A look at the 2006 FDA hearing on the safety of dental amalgams and possible toxicological concerns

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September 7, 2006

Abstract

In early September 2006 the FDA staff of the Dental Devices Branch released a 'white paper' on their evaluation of the research in the past 10 years that provided data that could be used to evaluate the safety of dental amalgams. This white paper was to be used to convince the FDA appointed 20 member external advisory committee of the safety of amalgams. It failed badly as the advisory committee voted 13 to 7 to not accept the conclusions of the white paper. The advisory committee asked for further research into the issue and expressed the opinion that the white paper did not present all of the relevant research. It is my opinion that the bulk of the research showing toxic effects from mercury were dismissed by the FDA staff using an invalid assumption that mercury toxicity can be determined by simply measuring urine or blood mercury levels. The FDA staff also took the position of questionable expertise in dismissing research done at major research universities and published in highly regarded journals. They also overlooked many important research papers by only using one search engine to identify the literature they would address, and only considered research done in the last ten years. This paper presents a few of the relevant articles overlooked by the FDA and gives a different evaluation of the research articles that were somewhat dismissed by the FDA staff using the outdated concept that urinary mercury levels can be used to determine if a toxic exposure has occurred.

Keywords: amalgams, toxicity, FDA hearing, urine mercury levels, mercury, chelation effects.

In September 2006 the FDA staff released a white paper [1] on their evaluation of the scientific literature regarding dental amalgam safety. This manuscript presents additional science countering this opinion, and challenges the FDA staff's interpretation of the science in their white paper.

A simple computer search of the literature confirms that mercury and organic mercury are extremely toxic agents and the mere presence of mercury in the body should be proof of toxicity. It has also been clearly shown by many, even the World Health Organization, that amalgams are the major contributor to human body burden. The EPA and National Academy of Sciences (NAS) report that 8 to 10% of American women have such high mercury body burdens that put to elevated risk for neurodevelopmental disorders any child they would give birth to. The Center for Disease Control states that 1 in 6 American children have a neurodevelopmental problem. So the problem or issue is not whether or not amalgams and the mercury they deliver is a health risk, this is an obvious fact according to the EPA and NAS. The real problem is how do we convince the controlling bureaucratic agency, the FDA, to admit that they have been wrong for many years in not evaluating the mercury release from dental amalgams.

One has to ask the simple question "Why are producers of amalgam products not required to produce data in the packages that describe the amount of mercury vapor that escapes daily from an amalgam of known weight and surface area under conditions that mimic the mouth with regards to temperature, pH and brushing?" In my opinion, the reason they don't is well known since to do so would quickly establish their amalgam products as dangerous to human health. A recent study on the levels of mercury in autopsy tissues and existing dental amalgams clearly states "Mercury levels were significantly higher in brain tissues compared with thyroid and kidney tissues in subjects with more than 12 occlusal amalgam fillings (all $P<0.01$) but not in subjects with 3 or less occlusal amalgams (all $P > 0.07$)."[2] Further, a 1984 NIDCR workshop came to the conclusion that there appears to be little correlation between toxic effects and the urine mercury levels showing the inadequacy of this approach [3].

The recent (prepared August 2006) FDA staff white paper[1] concludes that dental amalgams are safe. However, this claim is almost totally based on a fatal flaw in their evaluation procedure. This flaw is the old, widely used perception that safe or dangerous mercury exposures can be evaluated by measuring urine mercury levels. This concept has been developed and used consistently by some toxicologists for many years primarily, in my opinion, because it was easiest to do. Consider that other publications have shown that fecal mercury excretion is many times higher than urinary excretion in individuals with amalgams [4]. So urinary determinations are using an excretory route that accounts for much less than 8% of the mercury being excreted. Using urinary mercury also gives misleading information. Consider the data published by many authors in this area. Routinely you see shotgun patterns when plotting increasing number of amalgam fillings versus blood, urine, hair, or body tissues levels of mercury. This immediately tells one that there is not a linearity, or direct correlation, between the two factors being plotted and that other factors that need consideration must be identified. In my opinion, these factors are genetic susceptibility to mercury retention toxicity, exposure to compounds with synergistic toxicities based on increased retention, use of antibiotics, diet, etc. as elaborated on below.

Urine mercury is a measure of exactly that, the mercury being excreted by the kidney---not total mercury exposure, and a mercury toxic kidney is not as capable as a healthy kidney for excreting mercury. Yet, the FDA white paper evaluated most of

doi: 10.1588/medver.2006.03.00129

the research documents based on urine mercury levels that they designate as proof that toxic levels of mercury have not been reached. In my opinion, this approach has been proven to be very misleading. Even the ATSDR 1999 and 2005 reports creating an MRL (minimum risk levels) and the current EPA RfC (reference concentration) appear to based mostly on reports using urine mercury levels as a measure of toxic exposure. Even the data in the recent JAMA articles on the children's amalgam trial show that urine mercury levels are not an evaluation of dental amalgam mercury exposure (see below) as the children appear to lose the ability to excrete mercury in the urine with increased time of mercury exposure[5]. That is, even with increased amalgams the children's urinary mercury levels dropped after two years exposure to 7 years exposure by almost the entire increase that was initially caused by placement of amalgams within the first two years. Since the exposure has increased during the 2 to 7 years by placement of more amalgams this decrease does not reflect decreased exposure but indicates that the children are now retaining this mercury.

Does the above make sense? Consider another research project evaluated by the FDA white paper [1], that of Vamnes *et al.*[6]. This study described the initial blood mercury levels and the effect of chelation with DMPS on blood mercury levels of four cohort groups: Group1, 19 controls who never had amalgams; Group 2, 21 healthy persons with 43 existing amalgam surfaces; Group 3, 20 persons claiming self-reported symptoms with 37.5 surfaces; and Groups 4, 20 persons with amalgams removed (approximately 48 surfaces) 31.5 months earlier. The blood Hg levels were about 2.5, 5.0, 5.0, and 4.0 mcgs for the groups, respectively. The FDA white paper gave this evaluation "The data show that there is no difference in Hg blood levels in subjects with and without self-reported symptoms thought to be caused by amalgams and that chelation by DMPS is short-lived and has minimal impact on blood Hg levels. [1]" DMPS created a brief 24-30% drop in blood mercury that returned to pre-chelation levels within 2 hours. In my opinion, both (1) the rapid return of the chelated blood to pre-chelation levels and (2) the high blood Hg levels of those with amalgams removed when compared to the low levels in those who have never had amalgams demonstrate that amalgams contribute to a long-term, high mercury body burden that maintains a steady blood Hg level years after they are removed. Removal of blood mercury by chelation is rapidly brought back to pre-chelation levels by contributions from a high mercury body burden that is obviously not detected by blood or urine mercury levels. It is the amalgam induced body burden of mercury, not the blood or urine levels that cause toxic effects and this fact was not considered by the FDA white paper.

Consider, in the summary statement the FDA white paper stated "Chelation of Hg decreased blood and urine levels by 30% but for only a short time after which levels rapidly (within 2 hours) return to pre-chelation levels. Removal of a substantial number of amalgam restorations does not result in a large decrease in blood Hg levels, even 2-3 years after removal [1]." With this they again assume that mercury's toxic effect can be measured by blood and urine level which is the erroneous spin that all of the pro-amalgam supporters place on such data. The fact that mercury body burdens and mercury blood levels are markedly different between those who never had amalgams versus amalgam bearers and amalgam bearers with amalgams removed substantiate that amalgams contribute to a high mercury body burden that exists at least 3 years or longer after removal.

Retention of mercury by the body has to decrease the level of mercury in the blood and urine excretory routes. So the reality is that for those equally exposed, low blood and urine mercury levels identify the individuals who are not effectively excreting mercury from their body and the level of excretion varies from patient to patient. This leads to the shotgun pattern when plotting amalgams against mercury levels in various tissues.

However, the case against mercury levels produced by amalgams in the human body as being safe is growing. In Alzheimer's disease (AD) the aberrant biochemical events and the pathological hallmarks are well described. So is the research that shows that mercury, and only mercury, will produce the aberrant biochemistry and produce most of the pathological hallmarks in appropriate test systems [7, 8, 9 and references therein]. Also, a recent study has indicated that the increase in brain amyloid protein is due to an aberrant brain heme level and the heme synthetic pathway is one known to be extremely sensitive to mercury [10]. In spite of all this molecular level data the Alzheimer's Association of America supports the ADA in its plan to continue exposing Americans, some of whom are destined to become demented with AD, to a 40 to 60 year exposure to mercury from dental amalgams. It seems logical to me that this exposure, even if you don't want to think it causal for AD, would certainly exacerbate the rate of biochemical breakdown of the human brain of those who later suffer from AD type dementia.

The genetic inheritance of the APO-E4 form of apolipoprotein-E greatly increases the risk of early onset AD whereas inheritance of the APO-E2 form appears to be protective against AD. Both the E2 and E4 forms appear to do their biological functions well. One of these functions is to remove oxidized cholesterol from the brain, into the cerebrospinal fluid, across the blood brain barrier for removal from the blood by the liver. The second highest concentration of APO-E protein is in the cerebrospinal fluid. The one definite difference between APO-E4 and APO-E2 is the presence of two cysteines in the APO-E2 that are capable of mercury binding, and therefore mercury removal from the central nervous system. APO-E4 differs from APO-E2 in that these two cysteines have been genetically replaced by arginines that have no mercury binding capacity. Therefore, as previously reported, one of the most logical explanations of the different protective effects of the widely accepted, differential risk for AD based on APO-E geneotype can be explained by the loss of mercury binding capacity in the cerebrospinal fluid and brain by the proteins expressed by these genes [7]. It is this type of genetic susceptibility that may be evident in multiple biochemical pathways that place certain individuals at risk for mercury exacerbated or causal illnesses (see the comments on the heme synthesis pathway below). Also, the APO-E4 form appears as a risk factor for other neurological problems and illnesses, especially in patients with extensive amalgam fillings [11].

Mercury exposure to humans comes from various chemical forms such as elemental vapors, inorganic salts and organic-

doi: 10.1588/medver.2006.03.00129

mercurial such as thimerosal and phenylmercury acetate. All chemical forms of mercury have been proven toxic at very low levels. There is no doubt that mercury and mercury compounds represent the most dangerous form of metal toxicity since research on exposures show them to cause adverse effects in animals and humans at the very lowest levels of any metal. Mercury and mercury containing compounds are listed under California's Proposition 65 as compounds that need to be evaluated for their level of toxicity to ensure the safety of the citizens of California. Mercury vapor is one of the most toxic forms of mercury along with some of the organic mercury compounds. This is probably due to the efficient partitioning of vaporous mercury into certain body organs (e.g. Central Nervous system (CNS), kidney) and into specific cellular organelles (e.g. the mitochondria) based on mercury vapor's ability to easily penetrate cell membranes and the blood brain barrier. In this manner mercury vapor, Hg^0, is quite different from ionic Hg^{2+} and Hg^{1+}. For example, inhalation of mercury vapor (Hg^0) primarily affect the central nervous system whereas the kidney is the major organ affected by ingestion of the cationic forms of mercury.

Attempting to determine a lowest observable affect level (LOAEL) or no observable effect level (NOAEL) regarding mercury vapor exposure is, at best, a complicated procedure as explained by the analysis of published refereed research articles as presented below. The relative toxicity of mercury and organic mercury compounds vary extensively depending on: (1) delivery route (2) the presence of other synergistic toxic metals (3) different diets[12] (4) antibiotic exposure[12] (5) genetic type[13] with 8.7 to 13.4% showing sensitivity to a diagnostic patch test [14] and gender [9,15] (6) state of health and (7) age of exposure[16]. Based on the factors affecting mercury retention/excretion the obvious fact is that no exposure level can be determined that will predict the retention rate and subsequent mercury body burden of humans.

However, we now have a reliable measure of physiological toxicity of mercury exposure that is reflected in the "porphyrin profile". Porphyrins are small molecular weight organic compounds that are produced in a multi-step pathway and ends in the synthesis of heme. Evidently, different toxic metals and other toxic compounds may inhibit the porphyrin pathway in different manners ending up with a different urinary "porphyrin profile". Mercury toxicity has a unique "prophyrin profile" that today is not known to be produced by any other toxin. Recent research on dentists and dental technicians showed that 85% of these subjects had a porphyrin profile that was different from normals and symptomatic of mercury toxicity[17,18]. Also, 15% of the 85% had a more dramatic aberrancy which corresponded to a polymorphism in the CPOX4 gene[19]. This data clearly shows both the general toxicity of amalgam mercury vapor and an enhanced sensitivity of a genetic subset of the population.

To date we do not know the effects of amalgam mercury on the porphyrin profiles of children although this work was supposedly done by the group that did the NIDCR children's amalgam trials but the results were not reported in the initial papers[5,23]. What we do know is that there is a report that the majority of autistic children have an aberrant porphyrin profile and that this aberrancy was reversed by treating these children with a mercury chelator [20]. This new information has lead to many parents and their children having prophyrin profiles testing to establish if they have become mercury toxic.

The critical question is the effect of mercury vapor exposure on brain porphyrins profiles since an aberrancy has been reported in brain heme that has been associated with the inability to remove beta-amyloid protein from brain cells[10]. The effect on urinary porphyrins is well known but it is not know how brain heme is affected by mercury.

It should be noted that porphyrins lead to heme and heme is critical for several biochemical mechanisms. Heme is the oxygen carrying cofactor for hemoglobin, it is a critical cofactor for the P450 class of enzymes that are responsible for detoxifying organic type of toxins from the body, and heme is a necessary cofactor for one of the complexes in the electron transport system of mitochondria. Therefore, mercury inhibition of heme production could have a multitude of secondary effects that cause human illnesses. It has been pointed out to me that many autistic children are usually of very light complexion, indicating a lack of hemoglobin or oxygen carrying capacity, which is consistent with their abnormal porphyrin profiles.

In the FDA white paper [1] the elegant porphyrin work from the laboratories of Esheverria and Woods was soundly dismissed, as if the "experts" at the FDA knew more about this research than the authors and the reviewers of these manuscripts that were published in outstanding scientific journals [17.18.19]. The major criticism was the lack of non-dental controls or data on other metals, as if there weren't data on the general population in medical literature regarding normal porphyrin levels and the behavioral measures used. The work of Nataf et al. showing the same porphyrin aberrancies in many autistic children, who were never exposed in a dental office was also ignored.

In spite of the fact that 85% of the dentists and dental technicians tested showed mercury related toxicities in both behavior and physiological parameters, and 15% showed an increased mercury induced neurological deficits with polymorphism of the CPOX4 gene, the FDA and ADA still maintain that amalgams do not cause any significant medical problems because the urine and blood levels do not reflect that these individuals had reached a level of exposure that was toxic. I think it would be worthwhile to err on the side of caution and warn the members of the ADA, practicing dentists, of this concern instead of ignoring it for very questionable reasons. Again, the FDA/ADA miss the point that it is the mercury body burden, not the blood or urine levels that defines toxicity, and even body burden has to take into account genetic susceptibility parameters. It is my opinion, that the FDA/ADA staffs do not have the expertise to second guess the findings of these researchers. In doing so they highlight their inability to give fair-minded judgment to research which was done at a highly regarded research university and reviewed by excellent journal editorial boards.

It is obvious that lethality requires a higher level of exposure to mercury vapor than does neurological or developmental damage when considering infants *in utero*. Neurotoxicity, or a suppressed immune system in the parent, would be considered dangerous for developing and maintaining a pregnancy that leads to birth of a healthy child. Many children may appear normal and have apparently non-toxic levels of blood and urine mercury and still suffer from extreme mercury toxicity. For

doi: 10.1588/medver.2006.03.00129

example, young athletes and others who died from Idiopathic Dilated Cardiomyopathy (IDCM) have been found to have 22,000 times the mercury in their heart tissue whereas the muscle tissue samples from these patients did not [21]. This level, 178,400ng/g, would have generally been lethal to the kidney and CNS cells and has never been reported in any blood or urine sample. *In my opinion, the unexplained, abnormal partitioning of huge levels of mercury into specific organs in certain individuals essentially renders it impossible to identify a blood or urine level of mercury that is safe for all*.

Consider also that recent research has shown that mercury and ethylmercury have the ability to inhibit the first step (phagocytosis) in the innate and acquired immune response of humans at low nanomolar levels [22]. This clearly shows that mercury exposures quite below the average exposure can cause disruption of the immune system at all ages, but especially infants.

Recent reports, supported by the NIDCR, have come to the conclusion that amalgams are safe for use in all children [5,23]. However, there are numerous flaws with these studies that do not warrant such a conclusion and the papers themselves have been highly criticized both on ethical and scientific grounds by myself and other scientists (see http://web.mac.com/iaomt/iweb /iaomt_news/September).

First and foremost, these studies excluded all children with neurological problems (maybe caused by in utero mercury exposure from the birth mother's amalgams [24]) from the studies, and there are 1 in 6 children in the USA with neurological illnesses according to the CDC. So while a neurological healthy child may not respond to mercury toxic exposures as rapidly as a neurologically unhealthy child it seems untenable to call amalgams safe for general use in children which the authors did inaccurately conclude [5,23]. Also, one cannot measure accurately the effects of mercury exposure on the IQ of an infant exposed at birth since we do not know what it would have been without exposure---and a toxicity induced decrease in IQ, if the infant is not severely compromised, is difficult to establish.

Second, the data presented in these JAMA reported studies regarding urinary excretion of mercury [5:1788] (see Fig. 2 below) showed clearly that urinary mercury excretion increased in the first two years of amalgam exposure then dropped over 40% in the next five years to where the error bars of amalgam bearers and composite bearers overlapped. This indicates no significant difference in urinary mercury excretion between the two groups at the end of the study even though one set had an extensive set of amalgam fillings! In fact, the total increase in urine mercury caused by amalgam placement was lost by year 7.

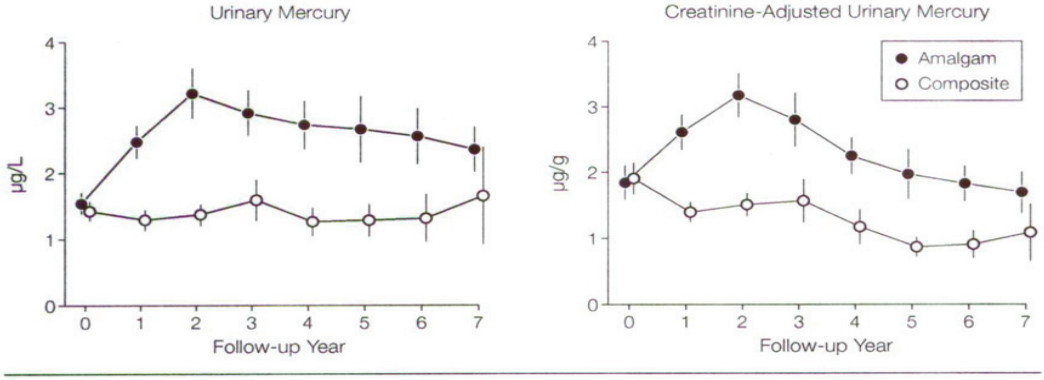
The rationale for this amazing data was not discussed in the published manuscripts as the authors appeared to consider urinary mercury as a "measure of exposure" and were content with a decreased excretion as being explained by a decreased exposure. However, mercury does not stop emitting from amalgams after two years and these children also received new amalgams after year two through year six. *What the authors did not consider was that the decreased urinary mercury levels were a measure of "a decreased ability to excrete mercury" via the kidney. The most straight-forward explanation for this data is that after two years exposure to mercury vapor from amalgams the children are losing their ability to excrete mercury through the kidney likely due to the well known nephrotoxicity of mercury.* This explanation is consistent with amalgam exposure affecting the porphyrin synthetic pathway and causing additional metabolic problems. This data, data from the articles that conclude dental amalgams are safe for all children, actually proves that basing any safety of dental amalgams on single day a year urinary mercury levels is totally invalid.

Third, according to most reports that have directly studied the issue, a very high percentage of mercury is excreted not by the urinary route but by the fecal route. One study found that the ratio was 12 to 1 with the fecal excretion being over 90% of the total [4]. Therefore, using a single, yearly spot urine analysis to account for mercury exposure appears to be a scientifically unacceptable procedure to evaluate the mercury exposure of these children based on the fact that urine most likely is a minor excretory route. Since this was supposed to be a complete study it seems as if measuring fecal mercury levels would have been done in at least a subset of these children to insure that the major excretory route for mercury was or was not being affected.

Fourth, why weren't the porphyrin profiles of these study children evaluated rapidly and reported in the initial papers? One would be surprised if they remained normal in light of the reported effects on the porphyrin profiles of dentists and dental hygienist exposed to mercury vapor that has been in the literature for some time now[5, 23]. In fact, the Children Amalgam Trial studies appear symptomatic of developing a study that will show no significant differences, while avoiding any experiments that have been shown to be more sensitive to mercury toxicity. Yet the FDA white paper accepted the conclusions of the authors of these papers without mentioning the obvious weaknesses.

Mercury based LOELs and NOELs from non-human data have another short-coming. For example, it has been known for some time that the relative toxicity of mercury containing com-

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



Error bars indicate 95% confidence intervals.

doi: 10.1588/medver.2006.03.00129

pounds appears to be dramatically affected by the presence of other compounds and heavy metals that synergistically enhance the toxicity of mercury. For example, mixing of an LD1 dose of mercury with a 1/20 dilution of an LD1 of lead produces a mixture with an LD100, not an LD2 or less that would be expected with additive toxicities[25]. Since there is considerable concern about the lead levels in the drinking water in our nation's capital it seems the citizens there would be under more toxic stress than in locations with little or no lead exposure. This data strongly implies that synergistic toxicity of mercury with other readily available toxic metals would dramatically enhance the toxicity and lower the LOEL and NOEL values.

What we do know from a study that measured mercury in brain tissue of infants is that the mercury levels in the brain stem of infants from California had a mean of over 55ng Hg/g wet weight of tissue. This is roughly 55 micrograms/kg. Assuming a kg of tissue is about 1 liter then the mercury concentration is about 275 nanomolar. It has been clearly shown that neurons in culture are destroyed by levels of mercury much less than 50 nanomolar with no synergistic compounds, such as lead, aluminum or cadmium, present to enhance mercury toxicity [9]. This level of mercury is especially toxic in the presence of aluminum and certain antibiotics and, most importantly, testosterone. Given the findings of elevated testosterone in the amniotic fluid of mothers who gave birth to autism spectrum children this has to be a concern. Also, the neurotoxicity of thimerosal to neurons in culture was decreased by estradiol [9] and a subsequent report showed that estradiol reduced cumulative mercury and associated disturbances in neuronal tissues of ovariectomized rats. These observations may explain the 4 to 1 ratio of boys to girls with autism as boys. The FDA white paper did not address these well known problems of synergistic toxicities with mercury.

Consider also that mercury from different exposures are at the least additive in their toxicity effects. A report from the National Center for Health Statistics, Center for Disease Control and Health in 2003 stated that approximately 8% of women of child-bearing age had concentrations of mercury higher than the USA EPA's recommended reference dose, below which exposures are considered to be without adverse effects[3]. This blood level in women caused more recent concern with data showing that cord blood was 1.7 times the level of maternal blood indicating that more than 8% of children being born are being exposed to toxic levels of mercury from their mother's blood. These individuals would definitely be more at risk during transient mercury exposures than would the general population and are certainly not comparable to animals in a pristine environment being exposed to only one mercury toxicant. Therefore, a 10-fold reduction for mercury in medicaments, as is common in converting a LOEL into a NOEL, most likely does not provide the protection factor as it would for exposures to most non-mercury toxicants that have less defined synergistic partners.

Reports have shown that diet plays a major role in the ability of mammals to excrete mercury[12]. Three different diets fed to adult female mice (high protein synthetic diet; standard rat chow diet; milk diet) dramatically changed the rate of fecal excretion of mercury. Mercury was introduced orally as methylmercury (MeHg) and diet caused differential rates of whole body mercury elimination. The results showed that mice fed a synthetic, high protein diet had the lowest tissues levels of mercury whereas those fed the milk diet retained the highest mercury levels. *This was confirmed by the total percentage of mercury excreted in the feces after 6 days of 43%, 29% and 11% in the high protein, rat chow and milk diets, respectively.* Therefore, diet plays a major role in the fecal excretion rates of mercury from an organic mercury compound. As expected, diet also affected the excretion rate of mercury from body tissues. The retention of mercury in the body of a child on a milk diet would be much higher than for a child not on a milk diet. Twenty-year-old studies report that suckling animals absorb about 50% of Hg^{2+} versus 5% in non-suckling animals [26]. Since the level of toxicity would likely increase with retention time, especially if the exposure rate to mercury were consistent over any significant period of time, then the diet can have a major affect on the calculated NOELs and minimum acceptable daily levels. Concerns about diet enhanced toxicity of infants on milk diets was not considered in the FDA white paper [1].

Toxicity is also known to vary with the chemical species of mercury that exists in the body's tissues. Diets can change this as it was observed that foods ingested played a major role in the mercury chemical species that existed in the mice given oral doses of MeHg. Hg^{2+} was the species found at the highest level in test animals on a synthetic protein diet (35.3%) and was the lowest in test animals on a milk diet (6.6%). It is reasonable to predict that diet changes the conversion of MeHg to Hg^{2+} and would likely do so for other organic mercury compounds, such as ethyl-mercury (Et-Hg), which is released from thimerosal. Since the toxicity of organic mercury compounds (e.g. MeHg versus EtHg) which partition similar to mercury vapor has been suggested to be greater than Hg^{2+} (inorganic mercury) and toxicity is partially determined by the rate that the compound is converted to Hg^{2+} after the chemical nature of the mercury source has allowed effective partitioning across the blood brain barrier.

Other studies confirm that the renal uptake and toxicity of circulating mercury is significantly enhanced in rats by the co-ingestion of the essential amino acid L-cysteine [27] and disease marker homocysteine[28]. Elevated blood homocysteine level is a major risk factor for cardiovascular disease. Therefore, humans with risk for cardiovascular disease would be more at risk for low level mercury exposure than others. This would also be true for Alzheimer's disease where elevated homocysteine has also been reported [29].

Medical status is of concern when considering mercury compound toxicity, especially when bacterial infections are being treated. Treatment of adult female mice with widely used antibiotics 7 days prior to MeHg exposure dramatically influenced mercury retention of tissues from mice receiving similar organic mercury exposures [34]. The calculated whole body mercury elimination half-times from day 1 to day 6 varied from 34, 10 and 5 days for mice fed a milk diet, mice chow or high protein diet respectively. *A remarkable 6.8 fold increase in retention half-life existed between a milk diet and high protein diet that was caused by antibiotic treatment that also changed the gut microflora*. Antibiotic treatment dropped the fecal mercury excretion to near zero in the high protein and milk diets and to less than 8% with the mouse chow diet. Therefore, it can be concluded that the relative toxicity of mercury and mercury

doi: 10.1588/medver.2006.03.00129

compounds would be dramatically increased if the test subject were on antibiotics.

The toxicity of mercury vapor is dependent on retention and excretion and these vectors are dramatically affected by diet and antibiotic treatment as well as other factors. This makes it nearly impossible to define a safe level of exposure, especially for mothers and their infants *in utero*. The process of placing or removing dental amalgam's in a pregnant mother has to increase the exposure of the *in utero* infant to elevated mercury vapors as it would dramatically increase the mother's blood mercury levels. It is well known that mercury vapor can cross the placenta, and is even concentrated in the cord blood versus the mother's blood. Other studies have shown that mercury increases in the birth hair of normal children in response to increasing dental amalgams in the birth mother[24]. Other similar studies point to aberrant mercury hair levels in children with neurological problems[24, 30]. There can be little doubt that the exposure of a pregnant mother to mercury vapor by aggressive dental amalgam treatment could cause harm to her infant *in utero*. Other reviews of the potential toxicity of dental amalgams has come to the conclusion that they are not safe for pregnant women nor children [31].

Finally, based on the exacerbation of mercury toxicity by variation in human sex hormone presence, dietary factors, other toxic metals, antibiotic usage, and genetic susceptibility factors prove there is no intelligent way that anyone can say they know that a specific exposure to mercury or urinary or blood mercury level would not cause a significant affect on their health, especially to an infant in utero or an aged ill person. The FDA's dismissal of the factors that enhance mercury toxicity and their use of mercury urine levels to measure exposure is totally invalid and represents a lack of knowledge of the most recent scientific literature.

We know that alcohol is a toxic material and mere presence in the blood stream or oral air can lead to a conviction. However, the presence of the more toxic mercury, known to have adverse effects of a more permanent nature in humans, is not judged by the FDA based on its mere presence. This FDA required that studies be done to prove mercury from amalgams caused a specific illness in humans. Yet the cost of such studies are such that only the USA government agencies such as the FDA or CDC could afford to do such studies or have the power to insist that the manufacturers of amalgams do so. However, this is something the FDA and CDC have steadfastly refused to require. No other compound, drug, etc. seems to have this special consideration, which is amazing in light of the known, potent neurotoxicity of mercury vapor.

The FDA white paper seems not at all concerned that our dentists and dental technicians may be suffering from an occupational exposure to mercury although research indicates this is a group that is physiologically and neurologically affected. Also, no other material has near the number of mimicking abilities of mercury with regards to producing the aberrant biochemistry and producing the known diagnostic hallmarks of Alzheimer's disease (AD). Many Americans have grams of mercury vapor releasing amalgams within two inches of their brains and it is inarguable that this minute by minute exposure for 20 to 50 plus years would not push those condemned to die with AD into dementia earlier, and at a great cost to their families and our medical system.

In spite of all of this published knowledge the FDA, American Dentistry and Medicine remains silent and in active denial that many modern man neurological diseases, which have no known etiology, may be caused or exacerbated by mercury. This ignores the "first do no harm" mantra of medicine. It seems as if the FDA has chosen to ignore this advice in the past as certainly there can be no doubt about amalgam's contribution to human mercury body burden and the opinion of the EPA and NAS that this mercury body burden is not healthy and most likely is quite damaging. In my opinion, it was obvious in the FDA hearing, in order to support the FDA white paper, that the pro-amalgams presenters were given much more presentation time than the scientists who were not supportive of amalgams. The FDA should address the external advisory committee's issue that the FDA white paper did not cover all the issues of mercury toxicity from amalgams and was overall incomplete in its assessment of the research regarding amalgam safety. I would suggest that the next FDA hearing be more balanced with those concerned about amalgams being given equal time to present the science to support their opinions.

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