

NIDCR funded research looked for mercury in all the wrong places

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Anyone who cares about the health of our children would be wise to consider the flaws in the two recent JAMA papers about studies that were conducted in Portugal and New England and that compared youngsters with dental mercury fillings with those who were amalgam free^{1,2}. In designing their studies, the authors of these two papers evidently ignored recent research findings about mercury toxicity, particularly the results strongly suggesting that the level of mercury in blood, urine or feces may be influenced more by the child's ability to excrete mercury than by his or her total mercury exposure.

The view that mercury toxicity can be traced to the child's inability to excrete the metal comes from a wide range of studies, including research on autistic children³. These children are one of the subsets of the population that do not effectively excrete mercury. Scientists have shown that in comparison to non-autistic children, autistic children have less mercury in their blood, urine or feces but have much more in their body organs. Also, the aberrant porphyrin profiles of autistic children indicate that their ineffective mercury excretion is the result of an early exposure to this metal⁴. The almost normal porphyrin profiles that are produced in children who have undergone mercury chelation treatments supports the view that mercury toxicity is based on a child's inability to excrete mercury, not on his or her total mercury exposure.

Why is the profile data relevant? Consider these facts: the inhibition of the porphyrin synthesis pathway curtails the production of the final product, heme, which binds and carries oxygen in the hemoglobin of blood. Heme is also a necessary component of the P-450 enzymes that are critical for detoxifying the body of pesticides, herbicides and other organic toxins. In our body's cells, heme is also critical for the electron transport system of mitochondria, the source of most of the body's energy (ATP).

A report in the February issue of the Proceedings of the National Academy of Sciences established that heme is needed to flush beta-amyloid from the brain, and if insufficient heme is present, the beta-amyloid forms "large toxic clumps" called amyloid plaques, a major diagnostic hallmark of Alzheimer's disease⁵. While many regard the amyloid plaques as the root of Alzheimer's disease, several recent studies suggest that the primary cause is toxins such as mercury because they prevent the body's normal removal, or excretion, of the amyloid protein.

Therefore, mercury inhibition of the heme producing porphyrin pathway could have major effects secondary to the primary site of mercury inhibition. Previous scientific papers by other investigators have reported that, when exposed to dental amalgam, the subset of the adult population with the genetic polymorphism (CPOX4) is at risk for developing aberrant porphyrin excretion profiles that significantly modify the effect of mercury exposure on urinary porphyrin excretion^{6,7}. Because some of the CPOX4 adults were more affected than others, it is likely that a smaller subset with an even stronger genetic susceptibility to mercury toxicity also exists. The authors of the two JAMA papers should have acknowledged these findings, and, of course, they should have included the porphyrin profile data on the children rather than dismissing this information with only brief comments. Those of us who are aware of the previous scientific papers on the impact of the CPOX4 genetic polymorphism on an adult's porphyrin profile have a hard time understanding why children – such as those in the two studies reported in JAMA – would not have been similarly at risk for the CPOX4 effect and thus tested to identify those with the polymorphism.

Below are my more 'other' comments about the two JAMA studies. The end of this summary provides information about the research publications relevant to my comments.

1. In the first line of the Portugal based study entitled, "Neurobehavioral Effects of Dental Amalgam in Children," Dr. Timothy A. DeRouen, et al., wrote that dental amalgam "emits small amounts of mercury vapor". This is not a scientific or quantitative statement, because what is a "small" amount of mercury? Reporting the exposure level of a toxin in any study is absolutely needed. It is a dereliction of duty to place a toxic material into any patient, but especially a child, and particularly if the level of toxic exposure is not defined or known. That the authors totally ignored the exposure level invalidated their conclusion that the measurements of the urine mercury levels demonstrated the safety of the mercury fillings.

The authors also did not report the level of mercury vapor to which the children in the studies were exposed daily. This is an irresponsible omission considering the fact that the material implanted in the children's teeth was 50% mercury, and previous studies have indicated that such fillings emit mercury vapors⁸. However, the authors' omission is not surprising since both the ADA and the FDA have steadfastly refused to conduct and publish the results of well-designed experiments on the impact of mercury vapor on human health. Have they stonewalled these experiments because they suspect that the level of mercury vapor emission from amalgams is too high to be accepted as safe? (Now it appears that the IRB boards of several prestigious medical schools are following ADA and FDA's lead.)

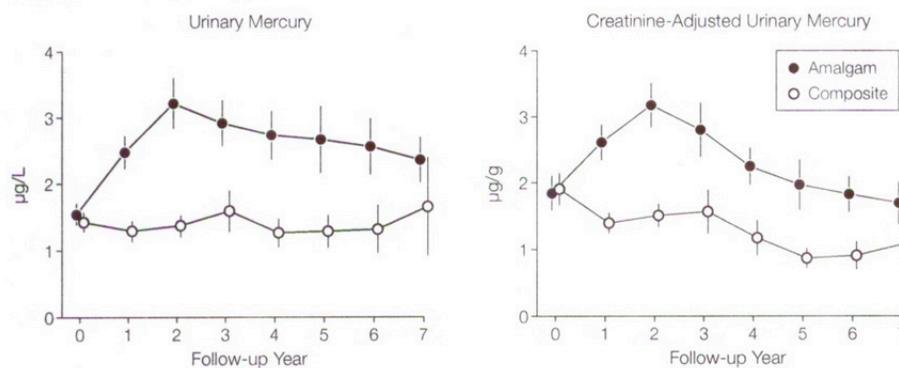
2. Since previous research has well documented that the amount of mercury in urine does not reflect a child's or adult's exposure under many conditions, it is baffling that the authors of the JAMA papers used urine, not fecal, samples to measure the children's mercury exposure⁹. It has been published and verified that over 90% of mercury that is excreted by humans is through the biliary transport system of the liver and that mercury is found in the feces, not the urine. One study reported that mercury in fecal materials was 13 times higher than the levels of the metal in the urine of the same patients^{10 11}. Also, most mercury excreted in the urine is bound to cysteine or other soluble, small molecule containing compounds. Therefore, the urine mercury excretion levels depend as much on the blood levels of cysteine or other small sulfur compounds as they do on mercury exposure. In addition, cysteine levels are influenced by diet. The bottom line is that these studies looked for mercury in all the wrong places. The take-home message from these JAMA papers is that if a researcher doesn't want to find data indicating excess exposure to mercury, he or she should look where the metal isn't -- in the urine.

3. Since the IRB of several prestigious universities approved this research even though it exposed children to an unknown daily level of mercury vapor, the public should be outraged and should demand that these institutions perform experiments on the same brand of amalgams, made outside of the mouth, of known weight and surface area and determine the amount of mercury that these amalgams released per day (with and without abrasion to mimic the daily effects of chewing). If these experiments were ever conducted, the public and the scientific community would have the data that the two studies described in JAMA failed to provide: determinations of the daily exposure of the children to mercury from these amalgams and the fraction of the amount excreted in the urine that did not account for the bulk of the mercury.

Research in my laboratory and studies by other scientists have demonstrated that the emissions of mercury vapors were much higher than the "estimates" made by pro-amalgam individuals. Chew et al.¹² showed that a study of long-term dissolution of mercury from a non-mercury releasing amalgam totaled 43.5 microgram/cm²/day Hg and this measure remained constant for 2 years. It should be noted that different amalgam preparations release mercury at vastly different levels, and the modern high copper amalgams have been shown to release much higher levels than other older type amalgams.

4. In Figure 2 on page 1788¹³, the authors of the two JAMA papers reported data that are quite damning of their conclusion that amalgams are safe to place in children. On the figure, the authors plotted the urine mercury levels at each year of the study. As expected, years 1 and 2 showed a steady increase in mercury exposure in the amalgam bearers when compared to the amalgam free children. Yet, during years 3 to 7, the level of mercury in the urine of the children with amalgam continuously dropped, approaching the levels of the amalgam free children. The authors implied, but failed to explain their reasoning, that restorative treatment in years 6, 7 and 8 would have increased, or at least maintained, the urine mercury levels. (The average life span of an amalgam before replacement is less than 10 years.) In the Chew study mentioned above, the amount of mercury released was steady for the study's two-year period.

Figure 2. Mean Urinary and Creatinine-Adjusted Urinary Mercury Concentrations by Treatment Group and Follow-up Year



Error bars indicate 95% confidence intervals.

Readers of the two JAMA papers also should consider the fact that 1 gram of filling contains 500,000 micrograms of mercury -- which over 100,000 days should emit a toxic 5 micrograms per day¹⁴. That is, before all of the mercury has been emitted, about 275 years have passed! Therefore, since amalgams do not stop releasing mercury vapor within 7 years, do you not wonder what caused the urinary excretion to drop after year 2? Urine mercury levels are, in my opinion, a measure of the amount of mercury being excreted by this route. After two years of exposure, the kidney route of mercury excretion appears to become less effective -- a development consistent with the well-known fact that increased mercury exposure inhibits its own excretion. However, the drop in urinary mercury could also be due to the fact that the mercury filled teeth were extracted during the course of the study, but that would invalidate the entire basis of these studies.

The mercury levels that have been measured in the body tissues of young athletes, nuns and other groups indicate that this toxic metal can be detected long after the dental mercury fillings have been installed. For example, in the heart tissue of young people who died from idiopathic dilated cardiomyopathy while under physical stress in athletic events, scientists have found 178,400 ng/g mercury -- 22,000 times more than the quantities measured in the heart and muscle tissue of individuals with other forms of cardiac disease¹⁵. For another example, consider the study published in the Journal of the American Dental Association regarding amalgams and Alzheimer's disease¹⁶. That paper, amazingly, reported no correlations between amalgams and brain mercury levels. Yet, in about 15% of the nuns in this study, brain mercury levels were in the micromolar range -- a very toxic level of mercury since much less (even 1,000 fold less) of mercury can kill neurons in culture. Again, even if everyone lived in the same location and ate the same food, certain individuals would appear to have less ability to excrete mercury when

compared to their family members and neighbors, The reason: mercury collects in certain tissues at levels much higher than have ever been found in blood, urine or hair, and it is primarily the retention of mercury (or the inability to excrete mercury) that boosts its toxicity from continuous, low level exposures.

Thus, the data in Figure 2 strongly indicates that after two years exposure to dental amalgam mercury, the children seem to lose their ability to excrete mercury through their urine pathway. Have they also lost the ability to excrete mercury through the fecal pathway, the major way that the body eliminates the metal? If the authors of the papers had answered this question, would they still have concluded that there was no health reason for discontinuing placing amalgams in children?

By revealing that children with amalgam may slowly lose their ability to excrete mercury after about two years of amalgam exposure, the studies reported in JAMA do add to the body of scientific knowledge about mercury toxicity. However, these experiments should have been conducted on nonhuman primates, not children. That children were “used” presents a question of ethics in medicine.

5. Except to state that there was no indication of kidney damage, the authors of the JAMA papers provide minimal information about porphyrin’s effects in the amalgam bearers. A more important question concerns the children’s ability to make heme: were their porphyrin profiles as aberrant as those that have characterized adults exposed to amalgams or autistic children? One has to question why this data was not included and discussed in detail by the authors.

6. Several scientific papers have revealed that mercury is a potent immune system suppressor¹⁷. Testing the immune response is an easy procedure to perform. Since the authors of the JAMA papers failed to conduct these tests, readers did not learn whether the children’s immune system showed the abnormalities, such as the inability of macrophage phagocytosis of microbes at very low levels, that were determined by previous research on mercury exposure. That the authors checked mercury’s effects on IQ but not the immune system, is questionable science since the study’s purpose was to determine whether mercury from amalgams is “safe” for use in children.

7. The research reported in JAMA excluded those children most susceptible to mercury toxicity -- a major failing of the studies’ design.

Excluded from the studies were children with “interfering health conditions,” which could be assumed to have included, autism and prior neurological disorders, even though the CDC has reported that 1 in 6 children in the U.S. has a neurodevelopmental disorder. However, in determining that amalgams should remain a viable clinical option in dental restorative treatment, the authors did not point out that their conclusion cannot apply to children with neurodevelopmental disorders.

In summary, the major problems with the studies published in JAMA is they:

1. Neglected to measure the amount of mercury exposure to children by first determining the amount of mercury emitted from an average sized amalgam outside of the mouth.
2. Used urine and blood mercury levels even though 90% plus of mercury is excreted in the feces. This obviates their conclusions (and what their data shows) that urine mercury levels are unreliable with regards to exposure.
3. Did not select the most sensitive clinical testing parameters for detecting mercury toxicity but instead used testing parameters that are known to fluctuate without known cause, or parameters that require long-term low level exposure to show an affect.
4. Did not state that their conclusions of amalgam safety should not include children with any prior neurodevelopmental or systemic illness.

5. Ignored the drop in mercury excretion in the urine after year 2 even though the mercury exposure from amalgams remained the same or increased. The drop in excretion is a sure sign that the body is losing its ability to excrete mercury in reaction to increased exposure to this toxic metal.

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- ³ Amy S. Holmes, Mark F. Blaxill, Boyd E. Haley Reduced Levels of Mercury in First Baby Haircut of Autistic Children, International Journal of Toxicology 22:277-285, 2003
- ⁴ GET FRENCH PORPHYRIN REFERENCE FROM BOYD
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- ¹¹ Skare I & Engqvist A. Amalgam restorations - an important source of human exposure of mercury and silver. LÄKARTIDNINGEN 15:1299-1301, 1992
- ¹² Chew et al. Clinical Preventive Dentistry 13(3) 5-7, 1991. In a study of long term dissolution of mercury from a non-mercury releasing amalgam it was determined that 43.5 microgram/cm²/day Hg was released and this remained constant for 2 years
- ¹³ **NOTICE:** In accordance with Title 17 U.S.C., section 107, some material in this email broadcast is provided without permission from the copyright owner, only for purposes of criticism, comment, news reporting, teaching, scholarship and research under the "fair use" provisions of federal copyright laws. These materials may not be distributed further, except for "fair use" non-profit educational purposes, without permission of the copyright owner.
- ¹⁴ Wataha et al. Dental Materials 10 298-303, 1994. The amalgam material with the trade name Dispersal Alloy made solutions in which it was soaked severely cytotoxic.
- ¹⁵ Frustaci et al. J American College of Cardiology 33(6) 1578, 1999. Data showed that individuals who died with IDCM (idiopathic dilated cardiomyopathy, the cause of young athletes dying during physical stress) had 22,000 times more mercury in their heart tissues than individuals who died of other forms of heart disease. Never has there been a urine or blood level reported that comes to the level of 178,400 ng/g tissue which is the same as 178.4 micrograms/g and one milliliter water weighs 1 gram. In the study under discussion they were talking about 3-5 micrograms/liter (1,000 milliliters) or so which compares to 178.400 micrograms/1000g in IDCM.

Where does this mercury come from as this disease kills intercity kids as much as anyone and they are not big seafood eaters.

¹⁶ Saxe SR, Snowdon DA, Wekstein MW, et al. Dental amalgam and cognitive function in older women: findings from the nun study. *JADA* 1995;126:1495-1501

¹⁷ Hultman, P. et al. Adverse immunological effects and autoimmunity induced by dental amalgam and alloy in mice. *The FASEB Journal* 8 Nov 1183-1190, 1994