavy metal toxicity.

The effects of food refining and its depletion of minerals aggravate the problem. The trace minerals are concentrated in the germ layer of grains. Heavy metals/trace mineral ratios are elevated with refined flour, since the heavy metals are concentrated in the remaining portion, and the trace minerals are discarded in the germ layer.

**Diagnosis**

As you can see from Table 1 on page 8, there is no first-line, conclusive lab test for diagnosing heavy metal toxicity. More tests are usually required to get a clear and accurate picture of blood or tissue levels. These tests include red blood cell mineral levels, blood and serum levels, and provocative testing.

Hair analysis is an excellent way to identify certain heavy metal toxicities. However, it is often over-utilized for diagnostic and therapeutic regimes. When evaluating results, one needs to rule out external contamination. Red blood cell mineral testing also gives a fair picture of mineral levels.

An ethylenediaminetetraacetic acid (EDTA), dimercaptoproprionsulfonic acid (DMPS), or dimercaptosuccinic acid (DMSA) challenge test can be performed to glean additional information. If a urine measurement is elevated after a challenge with a chelating substance, it can signify an increased body burden of that particular heavy metal. DMSA is used to chelate mercury, lead, arsenic, and cadmium.

An elevated lead level can obscure an elevated mercury level. Because lead accumulates in bone, measurements of lead in bone may prove to be a useful biomarker for a chronic accumulated dose. Studies show that heightened bone turnover (during pregnancy, lactation, and aging) may liberate an increased burden of lead, resulting in delayed toxicity.(26)

**Treatment**

A treatment regime starts with a review of an individual's diet, making sure it is rich in minerals and not a source of potential heavy metal (e.g., high-fish diets). In addition to food, one needs to look at the water source. Water can be contaminated with heavy metals. In addition, any toxic exposures from household products, hobbies, and occupational activities need to be explored and eliminated at the start of a treatment regime. If a person has "silver" amalgams, a biologically oriented dentist needs to evaluate the state of the amalgams and the potential for removal.

Note: Removing fillings can be an exhaustive and costly procedure. The benefit/risk ratio should be carefully evaluated before taking this step.

Supplemental minerals are also recommended. Adequate calcium, magnesium, zinc, selenium, chromium, iron, molybdenum, and manganese are some of the most essential minerals. The individual also needs adequate stores of sulfur and sulfhydryl compounds, such as glutathione and cysteine. Dietary sources of sulfur include garlic, onions, eggs, cruciferous vegetables (e.g., broccoli, brussels sprouts, cauliflower), and green leafy vegetables (e.g., kale,

spinach, dandelion, endive).

Nutritional agents that help with heavy metal toxicity include vitamin C, alginate, glutathione, methylsulfonylmethane (MSM), and minerals such as selenium and zinc. Amino acids and amino acid complexes, such as cysteine, methionine, seleno-methionine, S-adenosyl methionine (SAM), and alpha lipoic acid, all contain sulfhydryl groups and help chelate heavy metals out of the body.

Intestinal agents such as psyllium increase transit time in the bowel. The fecal route of excretion is important, especially with respect to mercury. Green products, especially chlorella, help absorb mercury and other metals and remove them from the colon. Cilantro is an herb with an affinity for mercury.

**Use of Chelating Agents**

A chelating agent is used in a detoxification program to help pull heavy metal ions out of the body. A chelating agent is a substance that can form several bonds to a metal ion. EDTA is a chelation agent used to remove lead, cadmium, aluminum, and other metals from the body. It is given in an intravenous drip and can be administered in the office over the course of a few hours. It is important to monitor renal function, since EDTA is excreted through the kidneys. The calcium is exchanged from the heavy metal, and the stable metal chelate is excreted in the urine. Other, beneficial minerals can be removed with chelation, so it is important to supplement with multi minerals.

DMPS is a chelating agent, used parenterally, for arsenic, mercury, and lead removal. Deferoxamine is a chelating agent used for iron overload. DMSA is a water-soluble, oral form of chelation, effective for mercury, lead, cadmium, and arsenic. DMSA effectively removes mercury from the blood, liver, brain, spleen, lungs, large intestine, muscles, and bone. However, DMPS was found to be the most efficient chelation method for mercury removal from the kidneys.(27)

DMSA enhances the excretion of inorganic and organic mercury. DMSA is excreted in the urine as a cysteine-DMSA complex.(28) When administering DMSA to patients, N-acetyl cysteine (NAC), at 250 mg/day, should be given. Higher doses can cause mercury to be carried across the blood-brain barrier. This can be minimized by administering branched chain amino acids (BCAA) with the cysteine.(29) The affinity of DMSA for metals is in this order: Cd++ > Pb ++ >Fe++ > Hg++ > Zn++ > Ni++.(30)

One study, using EDTA and DMSA, showed a decrease in tissue burden and an increase in urinary output of lead. The results of the combined therapy was better than each therapy alone. In addition, no increased burden of tissue metal toxicity was observed in the brain.(31)

DMSA can be given in 500-mg capsules every other day for five to six weeks, with one to two weeks off. Repeated courses are determined by the situation, treatment results, and evaluation on retesting for heavy metal levels, e.g., RBC mineral and/or provocative testing.

DMSA can be started one to three weeks prior to amalgam removal. In addition, 500 mg of DMSA can be taken on the day of the dental procedure. After the procedure, 20 g of intravenous vitamin C can be administered. It is important to consult a biologically oriented dentist who has been trained in these procedures and has the appropriate equipment.

**Conclusion**

While we have offered an overview of heavy metal toxicity, this article can only begin to survey the field. With awareness of the problem, avoidance of some of the sources of heavy metals, new testing techniques, removal, detoxification, and nutrient supplementation, we can start to tackle the health threat of heavy metal toxicity.

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