REVIEW ARTICLE

MERCURY ELIMINATION WITH ORAL DMPS, DMSA, VITAMIN C, AND GLUTATHIONE: AN OBSERVATIONAL CLINICAL REVIEW

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Tissue mercury levels in humans have increased during the past 50 years to an alarming concentration, with possible deleterious effects that may involve neurological, cardiovascular, and immunological pathology. This article reviews the protocol for the use of oral 2,3-dimercaptopropane-1-sulfonate (DMPS) and oral meso-2, 3-dimercaptosuccinic acid (DMSA) in combination with intravenous glutathione and high-dose vitamin C for treatment of high-level mercury. This protocol yielded an average 69% reduction of urine mercury by provocation analysis. (*Altern Ther Health Med.* 2006;12(3):70-75.)

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During the past 50 years, tissue mercury levels have increased in humans.[1-3] The cause of this is environmentally multifactoral and cumulative.[4,5] The implications of chronic low-dose mercury exposure resulting in high tissue mercury levels appear to have a direct effect on cellular metabolism and development. We see an increase in incidents of disease that is dependent upon the specificity of DNA to cellular, and eventually, organ system functions.[6] Some conditions that have been implicated by chronic high tissue mercury levels are central and peripheral neuropathy[7-9] (including autism[10] and Alzheimer's disease[11]), autoimmune disease,[12] and cardiovascular disease.[13,14] An in vitro study demonstrated the degeneration of the neurite membrane with exposure to mercury vapor.[15] Another study demonstrated that the fetus could have 70% higher blood levels of mercury than the pregnant mother. In the United States during the year 2000, more than 300,000 newborns who were exposed in utero to levels of methyl mercury higher than those allowable by US Environmental Protection Agency recommendations were at risk for adverse neurodevelopmental effects.[16,17]

Concerns about high tissue mercury levels as a contributing factor to various disease states have motivated clinicians to try to decrease these levels. Various methods of mercury detoxification have been undertaken with varying results.[18-21] This article describes a unique method of mercury binding and detoxification using oral DMSA and oral DMPS in conjunction with intravenous glutathione and high-dose vitamin C.

A variety of patients are included in this review. Some had current or past dental amalgams; some had been exposed to mercury-toxic regions; others regularly consumed fish. The possibility of excess tissue mercury as a contributing factor in their disease process was explained. The patients were then offered further testing for tissue mercury load via provocation.

METHODS

The tissue mercury load was determined using DMPS provocation.[22] DMPS provocation is the most reliable method of determining tissue levels of mercury other than obtaining tissue biopsies from multiple sites. Also, DMPS provocation can be reliably duplicated. Patients were instructed not to eat any fish or take any minerals or supplements for 2 days before the provocation. Patients collected a urine sample by completely emptying their bladders in the morning before taking the DMPS. Mercury levels subsequently analyzed in this sample were used as a baseline measurement. Next, patients took the prescribed amount of DMPS and drank 1 to 1.5 liters of water. The DMPS provocation is performed using oral DMPS 10 mg/kg up to a maximum of 500 mg as a one-time dose. The next 6-hour cumulative urine was collected, mixed well, and sent to Doctors Data, Inc, St Charles, Ill, for analysis. The urine sample underwent heavy metal urine screening using inductively couple plasma mass spectrometry (ICPMS) methodology.

According to Doctors Data, "Toxic metals are reported as µg/g of creatinine to account for urine dilution variations. Reference ranges are representative of a healthy population under non-challenged or non-provoked conditions."[23]

Doctor's Data results are reported in a graph format reflecting the expected range based on age and gender. Specifically, adult females with elevated mercury values are between 4.1 and

12 µg/g of creatinine, and very elevated are >12 µg/g of creatinine, while adult males with elevated mercury values are between 3.1 and 9 µg/g of creatinine, and very elevated are >9 µg/g.

Patients in the "very elevated mercury range," as reported in the DMPS provocation results, were candidates for this mercury elimination program. Their participation was discretionary. Additional laboratory analysis was performed at the beginning and end of the program to evaluate the patient's CBC, basic chemistry, RBC protein and vitamin level, as well as renal and hepatic status. Sensitivity to all medications was tested. Patients were also screened for a possible sensitivity to high-dose vitamin C via glucose-6-phosphate dehydrogenase deficiency (G6PDH) or hemochromatosis.

Our current mercury elimination program protocol is a modification of the Holmes and Cathcart protocol.[24-26] Our protocol consisted of 5, 2-week cycles or a cumulative 10-week program (Table 1). A cycle begins with taking an oral dose of 133 mg of either DMPS or DMSA (depending on the cycle) 3 times a day for 3 days. On the fourth day, an intravenous infusion of sodium ascorbate (pH balanced to 7.0) mixed with vitamins and minerals (vials A and B, respectively—see Table 2) in 500 mL of a sterile water solution was followed by a slow intravenous push of glutathione. The schedule of DMPS and DMSA with the vitamin C and glutathione is shown in Table 1. During the remaining 10 days of the cycle, patients received an oral mineral and vitamin supplement following the oral chelator and intravenous fluids. Again, patients were instructed not to have any fish or additional mineral supplements 2 days before the DMPS or DMSA oral administration. At the end of the first 2-week cycle, another 2-week cycle began.

Upon completion of the full 10-week program and a 10-day rest period, the patient underwent a repeat of the DMPS urine provocation.

TABLE 1 Mercury Elimination Protocol

	Treatment Cycle Number—2 weeks per cycle				
	1	2	3	4	5
Chelator—first 3 days of each cycle					
DMPS (133 mg TID) PO	X	X	X		
DMSA (133 mg TID) PO				X	X
IV infusion—fourth day of each cycle					
Ascorbate (vitamin C)	15 g	25 g	50 g	50 g	50 g
Calcium gluconate dosage	900 mg	900 mg	900 mg	900 mg	900 mg
Vial A (vitamin complex)*	X	X	X	X	X
Vial B (minerals)*	X	X	X	X	X
Magnesium	4 g	4 g	4 g	4 g	4 g
IVP (slow)—after IV infusion					
L-glutathione	750 mg	1500 mg	1500 mg	1500 mg	1500 mg

* Preparation by ApothéCure, Inc, Dallas, Tex

TABLE 2 Contents of Intravenous Infusion

Vial A: B Complex		Vial B: Minerals	
Pyridoxine	100 mg	Magnesium	2 g
Thiamin	100 mg	Zinc	10 mg
Riboflavin-5-phosphate	5 mg	Manganese	2 mg
Niacinamide	100 mg	Selenium	200 µg
Dexpanthenol	1 g	Molybdenum	250 µg
Hydroxocobalamin	1000 µg		
Folic acid	5 mg		

RESULTS

Our study group of 16 total patients was skewed based on concomitant ailments that were of a chronic nature with exposure to significant mercury from either a food source, environmental toxins, or amalgams. Twelve of the 16 patients (75%) showed extremely elevated levels of mercury with DMPS provocation. Of these 12 patients, 4 had amalgams removed before the provocation test. Six of the 12 patients with extremely elevated mercury levels elected to participate in the mercury elimination program. The mercury elimination program showed a significant reduction (see percent change) in mercury levels in 10 weeks. Their pre- and post-elimination DMPS mercury provocation test results are shown in Table 3.

DISCUSSION

DMPS is an antidote for the treatment of acute and chronic toxic metal poisoning that has been used extensively in Europe for more than 50 years. After oral administration, re-absorption of DMPS in the gastrointestinal tract, presumably by passive diffusion, occurs in 3.7 hours.[22,27] Approximately 50% of the orally administered DMPS is detected in the urine. Neither DMPS nor its metabolites are detected 12 hours after administration. Irrespective of the size of the administered dose, the highest concentrations of DMPS are achieved in plasma and the kidneys. High concentrations are also measured in the skin. In the remaining organs, particularly the brain, only very slight amounts are found.

Chronic illness may arise when mercury displaces trace elements. In many cases, the deficiency is asymptomatic. Zinc displacement is likely to result in a specific deficiency syndrome. Mercury masks the zinc deficiency by functioning as an inferior replacement to the zinc. Once mercury elimination with the use of DMPS occurs, a zinc deficiency syndrome is revealed. Long-term treatment with DMPS does not cause a zinc deficiency.

As measured in the plasma, more than half of the absorbed orally administered DMPS is excreted in the first 6 hours in the urine and feces. The greatest DMPS concentration in urine is in the first 2 to 3 hours after oral administration. Similar to the elimination of DMPS in plasma, the concentration quickly decreases in the organs. The kidneys excrete approximately 80% of DMPS, the remainder mostly by the hepato-biliary system. No accumulation of the active substance is observed after repeated administrations.

TABLE 2 Clinical Results

Patient	Age (years)	Chief complaint	Mercury Levels (µg/g creatinine) Before provocation (date)	After provocation	After treatment (date)	Percent change
WM	47	Increase in flu and colds requiring taking off work; current otitis with tinnitus in right ear; lethargy; SOB; eczema; multiple fungal sites (feet and mouth); food allergies	1.7 (1/25/04)	4.7	no treatment	
RC	21	IV drug abuse; depression; symptoms of ADD and psychotic behavior; neurotransmitter deficiency; paranoia; food allergies	1.3 (5/12/03)	3.2	no treatment	
CH	40	Recurrent candidiasis; IBS; prostatitis; discomfort at hepatic fossa; dyspareunia; food allergies	0.8 (6/15/03)	4.9	no treatment	
MG	80	Recent decline in health and short-term memory; history of amalgams; patient is concerned about possible mercury accumulation	<3 (9/15/03)	3.9	no treatment	
NH	59	Type 1 diabetes with onset at 55 years old; osteopenia chronic fatigue	0.7 (1/19/04)	12	no treatment	
SD	53	Recurrent headaches; recurrent allergies; weight retention; history of extensive dental work with prior amalgams, all removed 5 years before DMPS provocation	2.1 (3/21/04)	36	no treatment	
MM	54	Recurrent candidiasis from mouth to anus; IBS; hypothyroid; chronic fatigue syndrome; nervous and depression syndrome X; adrenal fatigue; amalgams throughout mouth	7.1 (8/31/03)	38	no treatment	
MY	71	Diabetes type 2; hepatic cavernous hemangioma; dental amalgams	1.7 (9/15/03)	21	no treatment	
MC	52	Microadenoma other posterior aspect of the pituitary; fatigue; osteopenia; insomnia; weight retention; recurrent UTI; recurrent ovarian cyst; DVT after taking BCPs; fibroid cyst of the breast; IBS; chronic fatigue; menopausal	0.5 (9/17/03)	38	no treatment	
MR	57	Generalized fungal body rash started 14 yrs prior when treated with high dose of prednisone for rash; current use of any cortisone increases rash; marked amount of amalgams with fractured molars with amalgams exposed; eczema; recurrent UTI; food allergies; asthma; IBS; recurrent vaginal candidiasis; perianal pruritus; parasites from living in Mexico city.	5.1 (8/26/03)	81	no treatment	
JN	27	Vulvadysdinia; migraines; depression; recurrent vaginal candidiasis; IBS; gastrointestinal dysbiosis with hemolytic *E coli*; developed a rash with DMSA treatment with prednisone and fluconazole with resolution; amalgams removed before mercury elimination program	1 (5/26/03)	14	8.1 (10/20/03)	42%
CW	46	Alcoholic/depression; symptoms of neurotransmitter dysfunction; amalgams removed before mercury elimination program; developed a rash with DMSA treatment with prednisone and fluconazole with resolution	0.9 (5/22/03)	20	3.3 (4/25/04)	84%
IY	74	Marked amount of amalgams; squamous cell cancer developed on cheek adjacent to fractured molars with amalgams exposed, touching mucous membranes; BPH; thromboembolism with primary blood dyscrasia of protein S deficiency; treatment with coumadin resulting in ankle skin necrosis	4.7 (8/24/03) 0.9 (7/6/03)	45 27	8.6 (4/11/04) 9.1 (10/8/03)	81% 66%
GB	32	Amyotrophic lateral sclerosis with marked muscle atrophy at the thenar aspects of both hands and bilateral upper extremity weakness; 10 years prior was a resident of Minamata Bay, Japan; had amalgams 1 year prior to DMPS provocation	4.2 (9/25/03)	33	9.6 (12/20/03)	71%
PH	59	Myocardial infarction at 40 years old, in father at 45 years old; multiple drug and food allergies; chronic upper UTI; unprotected amalgam removal; osteoporosis; pulmonary mass?; SOB; cardiac palpitations with arrhythmia; ASHD; hypertension	1.6 (9/29/03)	37	30 (5/2/04)	19%
PB	67	Multiple mycardial infarctions with intermittent angina; ASHD with angioplasty x3 ('96,'97,'01); recurrent SOB: ASHD; menopausal: depression, neurotransmitter deficiency; lethargy; syndrome x; hypertension; amalgams replaced with crowns; history of living below dairy farm with water source a well				

ADD=attention deficit disorder; ASHD=atherosclerotic heart disease; BCPs=birth control pills; BPH=benign prostatic hypertrophy; DVT=deep venous thrombosis; IBS=irritable bowel syndrome; SOB=shortness of breath; UTI=urinary tract infection. *Between before and after treament provocations

The elimination half-life of DMPS in plasma and blood when given intravenously is 1.1 and 0.9 hours, respectively. The elimination half-life of DMPS in plasma and blood when given orally is 9.9 and 9.1 hours, respectively. The oral form is used in both acute and chronic poisoning, whereas intravenous (IV) administration is used primarily in acute poisonings or when an oral treatment cannot be administered.[26] Animal experiments have shown that DMPS does not increase the metal level in the brain. DMPS is excreted rapidly via the kidneys after IV administration (50% of the total dose is excreted in 1 hour, and 90% is excreted in 24 hours). DMPS is also excreted through the hepato-biliary system with IV dosing.

Adverse effects of DMPS may be due to the increased presence of circulating heavy metal or related toxins. Skin reactions are similar to those of acute mercury toxicity. These skin reactions are similar to allergic reactions in nature, are generally mild, and include itching, nausea, dizziness, fever, weakness, skin reactions (eg, rash, urticaria) mucous membrane reactions, increased body temperature or shivering and fever. No cases of anaphylactic shock have been reported. Allergic reactions generally regress after withdrawal of DMPS within 3 to 5 days without treatment. Exclusively, rapid IV injection may have cardiovascular effects, such as dizziness, weakness, nausea, palpitations, and a feeling of chest pressure.

DMSA has been approved by the US Food and Drug Administration for treatment of lead intoxication. DMSA has a higher affinity for mercury than it does for lead. DMSA is only available as an oral preparation. When used at its recommended dosage, there is no significant excretion of essential metals. Blood levels following oral administration of DMSA appear to reach maximum concentration in about 3 hours. The elimination half-time (ie, the time for half of the substance to be converted or disappear) was 3.2 hours. Elimination of 20% of the total dose of DMSA appears in the urine. The remaining 80% of the total oral dose in the gastrointestinal tract either is not absorbed by the gut or is returned to the gut via the hepato-biliary system. This portion is available for further binding of mercury, which may occur with hepato-biliary circulation.

DMPS and DMSA combined are excellent chelators of mercury.[28] The pharmacokinetic parameters between DMPS and DMSA differ, resulting in a different point of elimination of mercury from the cells. According to rat studies, DMSA does not readily enter liver cells, as does DMPS; however, there is a marked difference between rat and human models. In addition, DMPS has a higher affinity for mercury (both inorganic and organic) than DMSA. Some studies report that DMSA is 3 times more effective than DMPS in removing mercury from the brain.[29] Also, DMSA has lower toxicity levels. DMSA is commonly used in Asia and Eastern Europe to manage environmental disasters involving excess toxic metal contamination. Some researchers believe that DMPS has a higher efficacy than DMSA because the terminal succinic acid group of the DMSA interferes with the succinic acid phase of the Krebs cycle, which slows the mercury binding process.[21] DMPS does not readily cross the blood brain barrier or increase the deposit of mercury into the brain. Studies performed at Doctors Data, Inc, indicated that oral DMSA (30mg/kg/day) for 1 to 3 days yields about one-fifth to one-tenth the amount of mercury in the urine as does a single IV or oral dose of DMPS (personal communication with David W. Quig, PhD, 2004). Therefore, DMPS is more effective for provocation. Oral DMPS and DMSA were selected for this mercury elimination protocol due to their different binding profiles. It is advantageous to give DMPS and DMSA orally because both are partially absorbed from the gastrointestinal tract, leaving the remainder available to bind to any mercury product that may circulate via the hepato-biliary system during this elimination process, thus increasing the excretion of the mercury.

Vitamin C given intravenously in high doses has been used to treat acute mercury toxicity, beginning with the pharmaceutical use of mercurial diuretics in the 1940s.[30] Historically, vitamin C has been used to treat a broad range of maladies from infectious disease to toxicity. Tom Levy, MD, JD, reviewed more than 1,200 medical and scientific journal articles on vitamin C and describes the overwhelming benefits of its use.[31] It was once believed that vitamin C increased the development of renal stones. This has been refuted by recent studies by The New York Academy of Sciences and a recent review of 20,000 patients.[32,33] Vitamin C use has some unique side effects, however. Individuals with glucose-6-phosphate dehydrogenase deficiency might experience red blood cell hemolysis with intravenous infusion, and individuals who are homozygous for hemochromatosis may develop an increase in iron uptake with vitamin C ingestion. It is not known whether people who are heterozygous experience a problematic increase in iron uptake.

Glutathione is present in millimolecular amounts in most cells.[34] As an endogenous thiol-containing molecule, it has a high affinity for binding its reduced sulfur atoms to the mercuric ion, thereby decreasing the glutathione availability for other cellular function and locking the mercuric-glutathione complex within the cell membrane. The addition of glutathione significantly enhances the release of mercury from the astrocytes, where the mercury and glutathione are complexes, thus increasing the availability of mercury for binding and excretion.[35] Glutathione is 50% as effective as DMSA in preventing inorganic mercury accumulation in renal cells.[36]

Conflicting data from an animal study using rats concluded that intraperitoneal vitamin C, glutathione, and lipoic acid did not reduce the elemental mercury tissue load.[37] This study investigated the induction of elemental mercury from the mercury vapor exposure of amalgams and did not measure the organic mercury (mostly methylmercury and ethylmercury), which are derived from seafood or vaccinations and the ready conversion of elemental mercury to organic mercury by the gastrointestinal flora. Organic mercury is more neurotoxic than elemental mercury. The author contends that vitamin C-producing animals should not be used as a comparison model for vitamin C usage. This includes all animals other than humans and guinea pigs. This contention has been supported by

Cathcart (oral communication with Robert F. Cathcart III, MD, February 2005) and Levy.[38] Cathcart suggests that the problem with mercury is not toxicity, but rather a sensitivity reaction. Toxicity leads to death, whereas sensitivity leads to an inflammatory process with pathological results. The specificity and magnitude of this sensitivity reaction may vary depending on genetics and influential environmental factors. Results indicate that the action of vitamin C may not be the displacement of mercury but rather the decrease in sensitivity to the mercury. This is similar to the property of acute vs chronic mercury exposure. Individuals may exhibit varied adverse effects; they may not experience all or even the same symptoms.[39] HL "Sam" Queen, CCN, CNS, founder and president of The Institute for Health Realities, Colorado Springs, Colo, suggests another limitation of the experimental model. He contends that vitamin C and GSH given by intraperitoneal instillation as opposed to the IV route restrict the delivery and concentration of both GSH and vitamin C (oral communication with Dr Queen, April 2004). The conclusion is that this model would not contradict the findings in this article.

OBSERVATIONS

Of the 6 patients undergoing the mercury elimination program, 2 had a break in the protocol. These breaks occurred either in the 5, 2-week cycles that were not consecutive or when the time span between the completion of the last cycle and the final DMPS provocation test was greater than 3 months. Both patients had final DMPS provocation results within the 69% reduction range.

Two people developed a rash with urticaria and pruritus that completely resolved with treatment with fluconazole and prednisone. In both instances, the rash occurred during the third cycle with DMPS and did not reoccur with the final DMPS provocation. As mentioned previously, it is unknown if the rash is a primary drug allergy to DMPS secondary to increased *Candida albicans* growth or an increase in circulating mercury. Compared to other fungal species, *C albicans* favors the mercurial environment and tends to proliferate and produce methyl mercury from inorganic mercury while other fungal and bacterial growth decline.[40]

Of the whole group in the mercury elimination program, only 1 patient showed less than a 69% reduction in the final DMPS provocation; this patient showed a reduction of only 19%. The patient was not included in the efficacy rate of the treatment because of outlier circumstances. The patient lived near a large dairy farm and drank well water that was contaminated and sometimes blackish in color. A stool sample was sent to Great Smokies Diagnostic Laboratory, Asheville, NC, for analysis. Results included severe bacterial dysbiosis with marked mycosal overgrowth, including high growth of the fungal parasite *Geotrichum*. The patient developed an intestinal parasite that might have interfered with the mercury binding treatment. The author has discussed this with other providers, and there is agreement that the anticipated results from mercury binding treatment in such circumstances would be seen only after treatment with antiparasitic medication. This requires further investigation.

Patient Outcomes

Mercury sensitivity is not a disease in itself but contributes to the underlying pathology of disease states. Our patients presented with multiple diagnoses and accompanying symptoms, including vulvadysdinia with chronic candidiasis, squamous cell cancer, neurotransmitter dysfunction with depression, drug and food allergies with chronic upper respiratory tract infection, and amyotrophic lateral sclerosis. All patients who experienced a reduction in mercury levels reported improved overall health, increased energy, and decreased symptoms. Chronic candidiasis and squamous cell cancer resolved as a possible result of the mercury extraction and other appropriate treatment protocols. Symptoms of depression and allergies were markedly reduced. The patient with amyotrophic lateral sclerosis showed no signs of disease progression during the 6-month timeframe of the study.

CONCLUSION

As environmental mercury levels continue to increase, a safe and standard mercury elimination and desensitization program needs to be developed. A program protocol including the use of oral DMSA and oral DMPS in combination with intravenous high-dose vitamin C and glutathione has shown substantial merit for consideration in treatment of patients with high levels of mercury. There might be a basis for a more formal study based on these pilot clinical observations.

Changes in our protocol would be consistent with closely following laboratory markers of inflammation and antibody response to mercury. A focus on the etiology of the rash with proactive management could yield useful data. Also, for central and peripheral neurological protection, there is some suggestion that using intravenous phosphatidyl choline and glutathione facilitates the intracellular removal of mercury and fat-soluble neurotoxins.[41]

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