Heavy Metal Sources, Effects, and Detoxification

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The human environment has exposed the human species to heavy metals since time immemorial, and antiquity is replete with examples of lack of knowledge about the impact that these elements can have on health. With the advent of industrial society, the overall environmental "load" has increased dramatically to the point where literally no one is unaffected. Heavy metals are present in virtually every area of modern consumerism—cosmetics, health care, medications, energy, transportation, and construction. This review focuses primarily on cadmium, lead, mercury, and nickel. These metals occur abundantly in modern life (see Table 1), and they have similar toxic actions on the human body. Other metals (arsenic, uranium, beryllium, strontium, and radium, for example) that have an adverse effect on human health are not within the scope of this article.

It is usually the environment that over- or understimulates the balance of the body's physiologic processes. It has long been a tenet of osteopathy and traditional medicine in general, that distortion of the normal movement of any cell, organ, or system precedes disease or degeneration. Heavy metals act to distort the normal function or movement of the body. The motivation for this paper came from the understanding that heavy metals are ubiquitous in the environment and in human physiology and that these metals produce a "cascade effect" in the body. This means that they will debilitate an organ or system and then another area that is removed from this is affected—not an uncommon scenario in the practices of most alternative practitioners.

Diagnosing Toxicity

Pure heavy-metal toxicity as a sole diagnosis is rare, but it is not unreasonable to suspect it as a contributing component to many, if not most, of the conditions that cause patients to seek medical attention. A significant complication in the recognition of heavy-metal toxicity is that the effects of heavy metals are often delayed because the metals accumulate in the body, where they have half-lives of many years.[1] Although the metals may have been present for long periods of time, they are overlooked as a causative factor in a patient's condition, which is frequently misdiagnosed. Simply looking at the number of people with mercury fillings or other nonprecious metals in their mouths provides support in favor of this point. The best way to address this "sleeping elephant" is to pay close attention to the patient's history. If a patient has suspected exposure to any heavy metal, including mercury or other nonprecious metal fillings, this must be primarily addressed to ensure stability of treatment and long-term prevention of other conditions. It is important for the health care provider to know enough about a patient's employment, residence, hobbies, and past and present lifestyles to be able to perform an investigative diagnosis. It may be presumed that heavy metals could be playing a role in a patient's difficult-to-diagnose condition. If possible exposure is not addressed in the treatment protocol, treatment results could be disappointing or the patient will show improvement and then have a recurrence of the old symptoms.

As is examined in detail below, exposure to any of the four heavy metals discussed here may damage multiple tissues, organs, and systems of the body. For example, any of the metals can seriously increase the heart's susceptibility to infective myocarditis, alter the mineral balance in heart muscle tissue, and profoundly depress the immune system.[2] Studies conducted by Eggelston[3] have shown this effect with nickel and mercury. The toxic effects of heavy metals on the kidneys—which concentrate heavy-metal–rich urine for elimination—have been long recognized, as have the effects of these metals on the liver, the principal organ of detoxification. Perhaps one of the most significant aspects of heavy-metal toxicity is the permanent effect on developing tissues. Tissues, organs, and systems that are exposed to heavy metals when the organism is young and developing incur permanent damage that is not reversible with current therapy. Table 2 summarizes some of the symptoms of heavy-metal toxicity commonly seen by health care providers.

The effects of any heavy metal on an individual may localize in specific areas or, as indicated previously, show up as symptoms that are far removed from the commonly associated conditions as reported in the literature. It is risky to assume that a patient whose symptoms do not appear in Table 2 is not, therefore,

Occupational and environmental cadmium exposure have been linked to prostate cancer and male infertility in studies.

Table 1. Common Sources of Heavy Metal Exposure

Food; food production, preparation, and packaging[a]	Cd	Pb	Hg	Ni
Acid rain; water	Cd	Pb	Hg	Ni
Energy production[b]	Cd	Pb	Hg	Ni
Dental fillings/dental work	Cd		Hg	Ni
Tobacco/tobacco smoke	Cd	Pb		Ni
Sewage sludge	Cd	Pb	Hg	
Medications[c]		Pb	Hg	
Incineration of trash and waste		Pb	Hg	
Mining and smelting	Cd			
Lead based paint		Pb		
Firing guns		Pb		
Household dust in older homes		Pb		
Lead solder in pipes		Pb		
Crematoriums			Hg	
Inexpensive earrings				Ni
Cosmetics[d]				Ni

Cd = cadmium; Pb = lead; Hg = mercury; Ni = nickel.

[a]Cadmium is used in some foreign-manufactured food and beverage containers and is a component of some phosphate fertilizers. Some wines contain significant amounts of lead, which also occurs in "tin" can food containers and some pottery glazes. The elevated tissue and blood mercury levels of fresh water and saltwater fish have been monitored for several decades. Nickel enters the human body through cookware and through hydrogenated fats, which are made with a nickel catalyst; [b]Many types of fuel contain lead. Coal burning releases mercury. Energy storage batteries contribute significant amounts of cadmium, lead, and nickel to the modern waste stream; [c]Use of a mercury-containing preservative in production of hepatitis B vaccines has exposed countless infants to this metal. Some imported herbal remedies have been found to have dangerous levels of lead; [d]Nickel has been found especially in eye makeup and hair colors (see Ref. 52).

affected by a heavy metal. This is the diagnostic challenge. However, treatment for toxicity to any one metal is usually very similar to treatment for the toxicity to others, and a good oral supplement usually contains ingredients that can address this without overwhelming the patient with extremely complicated treatment.

Cadmium

Cadmium has an extremely long biologic half-life of 15–20 years in human beings. (This is not uncommon for the heavy metals in general and, as such, presents one of the most challenging aspects of detoxification.) For many years, it has been recognized that exposure to cadmium can lead to such chronic adverse health conditions as renal tubular dysfunction, liver damage, myocarditis, pulmonary emphysema, kidney damage, immune-system depression, and distorted calcium metabolism with attendant osseous effects, possibly osteoporosis. In fact, cadmium and cadmium-containing compounds were classified as human carcinogens in 1993 by the International Agency for Research on Cancer.[4]

The sources of cadmium are diverse and a particular person's exposure may be from one or more sources. See Table 1 for a listing of some ubiquitous sources of cadmium exposure.

The literature suggests that particular periods in an individual's life and certain organs in his or her body are most seriously affected by the presence of cadmium. Tests of laboratory animals have shown that low-level, multigenerational exposure to inorganic cadmium can affect the nervous system. (Because the heavy metals under consideration pass the placental barrier and are present in mothers milk, there is a legacy of toxic burden build up passed from generation to generation.[5] This strongly suggests that human populations who are exposed to cadmium may be at risk of developing neurologic disorders.[6]

A study conducted in Belgium in 1997 substantiated that cadmium is neurotoxic to the peripheral nervous system. The researchers concluded that an elevated body burden of cadmium promotes the development of peripheral polyneuropathies (PNPs). This is significant, because as many as 24 percent of PNPs cannot be related to specific causes.[7]

The liver is a major target organ of cadmium toxicity, as it is of the other three metals examined in this review. Metallothionein, a cysteine-rich metal-binding protein, has been shown to play an important role in resisting cadmium-induced liver damage. Although exposure to cadmium does not appear to elevate liver enzyme levels, investigators have noted the following hepatic effects: granulomatous inflammation; nonspecific chronic inflammation; apoptosis; an ongoing attempt by the liver to regenerate; and formation of preneoplastic nodules.[8]

One must ask whether heavy-metal exposure is creaing large numbers of permanently physically and emotionally handicapped individuals.

Cadmium can cause renal disease directly but, in susceptible individuals with diabetes, hypertension, cardiovascular disease, and genetic predispositions, reserve renal capacity is compromised, which results in additional risk.[9]

Occupational and environmental cadmium exposure have been linked to prostate cancer and male infertility in studies conducted at the George Washington University School of Medicine, Washington, D.C, and New York University School of Medicine, New York City.[10,11] This would suggest that the male reproductive organs are a target for heavy-metal accumulation.

Among the metals covered in this article, cadmium is unique in its ability to produce pulmonary inflammatory disease and lung cancer.[1,2] Likewise unique is cadmium's interaction with calcium in the skeletal system to produce osteodystrophies.[12] The implication is the possible involvement of cadmium in osteoporosis. Interestingly, aluminum reacts with calcium in the same way.[12]

Lead

The toxic effects of low-level lead exposure have captured the attention of researchers, the media, and governmental authorities like those of no other heavy metal in recent times, with the exception of mercury, as mentioned below. Despite all this attention, lead persists today as a significant concern for inner-city residents, low-income individuals, and residents of the northeastern region of the United States. With the removal of lead in gasoline beginning in 1972 and concluding in 1995, a fourfold reduction in blood lead levels in U.S. children has been achieved.[5,13]

Because of fetal sensitivity to lead, much emphasis has been placed on fetal/maternal toxicologic issues, especially because heavy metals pass from the mother to the child via the placenta and lactation.[14]

Even if a child has not been exposed directly to environmental lead, the mother's body burden is transferred transplacentally to the fetus.[15] This fact raises some disturbing questions in light of findings presented at a conference on The Role of the Environmental Neurotoxicants on Developmental Disabilities, in New York City, on May 24–25, 1999, at Mount Sinai School of Medicine, Bronx, New York, where more than 300 health scientists and physicians examined the growing body of evidence linking environmental toxins to neurobehavioral disorders.[16] The inclusion of Parkinson's disease in the group's discussions was intended to signal the notion that exposures in early life may have an influence on the evolution of neurologic diseases as humans age.[16] One must ask whether heavy-metal exposure is creating large numbers of permanently physically and emotionally handicapped individuals.

Exposure to lead can damage DNA, depress the immune system, and result in anemia, hypertension, kidney disease, and increased tooth decay. Lead exposure is also associated with learning disabilities and reduced intelligence quotients.

The adverse effects of lead on the human body have been studied for the past 100 years. Because lead is retained in the body for so long (with a half-life in bone of 62 years) health care practitioners will see this problem for many years to come, although environmental levels are receding.[13] The cumulative studies have uncovered important information about how lead is processed, stored, and excreted by the body. One study found a 40 percent increase in dental caries and a 30 percent decrease in parotid gland functioning in people who had been exposed to lead,[13] over those who had not been exposed. Another study demonstrated that lead is mobilized from the bones of mothers who are lactating, resulting in milk lead levels that exceed those in the mother's serum.[13] This remobilization of lead stores in the body can also be the result of pathologic processes.[17] In fact, 45–70 percent of lead in the blood comes from long-term tissue stores.[17] The detri-

Table 2. Common Symptoms and Conditions Associated with Heavy Metal Toxicity

- Headaches
- Mineral imbalances (particularly calcium and zinc)
- Kidney dysfunction
- Fertility problems (in males and females)
- Abnormal pregnancy outcomes
- Chronic immune system depression
- Nonresponsive or recurrent *Candida albicans* infection
- Tinnitus
- Contact dermatitis from metal jewelry
- Learning disorders
- Panic attacks
- Broad mood swings
- Memory loss
- Fibromyalgia
- Demyelinization diseases (multiple sclerosis and amyotrophic lateral sclerosis)
- Alzheimer's disease

Please note: This is not a complete list. Individual symptoms can be highly variable and can be mixed with other symptoms.

Elevated blood levels of lead and lead poisoning still affect nearly one million children in the United States.

Table 3. Chemical/Pharmaceutical and Nutritional Metal Detoxification Methods

Conventional medical chemical therapeutic agents				
D/L-penicillamine	Cd	Pb		
D-penicillamine			Hg	Ni
Neomynophagen C	Cd			
EDTA	Cd			
British anti-Lewisite (BAL)	Cd			Ni
Succimer (DMSA)		Pb	Hg	
Edetate calcium disodium		Pb		
DMPS			Hg	
Dithiocarb[a]				Ni
Antabuse[b]				Ni
Nutritional supplements				
Zinc	Cd			Ni
Selenium	Cd		Hg	
N-acetyl cysteine	Cd		Hg	
Sodium alginate	Cd	Pb	Hg	
Thiamine	Cd			
Methionine	Cd			
Vitamin C		Pb		

DMPS = sodium 2,3-dimercaptopropane-1-sulfonate; EDTA = ethylenediaminetetraacetic acid.

[a]Dithiocarb generic is sodium diethyldithiocarbamate; [b]Antabuse generic is tetraethylthiuram

mental impact on the baby is obvious. Maternal toxic-lead exposure has been associated with the birth of low–birth-weight children and with impaired neurobehavioral development, aggressive behavior, and reduced stature in children.[15,18] In Baltimore, nearly 50 percent of the children screened in 1993 had blood lead levels exceeding the guidelines established by the Centers for Disease Control and Prevention.[19] Elevated blood levels of lead and lead poisoning still affect nearly one million children in the United States.[16] A particularly troublesome study indicates that lead is "unusually effective" in damaging the DNA sequence.[20]

In adults, anemia, hypertension, and kidney disease are the ramifications of chronic lead exposure.[18] Lead replaces zinc in the heme enzymes and conflicts with iron metabolism.[12,18,21] Immune-system depression was noted by Basaran and Undeger in their 2000 study of workers in a battery plant. T-cell helper lymphocytes immunoglobulin G, I M, C3, and C4 complement levels, chemotaxis and random migration of neutrophils were all significantly depressed.[20]

As a potent inhibitor of many of the enzymes in the brain, lead can induce functional problems. In particular, the disturbance of specific cerebral glucose substances may place lead exposure in question as a risk factor for some neurologic degenerative disorders, including some forms of Alzheimer's disease.[22]

Mercury

In the last 10 years, no heavy metal has received as much media or research attention as mercury. This attention is well-founded. Mercury, of the metals under discussion, is arguably the most neurologically toxic. Despite efforts to reduce the levels in the environment, mercury has been difficult to control. It is the only heavy metal, other than nickel, that is implanted into the bodies of millions of North Americans each year in the form of mercury-silver fillings. It is estimated conservatively by the U.S. Bureau of Mines 1991 *Minerals Yearbook*[23] that 50 tons of mercury are used by the dental profession in the United States alone each year. Because of this, people are exposed directly and environmentally. Use of mercury-containing dental amalgams has been curtailed by the governments of Sweden and Germany, and, to a lesser extent those of Austria, Norway, France, the United Kingdom, and Canada. It is not the purpose of this paper to discuss the nonhealth issues surrounding heavy metal exposure. However, when people's lives are damaged as a result of the use of a material that is no longer necessary in the dental profession, unrelenting attention must be called to this issue to facilitate change.

One study demonstrated a significant occurrence of neuropsychologic and motor control effects in a population of dentists compared to a control group of nondentists.

Most of the medical research on mercury centers on its effects on the central nervous system (CNS), the immune system, and the renal and reproductive systems. Mercury is absorbed by the body in several forms, organic or methylated, inorganic, and elemental. Each form has a different metabolic pathway. Excretion is primarily fecal via the liver and biliary avenues. However, some urinary elimination does occur.[16]

The CNS effects are well-documented. The inhibition of the binding of guanosine triphosphate to tubulin in the brain is similar to that noted in lesions seen in the brains of people with Alzheimer's disease.[24] Mercury appears to interact with tubulin and result in the disassembly of microtubules, which function to maintain neurite structure.[25] Mercury also disturbs the brain's neuronal protein metabolism.[26,27]

One important study demonstrated a significant occurrence of neuropsychologic and motor control effects in a population of dentists compared to a control group of nondentists.[28,29]

Another research group is exploring the possibility that mercury acts to demyelinate motor nerves, resulting in tremor-related conditions, such as multiple sclerosis, amyotrophic lateral sclerosis, and Parkinson's disease.[29,30]

Mercury exposure has two notable effects on the immune system: The metal can induce autoimmunity in rats,[31–33] which would support the concept of mercury's connection to the demyelinization diseases. Mercury also depresses cellular immune response.[33] Low-level mercury exposure inhibits most animal and human lymphocyte functions, including proliferation, expression of cell activation markers on cell surface, and cytokine production.[34,35]

There is significant increase in the kidney concentration of mercury after amalgam placement in monkeys, sheep, and humans.[36–39] The accumulation and degradation of such sulfhydryl-containing ligands as albumin and glutathione in the proximal tubular epithelial cells cause acute tubular necrosis. This produces a fall in glomerular filtration rate and ultimately triggers renal failure.[40]

Occupational exposure to mercury and its negative effect on fertility, pregnancy outcome, and fetal brain development has been documented in the literature. Heavy metals, in general, have been suspected of having a negative influence on the reproductive system; however, it is clear that additional research in this area would assist the diagnosis and treatment of patients with reproductive dysfunction.[41–44]

Two sources of mercury exposure pose potentially widespread and enduring health risks. Thimerosal, a derivative of mercury, has been used since the 1930s as an antibacterial additive to many vaccines, including those against hepatitis B, which are given routinely to infants. Results of pre- and postinjection blood samples indicate significant elevation of blood mercury levels. Because mercury is a neurotoxin, infant exposure is of great concern.[45] A second troubling observation is that mercury creates antibiotic resistance in oral, intestinal, and respiratory bacteria.[46,47] The implications of this are enormous when the prevalence of mercury-containing amalgam fillings is considered in light of the ever-increasing problem of antibiotic-resistant life-threatening infections.

Resources

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This high-level scientific group of dentists, M.D.s, and Ph.D.s supports mercury-free, nontoxic dentistry.

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This company provides a mercury detoxification product called Mercury Detox.

Nickel

Unlike the other metals discussed in this article, nickel is an essential trace element in several animal species, who expe-

Evaluation of a patient for heavy-metal exposure should entail a thorough diagnosis that includes hair analysis.

rience depressed growth, altered serum lipids and glucose levels, and lowered reproductive rates, in the face of nickel deficiency. However, a deficiency relationship in humans has not been reported in the literature.[48,49] Nickel is not a cumulative toxin in the human physiology, but the metal's abundance in modern culture creates ample opportunity for chronic long-term exposure.[50] Table 2 lists some common sources of nickel exposure.

The literature reports a broad range of toxic effects of nickel. They include acute pneumonitis from nickel-dust inhalation, rhinitis and sinusitis from nickel aerosols; cancer of the nasal sinus and lungs; and dermatitis and other related allergic reactions from cutaneous exposure to nickel alloys.[51,52] Cutaneous nickel allergy or dermatitis is very common, affecting between 15 and 30 percent of the population.[50] There are also reports of a nephrotoxic effect of excessive nickel exposure.[51] Supporting this study is the fact that liver and kidney enzyme activities increased after 15–30 days of cutaneous exposure to nickel.[51] The allergic/immune response probably has the greatest clinical significance in terms of the sheer number of individuals involved. Acute toxicity is almost exclusively related to industrial and workplace exposure. As such, the diagnosis of nickel toxicity is easier to target than are some other types of metal toxicities.

Although the amount of research on nickel toxicity is less than that for the other metals discussed here, the substantial and continuing opportunities for chronic exposure warrant the attention of every clinician and suggest that every attempt should be made to limit each patient's body burden of nickel.

Detoxification with Nutrients

Evaluation of a patient for heavy-metal exposure should entail a thorough diagnosis that includes hair analysis. Although this diagnostic tool has the limitation of no-limit values (except for mercury) for the metals discussed, reference ranges have been established.[52] The Environmental Protection Agency accepts hair analysis as a valid marker for heavy metal exposure.[53] Proper harvesting of the sample and skilled laboratory analysis are essential.

The removal of heavy metals from the body can be divided into two primary strategy categories for each metal discussed. The first is use of chemical therapeutic agents, frequently prescription drugs. The second approach uses commonly available nutritional supplements. This discussion gives preferential treatment to the nutritional approach, with only passing mention of the conventional chemotherapeutic agents.

Many approaches to heavy-metal detoxification have been taken over the years. The procedure described in this article is but one of these. This procedure is, however, based on sound science to validate the effectiveness and safety of the components. This in no way negates other techniques that may or may not have Western medical/scientific backing but are effective nonetheless. It is beyond the scope and breadth of this article to include them all.

Table 3 summarizes some of the most widely used chemical/pharmaceutical and nutritional methods of reducing the toxic load of heavy metals in people who have been exposed to these metals. The instances in which a single nutrient addresses several heavy metals reflects the fact that the biochemistries of the metals are similar.

One cannot overemphasize the significance of sulfhydryl compounds and glutathione in the human metabolic pathways concerned with heavy-metal detoxification. One of the major targets for binding heavy metals in proteins is glutathione, an important low-molecular-weight sulfhydryl compound in mammals. Metals readily bind to the sulfhydryl group, thus blocking availability of glutathione for other key cellular antioxidant activities.[54,55] Once inactivated, the glutathione cannot participate in its key function in phase-II liver detoxification.[55–57]

Two of the most important components of nutritional support for rebuilding glutathione are sulfur and the amino acid cysteine. Garlic, cruciferous vegetables, and eggs are good sources of nutritional sulfur. Because of its natural occurrence in the body and excellent bioavailability, methylsulfonylmethane (MSM) has been shown to increase the levels of the amino acids cysteine and methionine safely and effectively.[58] Both of these are key nutrients for glutathione synthesis and heavy-metal detoxification respectively.[59] In addition to providing sulfur, MSM is a free-radical scavenger and promotes cellular permeability.

Another beneficial supplement is sodium alginate. The literature is very clear that this naturally occurring sea product has broad and effective applicability in the removal of heavy metals and prevention of their absorption in the gastrointestinal tract. This compound has also been shown to promote the removal of radioactive metals such as strontium.[60,61]

Additional Detoxification Therapies

Four common therapies use treatment other than nutritional supplement detoxification protocols:

1. *Intravenous sodium 2,3-dimercaptopropane-1-sulfonate (DMPS)*—This is an accepted protocol for the removal of mercury, arsenic, lead, and cadmium. This treatment must be done under the care of a physician. Because all minerals with a similar valence will be removed, it is necessary to monitor kidney function because this is the path of excretion.
2. *Intravenous ethylenediaminetetra-acetic acid (EDTA)*—This treatment removes mercury, cadmium, and lead. The above guidelines apply but this method usually requires more treatments.
3. *Saunas*—This usually accompanies

Successful accomplishment of a heavy-metal detoxification protocol requires elimination of exposure before the cleansing process begins.

other metal-removal modalities. Treatment is usually 3 weeks in duration. The procedure also increases the secretion of essential trace minerals.[62]

4. *Homeopathic detoxification*—This method works best if used in conjunction with a nutritional program because it usually not sufficient when done alone.

The ease of any therapeutic regimen determines long-term patient compliance. Nutritional detoxification protocols require 3 months or more for acceptable clinical results. Heavy metals are not typically circulating freely in the body, but are locked in the cells and, as such, take time to release and remove. To facilitate treatment, products should be chosen that contain nutrients that will remove all four of the heavy metals discussed.

Successful accomplishment of a heavy-metal detoxification protocol requires elimination of exposure before the cleansing process begins. In the case of a patient with mercury amalgam fillings, exposure must be terminated via removal of the fillings. The detoxification protocol should begin approximately 2–3 weeks before the first dental removal appointment, and should continue as long as it is necessary.

If a patient has an extended history of exposure to heavy metals, the body burden may be significant. The patient may experience a reaction shortly after beginning the protocol. Symptoms will vary but may include unusual emotional behavior, vivid dreams, headaches, disturbed elimination (diarrhea or constipation), skin eruptions, or irritability. If this is overwhelming to the patient, simply discontinue the protocol and wait several days until the difficulty diminishes then begin again on a half-dosage schedule, gradually increasing to the target level. It may be necessary to conduct the entire treatment for 3 months and then repeat it after a 3-month break.

Conclusion

All of the above are simply suggestions and do not represent treatment advice. Any treatment suggested in this presentation should be designed and monitored by an appropriately licensed health care professional who is familiar with the treatment of heavy metal toxicity. □

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