RESEARCH ARTICLE

METALS IN MEDICINE

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The effects of toxicant metals on human health have been reported in peer-reviewed literature with increasing frequency. Toxicant metals are present in many diseases of aging, especially vascular diseases. Toxicant metals are a natural environmental phenomenon as well as a byproduct of industrialization. The historical experience of toxicologists who treated individuals poisoned by acutely toxicant metals is waning; very few of these cases have been reported during the past 30 years in the US. Researchers with a special interest in clinical metal toxicology have noticed a clinical correlation between metal detoxification by chelation therapy and clinical improvement of vascular diseases. Chelation therapy currently is being tested by the National Institutes of Health (NIH) for post-myocardial infarction patients in the Trial to Assess Chelation Therapy (TACT). This article's author is on the NIH Data and Safety Management Board of that study. He was asked to write this review article and include an update on the clinical, environmental, historical, and scientific elements of this expanding field. This article reviews toxicant metals in the environment and their potential health consequences. (*Altern Ther Health Med*. 2005;11(4):18-25.)

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The 2001 Institute of Medicine (IOM) report "Crossing the Quality Chasm: A New Health System for the 21st Century," exposed the current crisis in medicine.[1] Loosely translated, the report states that our current health system is in a terminal state and must be replaced. The IOM report states that the new health system will have to include complementary and alternative medicine, as well as preventive measures. In his editorial, "Paradigm Shift: The End of 'Normal Science' in Medicine, Understanding Function in Nutrition, Health and Disease," Mark Hyman, MD, explained the need for a change in the way medicine is practiced.[2] Jim Gordon's Report on the White House Commission calls for implementation of the Commission's recommendations, including expanding treatment options to include prevention and complementary and alternative medicine.[3] Furthermore, Gary Null's "Death By Medicine" states that the leading cause of death in the US is a combination of pharmaceutical, iatrogenic, and hospital-based causes.[4] Dr. Null's work emphasizes the need to scrutinize our current system. Improvement in perception, if not in fact, is needed.

David M. Eisenberg, MD, brought consumers' interest in complementary and alternative medicine (CAM) and their use of CAM to our attention.[5,6] Since the publication of his seminal article on this topic in 1993, a virtual evolution has occurred in healthcare delivery and consumer preference. Many baby boomers are not content with the care given to their parents, and they are taking increasing responsibility for their healthcare.[7] They have become interested in prevention, healthy lifestyles, and supplements. The disease care industry is booming, and many hospitals are reaching their maximum capacities.[8,9] Examination of the role of environmental pollutants of toxicant metals and persistent organic pollutants, their detoxification, and preventive medicine and nutrition are evolving into proactive health approaches.

The medical model of the US was developed before adequate clinical texts were published and before the wide use of computers. Medical students are taught how to diagnose and treat diseases. Symptoms are often considered non-life-threatening and are treated with an appropriate medication.

My personal estimate is that approximately 90% to 95% of physicians have excellent memories and cumulative minds and compassionately practice what they learned in medical school. The other 5% to 10% of physicians have associative minds or good memories and the ability to look for nuances of disease causation. They tend to do their own clinical observations, over time, and share them with their colleagues. Although their methods are not as scientifically rigorous academic methods, many of these physicians make clinical observations that are later confirmed scientifically. They tend to be problem solvers. This group may be trained in physical science, mathematics, or engineering before they enter medicine. Many of these physicians are

in private practice and often seek solutions to patients' problems that they might not have been taught in medical school. These physicians, like most physicians, are contributing to evolving medicine in the 21st century by expanding our perceptions and interests regarding what it means to be a medical doctor. One such area is the role that toxicant metals have in the seeming causation of diseases. This article outlines the history of metal detoxification and bring us through the past 50 years to our current state of knowledge. It is an attempt to show how our environment affects us.

HISTORY

In 1893, Alfred Werner, PhD, a Swiss chemist, proposed the theory of metal-ligand binding as a ring formation that provided the foundation for modern coordination chemistry. He discovered that the divalent cation of metals bound with the divalent anion of other chemicals to form a neutral substance. He received the Nobel Prize for Chemistry in 1913 for complexion chemistry, which describes the process by which metal-ligand complexes form. In 1920, two Americans, Morgan and Drew, defined chelation as a metal ion incorporated into an heterocyclic ring.[10] The Greek word *chelai*, meaning a bird's talon, wolf's claw, or crab's claw, was adopted to illustrate the grabbing of the metal cation, rendering it inactive. Chelation therapy has been used in industry and manufacturing ever since.

As World War II approached, Germany began to prepare for battle by inventing chemicals to replace those in short supply. Citric acid was used in German industry to precipitate metals. Franz Munz synthesized nitro triacetic acid (NTA) to be used in the printing and textile industries as a substitute for citric acid, which was in short supply. This was called Trilon-A.[10] A subsequent improvement, ethylene diamine tetraacedic acid (EDTA), was called Trilon-B.[10p8] After World War II began, a search for antidotes to arsenic and other nerve toxins began. This led to the development of British Anti Lewisite (BAL) as the first chelating compound to be used in medicine. EDTA was brought to the US in 1947, when Martin Rubin of Georgetown explored its use to chelate calcium from blood, leading to the development of the lavender top tube for hematological tests. His research led to the use of EDTA in humans to chelate lead and other metals.[11,12] As lead poisoning was relatively common in some industries, EDTA chelation therapy was used frequently. Some patients with lead poisoning had co-morbid conditions such as hypertension, angina, peripheral arterial disease, and memory problems. Many of the co-morbid conditions improved as the lead was detoxified.[13pp211-214]

Norman E. Clarke, Sr, MD, began his pioneering use of intravenous EDTA chelation for atherosclerotic coronary artery disease at Providence Hospital in Detroit. During the late 1950s and early 1960s, several papers were published by Clarke, Mosher, Meltzer, Kitchell, and others.[14,15] These papers showed safety and clinical effectiveness in reversing the symptoms of angina and other vascular diseases. In 1966, the American Heart Association (AHA) began supporting the operative approach to heart disease introduced by Michael Ellis DeBakey, MD. The AHA's support led to the development of our current approach to cardiac intervention and to the decline of chelation therapy. Some physicians who personally saw the benefits of chelation therapy formed societies to further its use, and a protocol was established.[13] In the more than 30 years the protocol has been in use, there have been no deaths or events of renal shutdown due solely to chelation therapy administered by properly trained physicians. Because many patients were paying out of pocket for this treatment, and rigorous double-blinded tests had not been performed, in 2002, the National Institutes of Health (NIH) funded a five-year, $30 million, double-blinded prospective study called the Trial to Assess Chelation Therapy (TACT). Gervasio Lamas, MD, a cardiologist and researcher from Mount Sinai Hospital in Miami, is the principal investigator.

CHRONIC TOXICANT METALS EXPOSURE?

During the past five years, the understanding of vascular disease has changed. Vulnerable plaque has replaced stenotic lesion as the main cause of vascular problems.[16] Questions about the long-term benefits of coronary artery bypass grafting (CABG) surgery have been raised.[17] Metals have been implicated in many of the diseases of aging as well as in neurodevelopmental diseases and autism spectrum disorders.[18-24] The American Board of Chelation Therapy (ABCT) has formally changed its name to the American Board of Clinical Metal Toxicology (ABCMT) because of the new scientific association of toxicant metals with multiple diseases.[25] The most authoritative information on the early work on metals in medicine is *A Textbook on EDTA Chelation Therapy*.[13] This textbook presents the clinical observations of the early pioneers in this field along with the evolving science of the time. Their clinical observations during the past 30 years have set the stage for the integration of new scientific observations of toxicant metals in recent scientific literature. The remainder of this article updates readers on the science of toxicant metals, their place in diseases, and their diagnosis and treatment. The continuing unofficial outcomes research of chelating doctors, now clinical metal toxicologists, is being understood better each year as scientific journals publish articles on toxicant metals and their effects.

Toxicologists are experts in acute poisoning from metals. Their protocols, methods of diagnosis, and treatments are valid for acute poisoning only, which has become rare in American medicine during the past 25 to 30 years. The new experts for the low-dose, accumulated toxicant metals and their health consequences are the clinical metal toxicologists. Previously denigrated as "chelation therapists," these physicians are correlating more than 30 years of clinical observations with the latest science. Although the pioneers of toxicology often did not treat patients, they are the repository of information about acute metal poisoning. They have little understanding and few clinical skills regarding the effects of toxicant metals in vascular and other diseases, such as macular degeneration and cataracts. Clinical metal toxicologists have decades of experience diagnos-

ing and treating thousands of patients with toxicant metal problems. Clinical metal toxicologists are an example of one of the bridges from our current medical paradigm evolving into the new medicine of the 21st century, as outlined by the IOM report, "Crossing the Quality Chasm, A New Health System for the 21st Century."

Doctors practicing toxicant metals detoxification have often treated vascular disease patients without assessing the body burden of toxicant metals. The new research paradigms emphasize scientifically-based outcome studies as a meaningful replacement for the more traditional, but unquestionably outdated, double-blinded, placebo-controlled, crossover studies that worked marvelously for infectious diseases. A few stories of real patients, although not rigorously scientific and without the benefit of test data showing the body burden of toxicant metals, will lead us to consider new scientific articles that update the role of toxicant metals. These patients were treated for vascular symptoms from a purely clinical or heuristic perspective.

ANECDOTAL EVIDENCE

A physician was told that he had idiopathic cardiomyopathy and that if he did not receive a heart transplant within the next six months, he might die. The physician began a course of intravenous treatment with EDTA. His symptoms cleared during several months of treatment, and he was taken off the transplant list. He subsequently studied chelation therapy, married another young physician, and had two children. He eventually opened the largest chelation clinic in a midwestern state and lived his life fully, until he died suddenly of a cardiac event while deer hunting. The physician lived 19 years after his first chelation treatment and saved his health insurance company approximately $750,000, the current cost of a heart transplant. He also had an excellent quality of life, with no hospitalizations or continuing illnesses. Why did he respond so well to chelation therapy? It could be that he had an idiopathic cardiomyopathy of the type studied by Andrea Frustaci et al in Rome, Italy.[26] Succinctly, Frustaci and colleagues found 13 patients who had greater than 12,000 times the normal levels of antimony and greater than 22,000 times the normal levels of mercury in biopsied myocardial cells. No such increase in toxicant metals was found in controls. The researchers hypothesized that the metals may adversely affect mitochondrial activity and myocardial metabolism and worsen cellular function. Could it be that they have discovered an idiopathic, organ-specific metal toxicity that leads to cardiomyopathy? Could the physician have had the same etiology for his cardiomyopathy, which may have responded to the detoxification of the toxicant metals? We may never know, but logic dictates that it is possible. The toxic metals may have been removed with chelation therapy, causing the patient's clinical symptoms to improve. These are the types of clinical observations that can alter the course of current medical treatments.

Another patient had renal failure. He was hypertensive and diabetic and had a nephropathy that his physician told him would soon require dialysis. He began a course of chelation therapy without obtaining a toxicant metals test. The patient never had to begin dialysis, and he served his community and his church for six years before his health began to decline and he died. Could this patient be similar to those studied by Ja-Liang Lin et al as reported in *The New England Journal of Medicine*?[27] The researchers' conclusions showed that "low level environmental lead exposure may accelerate progressive renal insufficiency in patients without diabetes who have chronic renal disease. Repeated chelation therapy may improve renal function and slow the progression of renal insufficiency."[27] Although this patient had diabetes, could he have also had low-level lead exposure? Unfortunately, he chose not to be tested for toxic metals, so we do not know. However, it is observed that diabetic patients often respond to chelation therapy.[17p412] Chelation therapy may increase vascular neogenesis, but it also detoxifies lead preferentially. According to Lin et al, "repeated chelation therapy can improve renal function and retard the progression of renal insufficiency for at least 24 months. At the end of the study, the difference in the glomerular filtration rate between the chelation and control groups was approximately 8.1 mL per minute per 1.73 square meters of body surface area. This finding implies that treated patients might delay dialysis therapy by about three years, given the rate of decline in the glomerular filtration rate of approximately 3.0 ml per minute per year."[27] The cost saving per patient getting chelation therapy in Taiwan, where this study was conducted, was estimated to be approximately $57,000 per patient.[27] Because the federal government pays for all dialysis in the US, this optional approach might benefit the patient and reduce government expenditures. Should all patients headed toward dialysis be tested for toxicant metals, especially lead? My answer is a resounding "yes."

My last example of a patient's clinical symptoms improving involves a case of peripheral arterial disease with intermittent claudication manifesting after the patient walked approximately 50 yards. The patient had been evaluated for peripheral arterial disease, and surgery was not indicated. He began a series of intravenous chelation treatments, which often help the clinical symptoms of intermittent claudication. He was not tested for toxicant metals. He received approximately 17 treatments, with little improvement. After his 18th treatment, he explained that while he was walking he felt a sensation in his legs like something had broken loose. Subsequently, he was able to increase his walking distance markedly without pain. Within six months of beginning treatment, he was able to walk three miles non-stop at a brisk pace. The patient did not care about the science behind his improvement or if his insurance paid for the treatments, he was ecstatic because he was whole again and could live a normal life. Could he have had lead or cadmium in his system? Increased lead and cadmium have recently been shown to be associated with peripheral arterial disease.[28] "Simultaneous adjusting for the other metal did not appreciably alter the association for either lead or cadmium."[28] Metal detoxification has been clinically observed for more than 30 years to relieve symptoms from a variety of vascular diseases and

appears to work primarily on the small vessels. The exact mechanisms require further study, and more research is required.

SOURCES OF TOXICANT METALS

Where do toxicant metals come from? With the advent of the industrial revolution, the presence of many metals, such as lead and mercury, in the environment has increased. Tobacco, which tends to bio-concentrate cadmium, is a major producer of metal. Arsenic has been used in the past in agriculture. Forest fires release metals, especially mercury, from stable seleno-mercurial compounds that are extraordinary stable in the tree during its life.[29] Volcanoes also spew out copious amounts of mercury. One study done with ice core drilling from a glacier in northwest Wyoming collated every major volcanic eruption with a heavy level of mercury.[30] Nature acts as our best filter, with plant life and trees trapping many toxins, including toxicant metals. Between nature and man, we have polluted the planet. Man's pollution is by far the most toxic. We are now paying a price for our environmental neglect. That price appears to be the increasing diseases of aging, such as vascular disease, congestive heart failure, and cancers. Could these diseases of aging have a common prime risk factor that is diagnosable and treatable?

TOXICANT METALS BURDEN AND TESTING

Most toxicant metals are divalent cations, although there are exceptions, such as ferritin and aluminum. A lifetime of exposure to low levels of these toxicant metals and their long half-lives allow them to accumulate in bones and soft tissues. Some sources of these metals are the thimerosal additives to vaccines, dental amalgams, fish, food, water, air, cosmetics, leaded gasoline, and lead paints. It is estimated that 35 million houses still have lead paint. This is a problem, as renovation of these houses exposes workers to high levels of lead. We live in a toxic world and are slowly but surely being exposed to and storing these toxic metals. Acute poisoning, at least in the US, is a rarity. How can we test for these metals that we have accumulated since birth?

The body excretes toxic metals primarily in the feces. Other organs that may detoxify the body of these metals are the skin and lungs. Toxic metals may also be excreted through hair and urine. The standard test for acute poisoning is a blood test. Unfortunately, blood tests are not a viable test for low-dose, chronic toxicant metals exposure. Once the patient is exposed endogenously (from tissue turnover) or exogenously (from accumulation of the toxicant metals in the environment), metals remain in the blood for a very short time. One test with animals showed 60% of radioisotope tagged toxicant metal was out of the blood within six hours.[31] Most of the metals go into red blood cells, where they can be measured as long as the red blood cells survive, approximately three to four months. If exposure to an exogenous source occurred more than four months before the patient was tested, it is likely that the blood test would measure near zero, although the body may contain large residuals of the metal.

The hair test has been used as a screening test, but it is discouraged in North America. Metal is detoxified through the hair in the vast majority of individuals. However, new information suggests that as many as 15% of us may have a genetic predisposition to an efflux disease that does not allow normal toxicant metals excretion. This work is championed by H. Vasken Aposhian, PhD, Boyd Haley, PhD, and others.[18] Studies of children with autism spectrum disorders show almost no metals, specifically mercury, in their hair. Toxic metals are seen in the hair of normal children.[18] This suggests that the higher levels of mercury in the brains of autistic children and the lower levels in the hair can be accounted for by an efflux disease similar to Wilson's Disease. These data were presented to the IOM in February 2004. Assuming that the individual has normal hair detoxification, what can we measure? The hair grows approximately one inch per month. If we take an adequate amount of hair as a sample and mark the scalp and distal ends of the sample, we can determine if metals have been detoxified. However, it is theoretically possible to detoxify with all organ systems so that the hair will reflect metals with no total body accumulation of the metals. In other words, the metals from tissue turnover and the exogenous exposure exactly equal the detoxification capability of the individual. Thus, hair, like blood, may act as a screening test. When it is positive, additional testing is required.

Feces testing can be done, but since the feces is the primary detoxification pathway with up to 90% of the toxicant metals being excreted in the feces, it may not be the best test for total body burden of toxicant metals. It is not routinely done. That leaves us with urine tests. I was taught in neurology residency training in the early 1970s that when symptoms cannot readily be explained, look for toxic metal poisoning. This was done using a 24-hour unprovoked urine test for toxic metals. I have used this over the years and have never seen a positive test. I then learned about chelation therapy and the provoked urine test.

Oral and intravenous chelating medication is used to provoke the metals sequestered in the patient. The urine is then collected for a specific number of hours, ranging from six to 12. It is sent to an appropriate laboratory and the urine is tested by Inductive Coupled Plasma Mass Spectrometers (ICPMS) and the results are obtained. The cost of this test is less expensive than blood, hair, and fecal tests, and it gives the best reading of the body burden of toxicant metals. Since I have been using this method of provoked urine testing, the majority of individuals who are screened test positive. Any excreted toxicant metals must come from the body stores. Further studies are required to establish acceptable normal levels in healthy patients. Now that we can measure toxicant metals, what should we look for clinically?

CLINICAL SYMPTOMS

Toxicant metals target many organ systems and are now being associated with many of the diseases of aging. Most physicians correct the diagnosed medical problem with medication.

We were not trained to think about detoxification to allow the body to maximize its own immune system and defenses to assist in returning our dynamic system to homeostasis, or to realize that we are truly homeodynamic. Lead targets the blood, bone, brain, gastrointestinal system, kidney, liver, and peripheral nervous system.[19] Other metals also affect most of these systems. We will continue to use lead as our example toxicant metal. Lead affects children in many ways. Decreased head circumference and decreased stature are often associated with lead toxicity.[19pp408-446] Neurobehavioral problems such as decreased IQ, hyperactivity, learning disabilities, and other behavioral problems are associated with lead toxicity. Reproductive issues include the delayed onset of puberty, decreased sperm count, decreased libido, and increased spontaneous abortions.[19pp408-446] In adults the emphasis shifts to the diseases of aging, particularly vascular diseases and cancer. Hypertension, stroke, heart attack, left ventricular hypertrophy, increased cholesterol, cardiac arrhythmias, renal failure, and peripheral arterial disease have been associated with lead toxicity.[19pp408-446] Cancers of the bladder, brain, lung, kidney, and stomach have also been associated with lead.[19pp408-446] What about the other toxicant metals?

Mercury is known to affect the brain and has been associated with the causation or exacerbation of degenerative diseases such as amyotrophic lateral sclerosis, Alzheimer's disease, multiple sclerosis, and Parkinson's disease.[20] The same article is quick to point out that "available evidence shows no connection," however.[20] This excellent review article on mercury states that mercury is associated with autism, the degenerative diseases of the brain mentioned above, neurodevelopmental diseases, vascular diseases, nephrotoxicity, and cancer. It points out that "the fetal brain is more susceptible than the adult brain to mercury-induced damage."[20] Specifically, methylmercury "inhibits the division and migration of neuronal cells" and "disrupts the cytoarchitecture of the developing brain."[20] Recent studies have correlated the explosive increase of autism with thimerosal, an additive to many vaccines that contains 50% ethyl mercury.[21] An article by Deth and colleagues, proposes a mechanism that might explain how mercury and other metals cause the neurodegenerative problems.[22] Waly et al suggest that "the ethylmercury-containing preservative, thimerosal, inhibited both IGF-1 and dopamine-stimulated methylation with an IC-50 of 1 nM and eliminated methionine synthase activity. Our findings outline a novel growth factor signaling pathway that regulates methionine synthase activity and thereby modulates methylation reactions, including DNA methylation. The potent inhibition of this pathway by ethanol, lead, mercury, aluminum, and thimerosal suggests that it may be an important target of neurodevelopmental toxins."[22] Further research is needed, but the vaccination programs would not be harmed if thimerosal was removed from all vaccines, as has recently been done in the United Kingdom.

POSSIBLE MECHANISMS OF ACTION

Although our understanding of all the mechanisms of action that metals affect is incomplete, we do have knowledge about several mechanisms. The need exists for further investigation in light of Dr. Deth's and colleagues' work on brain methylation inhibition by metals. Metals affect the DNA, messenger RNA, mitochondria, enzymes, hormones, free radicals and the immune system. Dr. Russ Jaffe has neatly organized a few of the known mechanisms in his lectures. The following list of mechanisms is taken from these lectures.[32] The toxicant metals act as: 1) metabolic uncouplers that cause bioelectrical short circuits; or 2) haptens that cause immune sensitizing of small molecules resulting in secondary autoimmunity; 3) enzyme inhibitors that bind to active sulfhydryl sites; 4) agents for depleting glutathione and ascorbate and agents for decreasing adenosine triphosphate; 5) concentrating agents in the brain's choroid plexus and kidneys; 6) inhibitors of thiamine (B-1) and pyrodoxine B-6); 7) inhibitors of glutathione binding, which leads to altered brain tubulin, disrupted nerve function and communication; 8) beta-tubulin disorders of the brain causing neurofibrillary tangles; 9) inhibitors of nerve cone growth with retrograde degeneration of neurite membrane; 10) the cause of most, if not all, aberrant biochemistry in Alzheimer's disease brain in the case of mercury;[33] 11) a toxicant, in the case of mercury, that passes the placental barrier, allowing toxicant metal in the mother to be transferred to the fetus; 12) an agent that decreases dopaminergic brain activity leading to neurodegeneration. These are 12 mechanisms by which toxicant metals affect our health. Together, Dr. Jaffe and Dr. Deth provide 13 mechanisms of toxicant metals. As more resources are poured into studying the basic mechanisms of toxicant metals, more mechanisms will be forthcoming.

RECENT STUDIES

Acute lead exposure has been known to cause encephalopathy. Because acute toxicity is now rare in the US, more attention is given to chronic, low-level exposure and its health consequences. From childhood on, negative health consequences of lead exposure are being discovered. Selevan et al suggest that "environmental exposure to lead may delay growth and pubertal development in girls,"[34] and that "blood lead concentrations, even those below 10 µg/dL, are inversely associated with children's IQ scores at three and five years of age, and associated declines in IQ are greater at these concentrations than at higher concentrations."[34] "For each increase of 10 µg/dL, IQ decreases 4.6 points. For each concentration below 10 µg/dL, IQ decreases 7.4 points."[34] The lead author of the article, Richard L. Canfield, PhD, said in a subsequent interview, "there is no safe level of lead." Zero lead tolerance has been the goal of clinical metal toxicologists, but reality and the industrial society we live in may preclude achieving that goal. The acceptable reference range of blood lead level concentrations have been reduced in 1960 from 60 µg/dL to 40 µg/dL, in 1970 from 40 µg/dL to 35 µg/dL, in 1980 from 35 µg/dL to 30 µg/dL, and in 1985 to its present level of 10 µg/dL.[35]

According to a recent study, vascular diseases also have been associated with lead interactions.[28] "Blood lead level is positively associated with both systolic and diastolic blood pressure,

and the risk of both systolic and diastolic hypertension among women aged 40 to 59 years is increased. The relationship between blood lead level and systolic and diastolic hypertension is most pronounced in postmenopausal women. These results provide support for the continued efforts to reduce lead levels in the general population, especially women."[36] Navas-Acien et al found that "individuals with blood lead levels of 20 µg/dL to 29 µg/dL in 1976 to 1980 (15% of the US population at that time) experienced significantly increased all-cause, circulatory, and cardiovascular mortality from 1976 through 1992. Thus, we strongly encourage efforts to reduce lead exposure for occupationally exposed workers and the 1.7 million people with blood levels of at least 20 µg/dL."[28] Navas-Acien et al also found that, "blood lead and cadmium, at levels well below current safety standards, were associated with an increased prevalence of peripheral arterial disease in the general US population. Cadmium may partially mediate the effect of smoking on peripheral arterial disease."[28] "Lead and cadmium are toxic and are associated with neurodevelopmental disorders, cancer, hypertension, cardiovascular events, renal failure, and peripheral arterial disease."[28] Second-hand smoke may be the real cause of cadmium toxicity.[28]

Lead affects the brain, vascular system, immune system, kidneys, and peripheral nervous system.[19,28,34-36] It must be remembered that one toxicant metal alone is, in and of itself, potentially unhealthy. When another toxicant metal is added, the effect is not additive, but synergistic. The good news is that we have made progress in decreasing our lead exposure by removing it from paints in 1977 and gasoline in 1982. In 1990, the Environmental Protection Agency's top three toxicants were lead, arsenic, and mercury. In 2003, they were arsenic, mercury, and lead.

MERCURY EXPOSURE

The top toxicant metal for 2000, mercury, is continually increasing in our environment. The mercurous vapor from dental amalgams, the methylmercury from fish, and the ethylmercury from vaccines have all been reported by the press. A short video is available to show the off-gassing of a 50-year-old amalgam filling that had been removed from a patient's mouth 15 years earlier.[37] These vapors can be absorbed into the blood. Some of the vapors reach the brain via the ethmoid sinuses. Is it coincidental that Alzheimer's disease has shown degenerative tracts often following the olfactory connections? The Environmental Protection Agency (EPA), which oversees sports fishing, has recommended severe restrictions on fish caught in fresh water for years. The US Food and Drug Administration (FDA), which oversees commercial fishing and its restrictions, had been much more lenient until recent years. The differences between the agencies' guidelines occurred because the EPA used the most recent data regarding mercury in fish, and the FDA used outdated toxicology data from the 1970s. The current administration brought these two agencies together in the summer of 2003, and joint recommendations came out in December 2003 and were updated in March of 2004.[38] The United Nations Environmental Program (UNEP) has a Global Mercury Assessment Working Group in Geneva. The worldwide threat of toxicant metals is understood, and its negative effect on the oceans' food supply is of concern. R.C. Srivastava, PhD, former co-chair of the Mercury Assessment Group, UNEP, and former deputy director of the Industrial Toxicology Research Center, Lucknow, India, speaks out on the dangers of mercury pollution.[39] Dr. Srivastava warns about the dangers of increased use of mercury in the chlor-alkalai industries and from coal burning that now may contaminate the food supply in the oceans. Ethylmercury, in the form of thimerosal in vaccines, is especially problematic.

According to Congressman Dan Burton (R-Ind), the incidence of autism in the US was 1 in 10,000 in 1979 and 1 in 150 in 2005.[40] Representative Burton, along with three additional congressional representatives, two physicians, and two scientists, held a press conference to protest the IOM's carefully worded statement implying there is no danger from thimerosal. The IOM meeting to investigate scientific evidence for the safety of thimerosal was held in February 2004. Dr. V. Aposhian, Dr. Haley, Jeff Bradstreet, MD, Mark Geier, MD, PhD, and David Geier spoke of the association of ethylmercury and autism, and others spoke against it. The latter group prevailed, although flaws were noted in their research protocols. The four congressional representatives have been holding hearings on toxicant metals since 1999 and have heard from most experts. Their overwhelming sentiments are that something is very wrong with our vaccination system that has delayed removing thimerosal from all vaccines.

A similar problem arose in the United Kingdom. Parents were not getting their children vaccinated because of the fear of their developing autism. Approximately 13% of the parents withheld vaccination from their children, causing the government to act in August 2004. Reuters announced on August 9, 2004, "Babies will no longer be given a vaccine containing mercury, the British government said on Saturday, after pressure from parents fearing a possible link with autism."[41] The unintended consequences of our vaccination programs may be devastating to our youth. It is time to get the mercury out of our vaccines.

There is increasing evidence of mercury associated with Alzheimer's disease. Dr. Boyd Haley, Chairman of the Department of Biochemistry, University of Kentucky, has published multiple papers on his research since the late 1980s.[42,43] He has successfully reproduced the changes seen in Alzheimer's disease in the brain homogenate of normal brains with the addition of mercury, in the form of both mercury chloride and thimerosal.[42,43]

Mike Godfrey, MD, of New Zealand, published an article showing why more Alzheimer's disease patients with onset before the age of 70, have APO-E4 genes.[23] Each parent donates an APO-E gene. The APO-E4 has two arginine sites, the APO-E3 one arginine and one cystein and the APO-E2 two cystein. Cystein will bind to mercury, whereas arginine will not. If two parents have APO-E2 genes, their offspring will have four sites to

bind mercury. An APO-E2 and APO-E3 parent will combine a total of three mercury-binding sites in their offspring. These children will have onset of Alzheimer's disease after age 90. Any combination of APO-E2 and APO-E4 or two parents with APO-E3 will contribute a total of two mercury binding sites. These individuals will have onset of Alzheimer's disease between ages 80 and 90. An APO-E3 and APO-4 parent combination will have one binding site for mercury in their children. The onset of Alzheimer's disease in these children will be between 70 and 80 years. If both parents have APO-E4 genes, their offspring will have no sites to bind mercury and will have onset of Alzheimer's disease before age 70.[25]

The work of Haley, Aposhian, Godfrey, and others makes a strong case that mercury may cause or at the very least exacerbate Alzheimer's disease. Studies looking at toxic metals, especially mercury, as a possible cause for Alzheimer's disease need to be conducted. The clinical metal toxicologists have clinical experience that early metal detoxification will often stabilize and even reverse early Alzheimer's disease. More research is needed.

SUMMARY

The purpose of this review article is to explore new approaches to old diseases. Larry Dossey, MD, wrote an editorial in 1998 citing some of the difficulties facing us who choose a different path.[44] Toxicant metals are increasingly being associated with multiple disease states. Dental amalgams have not been paid for by state insurance since 1990 in Austria, Germany, Denmark, and Sweden.[45] The Swedish parliament voted 100% to remove mercury from their environment in December 2003.[46] In March 2004, the first recommendations by the coordinating government agency were to remove all amalgam fillings from deceased persons before burial or cremation.[47] Although Europeans have written articles about amalgams,[24,48] this is still an area for improvement in the US. The Centers for Medicare and Medicaid Services (CMS) have authorized payment for in-office, intravenous metals detoxification in the District of Columbia, Delaware, Maryland, Texas, and Virginia, as well as the Indian Health Service. This is a great opportunity to collect meaningful data directly from patients. It is known that dialysis can be delayed at least two or three years by repeated in-office, intravenous metals detoxification;[29] it is hoped that all prospective dialysis patients would be tested for toxicant metals and treated appropriately. If detoxification of toxicant metals can become the standard in time, our health may improve markedly. Could toxicant metals be a diagnosable and treatable risk factor in many of the diseases affecting this nation? The clinical metal toxicologists are the experts in low-dose, chronic accumulation of toxicant metals and the symptomatic reversal observed with treatment. Many clinical metal toxicologists are participating in the NIH's TACT study. More research is needed in the basic science mechanisms of toxicant metals and common diseases. Additional clinical research, besides the TACT study, is also needed.

As Dr. Dossey said, "the resistance of Right Men to CAM conceals a fear that good science may be degraded or contaminated by bad science. Rigid barriers must therefore be erected to keep out the contaminating influences."[44] I believe toxicant metals and their detection and detoxification will be one of the exciting new fields in medicine. I have great hope for the future of medicine. I will close with these meaningful words from Dr. Dossey: "We have come a long way; it's not for nothing that we've acquired these scars. Progress has been possible because we have done good scientific work, and good science remains our best hope of accomplishing our primary goal—the improvement of the health of those we serve."[44]

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