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Introduction to the science surrounding mercury dental amalgam

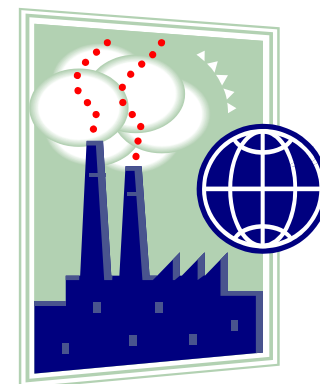
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January 22, 2013



Environment

- Mercury is a volatile toxic metal that does not decompose in the environment and is readily absorbed by animals
- Metallic mercury is not absorbed as readily by inhalation and absorbed even less when ingested
- Mercury bio-accumulates in the food chain, and many fish contain methylmercury.
 - Fish consumption is a significant source of exposure to mercury for many people.
 - In the absence of fish, amalgam is a major source of mercury body burden.
- Sources of mercury in the environment other than dental amalgam include coal fires, cement kilns, incinerators, releases from fluorescent lights, and gold mining and from naturally occurring minerals.



Toxicity of elemental mercury

- Mercury is a neurotoxicant and may affect many areas of the brain
- Toxicity from elemental mercury via:
 - oxidative damage of the cells and sulfur blockage
- Chronic mercury toxicity is associated with many nonspecific symptoms
 - Impaired detoxification
 - Developmental impacts
- Toxicity of low level, chronic mercury exposure is not well understood and many developmental and neurodegenerative disease may involve a combination of environmental exposures and genetic susceptibilities.

Evidence for toxicity

- The State of California through Proposition 65 recognizes mercury as a chemical known to the state of California to cause birth defects or other reproductive harm.
 - Dental offices with more than 10 employees are required to post notice
- Health effects from mercury in the environment are well recognized by the U.S. Environmental Protection Agency and the California Environmental Protection Agency and include impacts on neurological development, especially on the developing brains of fetuses, infants and children.

Animal data

- In experimental animal studies, offspring of pregnant rats exposed to elemental mercury experienced decreased birth weight at doses that also resulted in maternal toxicity.
- Adverse behavioral effects (ex. altered levels of spontaneous motor activity) were observed in adult rats whose mothers were exposed to mercury vapor during pregnancy into adulthood.

Morgan, D.L., et al. 2002. "Disposition of inhaled mercury vapor in pregnant rats: Maternal toxicity and effects on developmental outcome." *Toxicol.Sci.* 66(2):261-273.

Danielsson, B.R., et al. 1993. "Behavioural effects of prenatal metallic mercury inhalation exposure in rats." *Neurotoxicol.Teratol.* 15(6):391-396.

Fredriksson, A., et al. 1992. "Behavioural effects of neonatal metallic mercury exposure in rats." *Toxicology* 74(2-3):151-160.

Human epidemiology studies

- Numerous human epidemiology studies of amalgam and various health outcomes have been published. Many have not shown significant associations; some have found associations.
- Key studies: Portuguese and New England Children's amalgam trials
 - Randomized control clinical trials (gold standard)
 - Initial publications found no significant results between neurobehavioral outcomes and amalgams.
 - Children with amalgams did have higher urinary mercury levels than the controls.

Bellinger, D. C., et al. "Neuropsychological and renal effects of dental amalgam in children: a randomized clinical trial *JAMA* 295 (15): 1775–1783." *Find this article online* (2006).

DeRouen, Timothy A., et al. "Neurobehavioral effects of dental amalgam in children." *JAMA: the journal of the American Medical Association* 295.15 (2006): 1784-1792.

Children's amalgam clinical trials cont.

- Re-analysis of the Portugal clinical trial looked for a relationship between mercury levels (from amalgams) and neurological test performance grouped by a genetic variant (CPOX4)
 - Data was analyzed by a genetic variant (CPOX4). CPOX4 is hypothesized to modify the ability to detoxify mercury, impacting neurobehavioral functions
- Used better exposure assessment (measured urinary mercury levels unlike amalgam or no-amalgam grouping used before)
- Results: statistically significant dose-related adverse neurobehavioral effects in boys with the CPOX4 gene

Exposure

- Estimates of the amount of mercury released from dental amalgams range from 3 to 17 micrograms per day ($\mu\text{g}/\text{day}$).
- Dental amalgams are the most significant source exposures to mercury (*in the absence of fish consumption or living next to a waste site or incinerator*) and amalgams can contribute **75%** of your total daily mercury exposure (ToxProfiles from Agency for Toxic Substances & Disease Registry, CDC)
- The FDA assumes an average exposure of 5 ug per day.

Mercury standards and exposure

- The US EPA's Reference Concentrations (RfCs) is **0.3 ug/m³** of air (1995).
- The California EPA's chronic Reference Exposure Level (REL) is **0.03 ug/m³** of air (2008).
- Using the Cal/EPA standard, the exposure would no longer be safe
 - The FDA does not take into account sensitive populations or the range of variability in exposures.

Children and Sensitive Populations

Exposure among children:

- Children in the 2003-2004 National Health and Nutrition Examination Survey had mean urinary levels of mercury of **0.358 ug/g**
 - In contrast, the boys from the Portuguese amalgam trial (Woods *et al.* 2012) had **1.4 ug/g** when they started the study and **2.2 ug/g** in the year 2 study follow up
- Higher blood mercury concentrations were found in children with dental amalgams who also grind their teeth or chew gum, compared with those who do not (Hertz-Picciotto).

Exposure among pregnant women:

- Dental amalgams and pregnant women have been studied. The number of amalgam fillings in women during pregnancy was significantly associated with mercury concentrations in neonatal hair (Razagui) but not in amniotic fluid (Luglie).

Hertz-Picciotto, Irva, et al. "Blood mercury concentrations in CHARGE study children with and without autism." *Environmental health perspectives* 118.1 (2010): 161.

Razagui, I.B., and S.J. Haswell. 2001. "Mercury and selenium concentrations in maternal and neonatal scalp hair: Relationship to amalgam-based dental treatment received during pregnancy." *Biol.Trace Elem.Res.* 81(1):1-19.

Luglie, P.F., et al. 2005. "Effect of amalgam fillings on the mercury concentration in human amniotic fluid." *Arch.Gynecol.Obstet.* 271(2):138-142.