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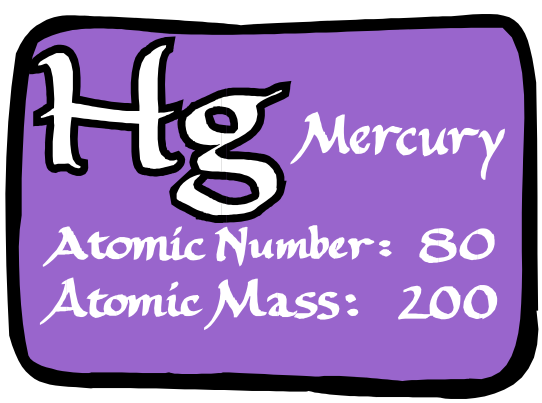
Mercurialism

Part one of a three part series:

Mercury is a well known neurotoxin that comes in various forms. Scientists have learned that all forms of mercury have the potential for toxicity. The first part of this series will discuss three common sources of mercury - methylmercury, ethylmercury, and mercury vapor. Discussion will include history, sources, disposition kinetics, and the effects/relative toxicity of exposure to each form. Next month, in part two, we will examine the various types of tests for mercury poisoning, the advantages and disadvantages of each method, and how to interpret the results. Finally, in part three, we will discuss treatment modalities for mercury toxicity.

Methylmercury

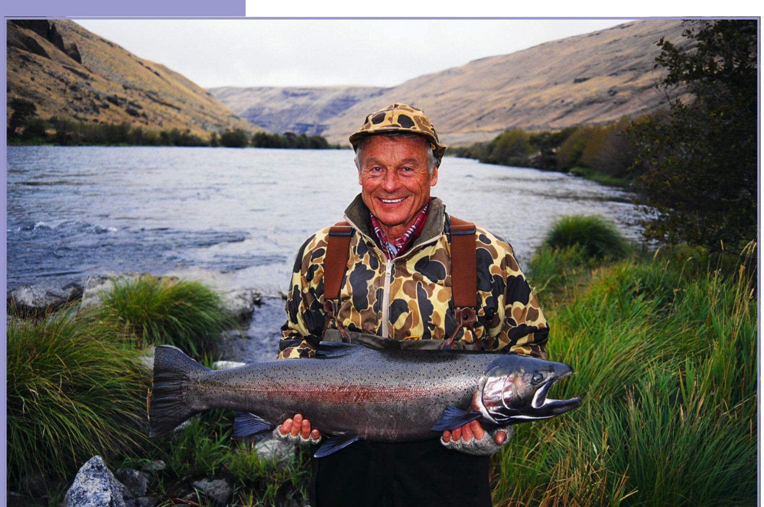
Methylmercury was first synthesized in a chemical laboratory in London in the 1860's, resulting in the deaths of two of the laboratory technicians (Clarkson, 2002). In the early twentieth century mercury was shown to have antifungal properties leading to its application to seed grains and cereal crops in particular (Clarkson, 2002). By the late 1950's and early 1960's there were several serious outbreaks of mercury poisoning in developing countries, including one in rural Iraq which hospitalized 6,000 Iranians and poisoned nearly 40,000 who consumed homemade bread made with flour from treated grains (Bakir et al, 1973). Predatory birds in Sweden also developed neurologic disorders after consuming small, grain-eating mammals that had consumed treated grains (Clarkson, 2002). Analysis of the bird's feathers showed a substantial increase in mercury and the increase in mercury was initially only shown in the feathers of birds from this area of Sweden where mercury was being used as an agricultural fungicide (Clarkson, 2002).



> **“Food containing mercury, such as fish, has been identified as a health risk .”**

Scientists eventually found equivalent mercury in the feathers of birds from other areas that had not eaten treated grain and it was quickly realized that microorganisms in the aquatic environment converted inorganic mercury to methylmercury, evidence of biomethylation and bioaccumulation in higher organisms (Clarkson, 2002). Therefore, methylmercury is most commonly found in fish and it was soon found in all species of fish and fish-consuming animals (Clarkson, 2002). Consumption of food containing mercury, such as fish, has been identified as a health risk and the methylmercury in these food products is 95% absorbed (Hightower & Moore, 2003).

Most methylmercury is eliminated from the body by demethylation and is excreted as inorganic mercury in the feces (Clarkson, 2002; Clarkson, 1997; Hightower & Moore, 2003). Methylmercury is present in the body as a water soluble complex and attaches to the sulfur atom of thiol ligands (Clarkson, 2002). What's most damaging is the fact that methylmercury enters the endothelial cells of the blood-brain barrier with l-cysteine, where biotransformation into inorganic mercury via demethylation takes place (Clarkson, 2002; Hightower & Moore, 2003). It also crosses the placental barrier into developing fetal tissue (Bjornberg et al, 2005; Hightower & Moore, 2003). Once demethylation occurs, the half-life of mercury can be measured in years therefore it is not easily eliminated from the body (Clarkson 1997; Davis et al, 1994; Hightower & Moore, 2003; Pedersen et al, 1999). People react in varying ways when exposed and genetics has been shown to have a strong influence on the susceptibility of the immune system to methylmercury (Goth et al, 2006; Havarinasab & Hultman, 2005; Lawler et al, 2004; Silbergeld et al, 2005).



The body removes methyl Mercury as a complex through the use of reduced glutathione (Ballatori & Clarkson, 1985; Dutczak & Bllatori, 1992; Dutczak & Bllatori, 1994). Perhaps this is the reason many mercury toxic individuals have low or undetectable glutathione levels. The half life of mercury is roughly 45 to 70 days therefor individuals with long-term, chronic exposure easily achieve a high body burden due to the slow excretion rate (Clarkson, 2002). Thiol containing agents, such as N-acetylcysteine (NAC) which is also a precursor to glutathione, enhance methylmercury excretion by carrying mercury secreted in the bile to the feces for elimination (Ballatori et al, 1998).

"Adverse effects… include paresthesia, ataxia, dysarthria, constriction of the visual field, loss of hearing, lost of neuronal cells, and damaged protein synthesis."

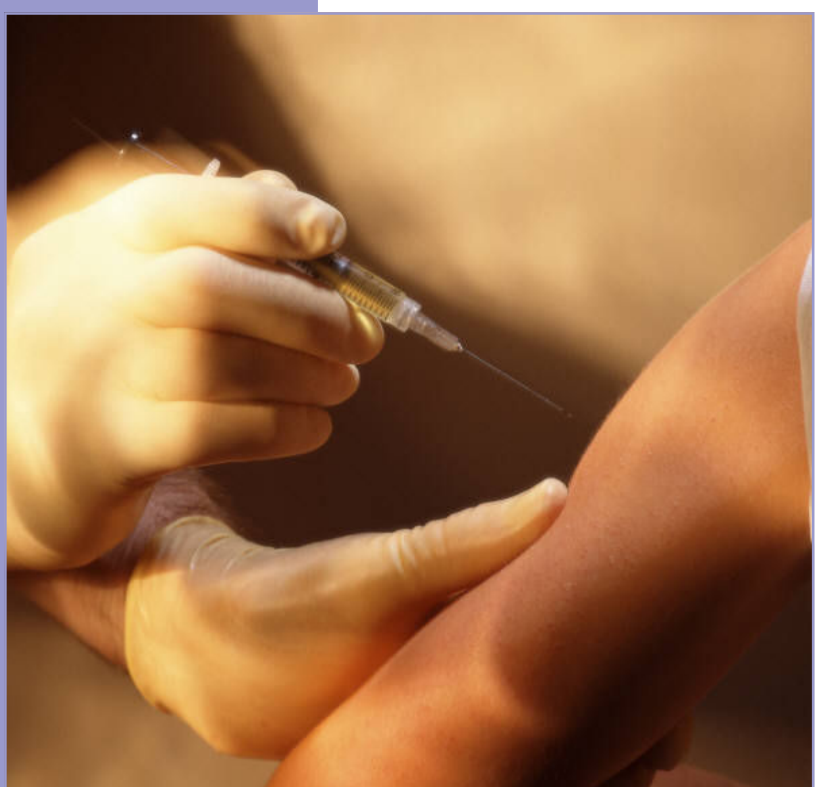
Adverse effects of methylmercury occur mainly on the neurological and central nervous systems and are characterized by a latent period of several weeks to several months between the time of exposure and first appearance of symptoms (Clarkson, 2002). General symptoms of methylmercury toxicity include paresthesia (partial paralysis), ataxia (stumbling gate), dysarthria (slow speech), constriction of the visual field, loss of hearing, lost of neuronal cells, and damaged protein synthesis (Clarkson, 2002). It has been shown that mothers with mild effects of methylmercury often give birth to offspring with severe brain damage (Clarkson, 2002). A milder syndrome has also been identified in which children, otherwise appearing normal, have a history of delayed development, neurologic abnormalities such as brisk tendon reflexes, and correlated elevations in blood pressure as related to the quantity of prenatal methylmercury exposure (Clarkson, 2002). A dose-response relationship was found between the mercury levels in prenatal hair samples and the number of abnormal offspring showing these developmental delays and abnormal neurologic findings (Clarkson, 2002; Marcia et al, 1987; Cox et al, 1989). Autopsy of infant brains showed damage to neuronal cell division and migration (Clarkson, 2002).

Ethylmercury

Ethylmercury, on the other hand, is most often seen as sodium ethylmercurithiosalicylate (thimerosal), an antiseptic added to cosmetics and vaccines since the early 1930's (Clarkson, 2002; Goth et al, 2006). The history of ethylmercury is very similar to that of methylmercury. Despite being given a clean bill of health by the FDA in 1976, the U.S. EPA later lowered the allowable safety limit and, as a result, recent reviews of thimerosal by the FDA have raised questions about public health risks (Clarkson, 2002). In 1999, thimerosal was withdrawn from many vaccines due to concerns over organic mercury being a known neurotoxicant, though it continued to be included in influenza, diphtheria toxoid, diphtheria toxoid and acellular pertussis, and tetanus toxoid vaccines (Centers for Disease Control & Prevention, 1999). Many parents are concerned over the potential that the rising rates of autism may be linked to the thimerosal contained in MMR vaccines, which are given to children at the age of 18 months when autism suddenly develops.

"There is limited toxicologic information about thimerosal."

There is limited toxicologic information about thimerosal and most estimates of heath risks were previously based on the assumption that ethylmercury was toxicologically similar to methylmercury (Burbacher et al, 2005; Clarkson, 2002). However, scientists have since found that methylmercury is not a suitable reference for ethylmercury toxicity (Burbacher et al, 2005; Clarkson, 2002). Similar to methylmercury, ethylmercury has produced several cases of poisoning, the most recent being in China in the 1970's after victims had consumed rice treated with ethylmercury chloride applied to prevent seed born disease (Clarkson, 2002;Jalili, MA & Abbasi, AH, 1961; Zhang, J, 1984).



The disposition of ethylmercury from thimerosal is likely different than that of methylmercury. Originally, it was believed that the thimerosal molecule would remain intact after injection for long enough to allow it into the bloodstream to be transported to the kidneys for rapid excretion (Clarkson, 2002). However, it was later found that immediately after injection the ethylmercury cation may dissociate from the thiosalicylic acid moiety and bind to surrounding thiol ligands, resulting in immediate release to surrounding tissues where it is most likely to induce damage (Carty & Malone, 1979; Elferink, 1999; Clarkson, 2002; Ulfvarson, 1962; Tan & Parkiin, 2000). Evidence now shows that the surrounding body tissues may be impregnated with mercury after injection (Carty & Malone, 1979; Elferink, 1999; Clarkson, 2002; Ulfvarson, 1962; Tan & Parkiin, 2000). "Toxicologically, ethylmercury in thimerosal is assumed to follow the same pathways of disposition as ethylmercury absorbed into the body from other ethylmercury compounds" (Clarkson, 2002) with the exception that inorganic mercury accounts for about 50% of the total mercury in blood samples in ethylmercury exposure as opposed to 10% in cases of methylmercury exposure indicating ethylmercury breaks down into inorganic mercury more rapidly than methylmercury.

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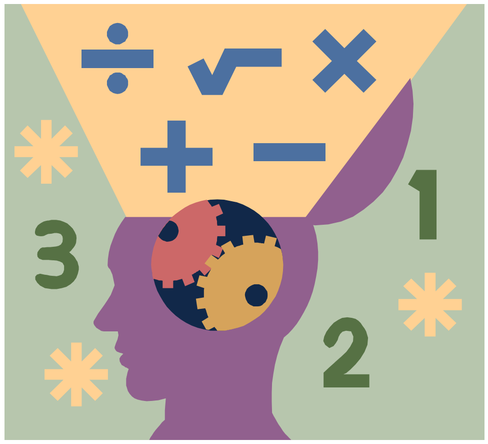
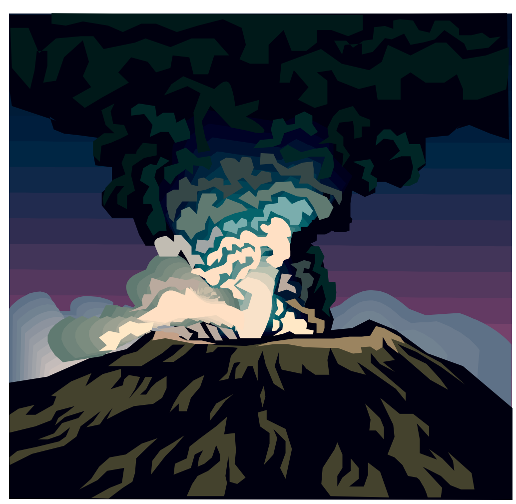


As with methylmercury, genetics has also been shown to have a strong influence on susceptibility of the immune system to ethylmercury (Goth et al, 2006; Havarinasab & Hultman, 2005; Lawler et al, 2004; Silbergeld et al, 2005). Adverse effects of ethylmercury result in milder neurological symptoms as than methylmercury, however they also include renal damage, kidney damage, contact allergy (Clarkson, 2002), brain growth abnormalities, and histologic abnormalities (Goth et al, 2006). It is quite clear that there is insufficient evidence to make a determination that the ethylmercury in thimerosal is safe for human use, as little is known about the disposition and toxicity of thimerosal in human infants and adults alike.

Mercury Vapor

Current sources of mercury vapor include the burning of fossil fuels such as coal, waste incineration, volcanoes, and dental amalgams (Clarkson, 2002). As a chemically stable monotomic gas, mercury vapor can remain stable in the air for at least a year, making it an opportune pollutant that easily recycles itself after evaporating by returning to the earth in the form of contaminated rainwater which can once again evaporate in a vicious cycle (Clarkson, 2002). Mercury in its liquid form was found to be useful for making mirrors, extracting gold and silver, manufacturing scientific instruments such as thermometers, designing household gas regulators, and has also been used as an ointment for treating skin (Clarkson, 2002). At one time mercury was used to clean hats, resulting in occupational exposure to the mercury vapor that has since been associated with the neuropsychologic symptoms known as "Mad-Hatter Syndrome" (Factor-Litvak et al, 2003).



"Dental amalgams, also known as silver dental fillings, are the main source of human exposure to mercury vapor."

Dental amalgams, also known as silver dental fillings, are the main source of human exposure to mercury vapor and are used to restore teeth after drilling of cavities. Amalgams contain as much as 50% inorganic mercury which has been demonstrated to cause systemic absorption of mercury vapors as they rise from the fillings (Berlin, 1969; Berlin et al, 1975, Hurch et al, 1980; Newton and Fry, 1978; Takahara et al, 1970; Watanabe, 1969). Much controversy exists over the safety of amalgam fillings (Skare & Engqvist; 1994, Factor-Litvak et al, 2003), particularly because concentrations of mercury vapors have been shown in the air of the oral cavity that exceed occupational health standards (Clarkson, 2002). Despite this, proponents have claimed that since the oral cavity is such a small area, the quantity of mercury really isn't a concern. However, there is still concern over body burden from multiple sources when a human being consumes methylmercury by eating fish, receives ethylmercury in the form of thimerosal from vaccinations, breathes environmental emissions of mercury vapor in the air, and has their own ongoing source of mercury vapor in their oral cavity. Scientific studies have linked amalgam restorations to psychiatric, neurologic, and immunologic effects (Fung & Molvar, 1992; Hanson & Pleva, 1991; Weiner et al, 1990). Mercury levels in autopsy tissues samples have been shown to correlate with the total number of amalgam restorations (Clarkson, 2002). It is estimated that amalgams release two to seventeen micrograms per day of mercury with additional release during chewing and when consuming hot foods and beverages (Clarkson, 2002).

About 80% of inhaled mercury vapor is retained in the body (Clarkson, 2002). Up to 15% may be exhaled within a week after exposure and the halftime of the mercury vapor is approximately 48 hours (Clarkson 2002). Once the vapor is dissolved it is carried in red blood cells to the tissues of the body and it crosses the blood-brain barrier as well as the placental barrier (Bjornberg, 2005; Clarkson, 2002). Once inside a cell, mercury oxidizes into inorganic mercury and just over 1% of the body's burden is excreted per day in the urine and feces (Clarkson, 2002).

"Clearly, the neurotoxin known as mercury has a negative effect on humans and animals alike."

Signs and symptoms from various research studies on poisoning from inhaling mercury vapor including damage to the brain, kidneys, severe lung damage leading to death from hypoxia, flu-like symptoms, pulmonary toxicity leading to death by hypoxia, memory loss, emotional liability, depression, insomnia, shyness, fine tremors, increased excitability slowed nerve function, decreased performance on psychomotor tests, changes in mood, changes in behavior, alterations in mood, decreased performance on neuropsychological tests, dementia, decreased cognitive function, Alzheimer's disease, and adverse effects on the kidneys (Clarkson 2002; Eheverria et al, 1995; Factor-Litvak et al, 2003; Ngim et al, 1992). Cutler (1999) believes that any number of human health disorders can be related to mercury toxicity including allergic asthma, autoimmune diseases, amytrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, schizophrenia, borderline personality disorder, attention deficit hyperactivity disorder, panic attacks, depression, learning disabilities, obsessive compulsive disorder, manic depressive disorder, rheumatoid arthritis, multiple chemical sensitivities, environmental illness, chronic fatigue, fibromyalgia, sciatica, gastritis, irritable bowel syndrome, Crohn's disease, sleep problems, and many other conditions.

Conclusion

Clearly, the neurotoxin known as mercury has a negative effect on humans and animals alike. Regardless of form, there is sufficient evidence to believe that any form of mercury is toxic (Clarkson, 2002). Nearly unavoidable, mercury has found its way into human bodies. Next month we will examine testing methods for mercury toxicity and cover the reliability and validity of each method.

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