Environmental Research 164 (2018) 65–69

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Review article

Mercury exposure and health impacts in dental personnel

Jan Aaseth[a,b,*], Bjørn Hilt[c,d], Geir Bjørklund[e,**]

[a] Research Department, Innlandet Hospital Trust, Brumunddal, Norway
[b] Faculty of Health and Social Sciences, Inland Norway University of Applied Sciences, Elverum, Norway
[c] Department of Occupational Medicine, St. Olav's University Hospital, Trondheim, Norway
[d] Department of Public Health and Nursing, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology, Trondheim, Norway
[e] Council for Nutritional and Environmental Medicine, Mo i Rana, Norway

ARTICLE INFO

Keywords:
Metallic mercury
Health effects
Mercury toxicokinetic
Mercury toxicodynamic
Dental practice

ABSTRACT

Based on toxicological, clinical, and epidemiological knowledge, the present paper reviews the status regarding possible deleterious health effects from occupational exposure to metallic mercury (Hg) in dental practice. Symptoms from the central nervous system are among the health problems that most often are attributed to Hg exposure in dentists and dental nurses working with amalgam. Uncharacteristic symptoms of chronic low-level Hg vapor exposure including weakness, fatigue, and anorexia have been observed in numerous studies of dental personnel. It is crucial to protect both human health and the environment against negative effects of Hg. In line with this, the use of dental amalgam in industrial countries is about to be phased out. In Norway and Sweden, the use of the filling material is banned.

1. Introduction

In spite of concerns regarding mercury (Hg) toxicity, dental amalgam is still worldwide a commonly used dental restorative material. The World Health Organization (WHO) has recommended phasing out dental amalgam and change to alternative materials (WHO, 2007). However, these alternatives may be too expensive for middle- and low-income nations and amalgam is therefore still a preferred dental restorative material in large parts of the world.

Numerous studies have shown that dental personnel's work with amalgams involves a risk for exposure to undesired metallic Hg levels. Early reports indicated that chronic Hg exposure for dentists was associated with reproductive disturbances and allergies (Bjørklund, 1991). Some reports also showed associations of occupational Hg exposure with neurological and/or cognitive problems (Shapiro et al., 1982; Bittner et al., 1998), fibromyalgia, and chronic fatigue syndrome (Sterzl et al., 1999; Stejskal et al., 2013; Stejskal, 2014; Bjørklund et al., 2018). Based on numerous reports, Hg is a global concern due to its environmental and health effects (Bjørklund et al., 2017).

Norway and Sweden have banned the use of amalgam, reportedly because of environmental reasons (Ministry of the Environment, 2007; Swedish Chemicals Agency, 2008–2012). In Denmark, Finland, Estonia, and Italy, the use of dental amalgam is less than 5% of all tooth restorations (BIO Intelligence Service, 2012). In Switzerland and Japan, the use of the filling material is about to be banned (BIO Intelligence Service, 2012). The health authorities of France have recommended Hg-free alternatives for amalgams for pregnant women. In Finland, Austria, Germany, and Canada, the use of dental amalgam have purposely been reduced for children, pregnant women, and subjects with kidney problems (HEAL, 2007). Other industrial countries are also in the process to phase out the use of dental amalgam (UNEP, 2016).

The aim of the present paper is to review the status regarding possible deleterious health effects from occupational exposure to metallic Hg in dental practice, based on toxicological, clinical, and epidemiological knowledge. The literature search was carried out using PubMed and Web of Science, supplemented with Google Scholar and the reference lists of relevant papers.

2. Elemental, inorganic, and organic mercury

Elemental Hg (Hg^0, atomic number 80) is liquid at room temperature. Mercury is the only metal element known to melt at a relatively cold temperature. The reason for this is the unique electron configuration of Hg ([Xe] $4f^{14}$ $5d^{10}$ $6s^2$), where electrons fill up all the available shells, 1s, 2s, 2p, 3s, 3p, 3d, 4s, 4p, 4d, 4f, 5s, 5p, 5d, and 6s subshells. This configuration explains the fact that Hg^0 under usual conditions resists removal of electrons (Norrby, 1991). Therefore, Hg behaves almost like a noble gas element, which at relatively low

* Corresponding author at: Faculty of Health and Social Sciences, Inland Norway University of Applied Sciences, 2411 Elverum, Norway.
** Correspondence to: Council for Nutritional and Environmental Medicine, Toften 24, 8610 Mo i Rana, Norway.
E-mail addresses: jaol-aas@online.no (J. Aaseth), bjorklund@conem.org (G. Bjørklund).

https://doi.org/10.1016/j.envres.2018.02.019
Received 9 January 2018; Received in revised form 11 February 2018; Accepted 13 February 2018
0013-9351/

temperatures melts and easily forms weak bonds.

Elemental Hg is used in dental amalgams and various domestic and industrial applications. Mercury liquid (Hg^0) is practically not absorbed in the gastrointestinal tract. However, at room temperature, Hg^0 volatilizes to vapor that is readily absorbed upon inhalation. This lipophilic form of Hg can, once it is absorbed, easily cross the placenta and the blood-brain barriers. Intracellularly Hg is rapidly oxidized by catalase into inorganic Hg (Hg^{2+}) (Eide and Syversen, 1983), which in the brain is retained for years (Berlin et al., 2015). Dental amalgam emits Hg vapor, which upon inhalation is absorbed and moved into the bloodstream (Jokstad et al., 1992; Clarkson et al., 2003).

In contrast to Hg vapor, inorganic mercuric (Hg^{2+}) salts occurring in industrial and domestic products (Ozuah, 2000) are not lipophilic and therefore do not easily cross the blood-brain barrier. Organic Hg compounds can, however, penetrate into the brain, and subsequently be metabolized to inorganic Hg, which is retained for years (Magos et al., 1985; Takeuchi et al., 1989; Vahter et al., 1995). Thus, organic Hg exposure may represent an additive burden for amalgam-exposed workers. Organic Hg exposure mainly occurs as methylmercury (MeHg, CH_3Hg^+) from fish or ethylmercury ($C_2H_5Hg^+$) from the compound Thimerosal, which is used as an antifungal and antiseptic agent in vaccines. Still, the safety of Thimerosal is debated (Guida et al., 2016; Dórea, 2017).

3. Laboratory tests for mercury exposure

Specimens that have been used as biomarkers of Hg vapor exposure include urine, blood serum, hair, and toenails, among which urine is considered the most reliable biomaterial. Whole blood is less applicable than blood serum and urine since organic Hg is the dominating form of Hg in the erythrocytes. And routinely used hair analyses do not distinguish between organic and inorganic Hg. Furthermore, proper reference values for Hg in hair and toenails are still lacking.

Several studies have shown that dental personnel have higher Hg concentrations in urine than the average population. In Scottish dentists, the mean urinary Hg levels were four times higher than in control persons (Ritchie et al., 2002). In Cuba, Iran, and Egypt it has also been found that dental personnel had higher urine Hg levels than control persons (Ibarra Fernandez de la Vega et al., 1992; Karahalil et al., 2005; Samir and Aref, 2011). In Norway, a prospective study of urine Hg levels in dentists found a decline from 1960 to 1990. Also, the researchers found that dental nurses during these decades had higher Hg values than dentists (Lenvik et al., 2006; Svendsen et al., 2010). A positive association between the current level of Hg vapor in the working atmosphere and urinary Hg concentrations has been reported (Ritchie et al., 2002; Neghab et al., 2011).

It is important to emphasize that Hg levels in urine and blood can decrease relatively rapidly when the exposure has ceased, even when the amounts in critical organs (brain and kidneys) remain high. Mercury has a complicated metabolism with various half-lives in different organs. Therefore, a suitable indicator medium that reflects the actual Hg concentrations in the critical organs is not available.

4. Kinetics and toxico-dynamics of elemental mercury

After occupational exposure to Hg vapor, inorganic Hg is found in the brain of dental personnel (Nylander et al., 1989; Berlin et al., 2015). Numerous autopsy studies that were undertaken many years after the Hg vapor exposure have found significant inorganic Hg deposits remaining in the brain (Nylander et al., 1989; Opitz et al., 1996). The inorganic Hg accumulation in the brain is likely to continue during long periods with chronic sub-clinical exposure. Once inorganic Hg has been deposited in the brain, it apparently has a cerebral half-life of several years (Vahter et al., 1995).

Vicinal thiol groups in membranes and enzymes are considered to constitute critical biochemical sites of the Hg^{2+} toxicity (Aaseth et al., 2016), e.g., the sulfur groups on tubulin in the neuronal cytoskeleton (Syversen and Kaur, 2012). An enzyme system vulnerable to Hg toxicity is presumed to be pyruvate dehydrogenase because of its dependency on several nucleophilic groups in cofactors, e.g., the sulfur groups in thiamin and lipoic acid. The substrate of this enzyme complex, pyruvate, is imported to mitochondria by a specialized transporter, and then converted into an acetyl-group that is subsequently attached to coenzyme A (CoA) for entrance into the citric acid cycle to yield substrates for the respiratory chain. Insufficiency of this enzyme may thus lead to fatigue and weakness (Fluge et al., 2016), that is frequently seen in individuals exposed to Hg vapor (Berlin et al., 2015).

5. Studies on mercury toxicity in dental practice

The immune system and especially the central nervous system are considered critical targets in long-term exposure to Hg (Berlin et al., 2015; Nagpal et al., 2017). Early symptoms of chronic Hg vapor poisoning include weakness, fatigue, anorexia, and loss of weight (Hilt et al., 2014; Berlin et al., 2015). A decreasing trend of the systolic blood pressure has also been reported (Goodrich et al., 2013). The tendency to motoric incoordination and the characteristic mercurial tremor usually occur at somewhat higher exposure (Berlin et al., 2015). At these stages, Hg vapor poisoning can be seen as an imitator with many different and unspecific symptoms. Upon studying dental staff, Neghab et al. (2011) reported a statistically significant relationship between muscular and neuropsychological disorders and the quantity of amalgam used per day. A statistically significant association between visual long-term memory and previously measured Hg concentration in urine was found in a Norwegian study (Sletvold et al., 2012). In another study, dentists had significantly more memory disturbance than controls (Ritchie et al., 2002). Two Norwegian surveys of dental assistants reported memory loss, concentration problems, psychosomatic symptoms, sleep disturbance, fatigue, and other signs of cognitive dysfunction (Moen et al., 2008; Hilt et al., 2009). A retrospective study in Denmark (Thygesen et al., 2011) disclosed a significant association between the number of working years in dentistry and the reported Hg related symptoms.

Meta-analyses of Hg exposed workers (Meyer-Baron et al., 2002, 2004) have shown that deficient motor performance had a distinct relationship to long-term Hg exposure. However, the capacities for memory and attention were also affected, according to the included studies, although less pronounced (Meyer-Baron et al., 2004). Upon inclusion of studies where Hg exposure had ceased, the meta-analyses showed that registered effects did not change, indicating that the deleterious effects persisted for several years after Hg exposure. Comparing Hg exposed workers and control subjects, the meta-analyses indicated a critical Hg^0 exposure level for the development of toxic effects corresponding to urinary levels of about 300 nmol Hg/L. This limit has, however, been challenged by the fact that urinary levels are not always entirely valid indicators of occupational Hg burden over time, and by research that has unveiled effects at even lower levels (Echeverria et al., 1998). The neurophysiological registrations by Chaffin et al. (1973) using electromyography, as well as a Swedish study (Langworth et al., 1997), reported signs or symptoms in about 5% of an exposed population at somewhat lower exposure levels. Reduced color vision (Fell et al., 2016) and changes in brain signals induced by visual stimulation (visual evoked potentials) have also been observed at long-term low-level Hg exposure (Ellingsen et al., 1993).

Subjects with autoimmune diseases may be sensitive to the low levels of Hg released from dental amalgam (Sterzl et al., 2006; Bjørklund et al., 2018). An accentuated inflammatory response has been observed in Hg sensitive individuals (Berlin et al., 2015). Typical responses are changes of the gums and ptyalism. Björkman et al. (2012) reported increased blood plasma levels of the pro-inflammatory biomarker interleukin-8 (IL-8) in a group of 20 amalgam-sensitive patients, compared to controls, and the IL-8 increase was normalized after removal of