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Scientific Comment

Amalgam studies: Disregarding basic principles of mercury toxicity

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Abstract

Dental amalgam, which has been used for over 150 years in dental practice, consists of about 50% metallic mercury. Studies on animal and humans show that mercury is continuously released from dental amalgam and absorbed by several body tissues. It is widely accepted that the main source of mercury vapor is dental amalgam and it contributes substantially to mercury load in human body tissues. There is still a controversy about the consequences of this additional mercury exposure from amalgam to human health. Many studies were performed to evaluate possible adverse effects. In this comment, these studies were analyzed with regard to their methodical quality by considering the newest findings on mercury toxicity and metabolism. In sum, a number of studies are methodically flawed drawing inaccurate conclusions as to the safety of dental amalgam.

Key words: Dental amalgam – mercury – toxicity – adverse effects

The use of dental amalgam in most developed countries for over 150 years triggered a scientific and political discussion about the rationale for using mercury in amalgam. The question arises as to why opinion differs so widely, in spite of the fact that a number of studies addressing this problem have already been conducted. One possible reason may be that some studies show substantial methodological flaws or simply disregard the basic principles of toxicological research on metallic mercury (Hg^0).

It is known from animal research that mercury vapor is emitted continually from dental amalgam and is absorbed and accumulated in organs tissues (Danscher et al. 1990; Hahn et al., 1989, 1990; Lorscheider et al., 1995; Lorscheider and Vimy, 1991; Vimy et al. 1990). Humans with amalgam fillings have significantly elevated mercury levels in blood (Becker et al., 2002; Gottwald et al., 2001; Kingmann et al., 1998; Pizzichini et al., 2003; Zimmer et al., 2002), about 3–5 times more mercury in urine (Becker et al., 2003; Gottwald et al., 2001; Kingmann et al., 1998; Zimmer et al., 2002) and 2 to 12 times more mercury in their body tissues (Drasch et al. 1992, 1994; Egglestone and Nylander, 1987; Lorscheider et al., 1995; Nylander, 1986; Nylander et al., 1987) than individuals with-

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out dental amalgam. Blood and urine concentrations are not necessarily indicative of mercury load in body tissues (Lorscheider et al., 1995) or severity of clinical symptoms (Drasch et al., 2002). Research on sheep and monkeys with dental amalgam have shown that blood Hg levels remained low, whereas tissue Hg levels were raised (Hahn et al. 1990; Lorscheider et al., 1995; Vimy et al., 1990). The half-life of metallic mercury in blood is quite short (about 3 days) because it quickly penetrates into other body tissues. Thus, the levels of mercury in blood only reflect recent exposure to mercury vapor. Urine Hg levels mainly reflect the cumulative dose of inorganic mercury in the kidneys and there exist only weak to no correlations with levels in other target tissues (Clarkson, 2002; Drasch et al., 1997; Weiner and Nylander, 1993). When exposure to mercury ceases, a half-life of 1 – 18 years can be expected in the brain and bone structures (Lorscheider et al., 1995; Opitz et al., 1996; Sugita, 1978).

In summary, the above mentioned studies suggest that:

1. Mercury levels in blood and urine do not necessarily correlate with Hg body exposure or clinical signs of mercury poisoning.
2. In the population large Hg concentrations in body tissues derive mainly from dental amalgam.

Recently, Bailer et al. (2001), Gottwald et al. (2001) and Zimmer et al. (2002) compared two groups exposed to amalgam (all female, one group of patients who claimed to be suffering from symptoms they related to their amalgam fillings and the other group, which did not report any association between complaints and their fillings) in terms of mercury levels in body fluids and psychometric tests. The mean number of amalgam fillings was identical in both groups. They found equal Hg levels in both amalgam groups. Bailer et al. (2001) and Zimmer et al. (2002) conclude: "Thus, mercury released from amalgam fillings was not a likely cause of complaints reported by the amalgam sensitive subjects". Because individuals with self-related amalgam symptoms suffer significantly more often from psychological disorders Gottwald et al. (2001) conclude: "Whether patients feel impaired by their amalgam fillings obviously does not depend on the exposure to mercury" (p. 226) and "Our finding suggests that psychotherapy or psychiatric treatment is the adequate therapeutic approach for many patients with amalgam-related complaints" (p. 227).

It is not clear why these authors come to such a conclusion. A fundamental question should arise: Why do some individuals suffer from amalgam exposure while others do not?

In contrast to Bailer et al. (2001), Gottwald et al. (2001) and Zimmer et al. (2002) other research groups have offered a partial answer to these question. They found that patients suffering from symptoms like fatigue, irritability, mood, poor concentration, headaches and insomnia due to their amalgam fillings exhibit significantly more frequently the presence of the apolipoprotein E4-allele than healthy controls (Godfrey et al., 2003). It is known that the presence of this allele is a major risk factor for developing Alzheimer's disease (Farrer et al., 1997; Ritchie and Dupuy, 1999). It is not known why, but a possible link could be the fact that Apo-E-4 has reduced detoxifying abilities due to the lack of thiol-groups. In contrast Apo-E-2 and Apo-E-3 can bind and detoxify heavy metals like mercury (Godfrey et al., 2003; Mutter et al., 2004; Pendergrass and Haley, 1996) and lead (Stewart et al., 2002).

Other researchers found that individuals with self-related amalgam complaints have significantly lower selenium levels or altered distribution of trace elements in their blood than individuals with amalgam who do not seem to display any symptoms (Hol et al., 2001; Lindh et al., 2001). In addition, Pizzichini et al. (2003) showed that the total antioxidative plasma activity was significantly reduced in individuals with dental amalgam.

In scientific research on the toxic effects of substances, it is necessary to compare at least two samples: one that is exposed to the substance in question and one that isn't. One of the main dilemmas in so called amalgam studies is that the vast majority do not incorporate true control groups which have genuinely not been exposed to dental amalgam. What is neglected is the possibility that "non-amalgam" controls may at some point in their earlier life have had dental amalgam fillings over a long period of time and may thus display a higher body mercury load. These studies cited by many authors and institutions (Berlin, 2003; BfArM, 2003; Clarkson, 2002; Dodes, 2001; Gottwald et al., 2001, 2003; Harhammer, 2001; Zimmer et al., 2002, 2003) as proof of the putative harmlessness of amalgam, do not use "proper" non-amalgam control groups:

The Swedish twin study (Björkmann et al., 1996) actually only compared 57 twin-pairs in a co-twin analysis, and not 587 as mentioned by some authors (BfArM, 2003; Gottwald et al., 2003; Harhammer, 2001). As the average age of the people making up the sample was 66 years, 25% had no teeth at the time of investigation, many had missing teeth and an

unknown number had crowns using other dental materials. Root fillings with amalgam and amalgam fillings under crowns was not calculated. As an allegedly "non-amalgam" group, they were compared with individuals who still had dental amalgam fillings. The authors found that individuals with more fillings (more own teeth) had a better health status. It is fair to assume that individuals with few or no teeth or teeth that have been restored with dental materials other than amalgam had probably had dental amalgam previously for a longer period of time, which may be associated with a higher mercury body exposure than the "amalgam group".

Ahlqwist et al. (1988, 1993, 1999) conducted a prospective study on 1462 women. They determined the number of dental amalgam, diagnosed a total of 30 defined symptoms and measured Hg levels in blood (stored for 20–30 years until analysis). The average age of the study population was roughly 60 years. The "non-amalgam-group" consisted of women with up to four amalgam fillings or without teeth (about 15% throughout the study) or many women with dental restorations using materials other than amalgam (implants, crowns, pontics). Here again, the amalgam group (more than four amalgam fillings) turned out to be healthier than the "non-amalgam-group" in nearly all the parameters tested, although they had higher serum Hg levels. The possibility that the "non-amalgam group" had formerly had dental amalgam and possibly a longer period of exposition to mercury vapor from dental amalgam was not taken into account. Interestingly, the authors dismissed our request that they provide us with the data for the purpose of reanalysis.

Elevated mercury levels were not found in the brain of patients with Alzheimer's disease (AD) compared to controls when exposed to dental amalgam (Saxe et al., 1999). However, Saxe et al. overlooked the fact that (i) there was a positive correlation between amalgam induced mercury load and mercury content in the brain in the control group, and (ii) measuring the nucleus basalis meynert and thalamic nuclei that is pivotal because they are predominantly involved in Alzheimer patients for which other studies have shown elevated Hg levels (Pendergrass and Haley, 1997; Thompson et al., 1988). In another study by Saxe et al. (1995) of a sample of 129 nuns, no differences in mental health were found between those who had amalgam and controls. However, 72% of the controls had no posterior teeth and thus had had a similar amalgam history.

In an alleged "meta-analysis", which was technically a review of selected literature, Dodes (2001) concluded in his abstract that "Amalgam restoration remains safe and effective". Dodes (2001) did not perform any sort of recalculation or proper analysis to underpin his conclusion, especially since it was solely founded on the above mentioned studies (Ahlqwist et al., 1988, 1993, 1999; Björkmann et al., 1996; Saxe et al., 1995, 1999). As a side note, it should be pointed out that this publication (Dodes, 2001), together with those by Saxe et al. (1995, 1999), was published in a dental association trade journal. Even in 2002, the editors of this journal started a media campaign to promote the use of dental amalgam, claiming that amalgam is a "stable alloy, similar to sodium chloride" (Larkin, 2002). This statement is not tenable, and others have already commented on it (Guzzi, 2002).

The multi-center study (Melchart et al., 1998) cited by Gottwald et al. (2003) did not consider the former dental status of the control group (Weidenhammer, personal communication 2003). Melchart et al. (1998) found that amalgam removal resulted in a significant improvement in amalgam-related symptoms. Furthermore, Lindh et al. (2002) showed that the removal of amalgam and other dental metals in 463 patients lead to an improvement in over 70% of the patients in frequently observed symptoms (e.g. fatigue, depression, muscle and joint pain, headaches, dizziness, stomach trouble, forgetfulness). A placebo effect can be excluded because: 1. The patients were chronically ill for many years without relief, despite numerous treatment efforts by a number of physicans. 2. Many patients experience a worsening of symptoms during the amalgam removal period. 3. The improvement in health continued years after the treatment (Lindh et al., 2002).

Engel (1998) also reported a significant (70%) improvement in most of these symptoms in patients after amalgam removal. Sterzl et al. (1999) showed that patients with chronic fatigue syndrome (CFS) and autoimmune thyroiditis showed an improvement in their health status after the replacement of amalgam fillings by composite. Individuals with multiple sclerosis (MS) whose dental amalgam had been removed were compared to MS controls with amalgam (Siblerud and Kienholz, 1994). The sample with amalgam fillings had significantly more neuromuscular exacerbations during the one year study period than those who had had their amalgam fillings removed. It was also shown that the MS typical electrophoretic band changes in cerebro spinal fluid proteins was normalized after amalgam removal (Huggins and Levy, 1998). 71% of patients with autoimmune diseases (including MS) improved objectively after amalgam removal (Prochazkova et al., 2004).

That amalgam fillings could be a source of Hg nephrotoxicity was demonstrated by Boyd et al. (1991) in an animal model and recently by Mortada et al. (2002) in 101 humans. In the latter, two groups were studied by matching them for gender, age, residence area and socioeconomic status. The group with dental amalgam (49 persons) had only had an average 4.4 amalgam fillings (range 1 – 8) for 1 – 60 months. In comparison with the control group which had not dental amalgam fillings, the amalgam group showed significantly higher urinary excretion of N-acety-ß-D-glucosaminase (NAG), y-glutamyl-transferase (y-GT) and albumin. NAG and albumin correlated significantly with the number of fillings.

Animals and in in-vitro studies have shown that exposure to inorganic and metallic mercury cause neuronal damage (Cedrola et al., 2003; Leong et al., 2001) and biochemical alterations (inclusive induction of β-amyolid) found in Alzheimer's disease (Duhr et al., 1993; Ely, 2001; Mutter et al., 2004; Olivieri et al., 2000, 2002, Pendergrass et al., 1997), even at very low levels. Other metals like Al, Cd, Pb, Mn, Zn, Fe, Cr, Cu, were not able to cause this types of neuronal alterations.

Hg levels in human placentas correlate with the number of maternal amalgam fillings and a substantial amount of Hg from amalgam reach the fetus (Ask et al., 2002; Drasch et al., 1994). Mercury from dental amalgam in pregnant women may also contribute to development of autism in their children (Holmes et al., 2003). In this study mothers of 94 autistic children had statistically more amalgam fillings during pregnancy than 49 mothers of normal controls. In contrast to their higher mercury exposure during pregnancy, these autistic children had reduced mercury levels in their first haircut. This may reflect a reduced capacity to excrete mercury from their body which in turn may lead to elevated brain-mercury levels (Holmes et al., 2003).

The neurobehavioral and psychological effects resulting from exposure to low levels of Hg from dental amalgam has been described (Echeverria et al., 1998; Siblerud 1989, 1992; Siblerud et al., 1993, 1994). Low dose exposure to inorganic mercury may be a co-factor in the development of autoimmune diseases (Bartova et al., 2003; Hultman et al., 1994; 1998; Prochazkova et al., 2004; Stejskal and Stejskal, 1999; Sterzl et al., 1999; Via et al., 2003). There are also possible adverse health effects for dentists and their staff caused by occupational exposure to mercury through amalgam (Echeverria, 2002; Echeverria et al., 1998; Ngim et al., 1992; Nylander and Weiner, 1991; Ritchie et al., 2002).

In a recent risk analysis (Berlin, 2003) it was suggested that the frequency of pathological side effects from amalgam due to genetically determined high sensitivity is about 1%. The German Commission on Human Biological Monitoring states that genetically susceptible persons may develop immunological reactions to amalgam. The portion of susceptible persons in the general public is about 1 – 4%. (Kommission Human-Biomonitoring, 1999). Richardson (1995) even concludes that approximately 20% of the general public may experience sub-clinical central nervous system and/or kidney function impairment due to amalgam fillings.

Taken together, these results question the safety of dental amalgam.

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