The Dental Amalgam Toxicity Fear: A Myth or Actuality

Monika Rathore, Archana Singh¹, Vandana A. Pant¹

Departments of Pedodontics and ¹Periodontics, BBD College of Dental Sciences, Lucknow, Uttar Pradesh, India

ABSTRACT

Amalgam has been used in dentistry since about 150 years and is still being used due to its low cost, ease of application, strength, durability, and bacteriostatic effect. When aesthetics is not a concern it can be used in individuals of all ages, in stress bearing areas, foundation for cast-metal and ceramic restorations and poor oral hygiene conditions. Besides all, it has other advantages like if placed under ideal conditions, it is more durable and long lasting and least technique sensitive of all restorative materials, but, concern has been raised that amalgam causes mercury toxicity. Mercury is found in the earth's crust and is ubiquitous in the environment, so even without amalgam restorations may raise these levels slightly, but this has no practical or clinical significance. The main exposure to mercury from dental amalgam occurs during placement or removal of restoration in the tooth. Once the reaction is complete less amount of mercury is released, and that is far below the current health standard. Though amalgam is capable of producing delayed hypersensitivity reactions in some individuals, if the recommended mercury hygiene procedures are followed the risks of adverse health effects could be minimized. For this review the electronic databases and PubMed were used as data sources and have been evaluated to produce the facts regarding amalgam's safety and toxicity.

Key words: Amalgam, mercury, myth, restoration, safety, tooth, toxicity

INTRODUCTION

Amalgam, an alloy of mercury (Hg), is an excellent and versatile dental restorative material. It has been used in dentistry since 150 years due to its low cost, ease of application, strength, durability, and bacteriostatic effects.^[1] Popularity of amalgam as restorative material is decreasing these days due to concerns about detrimental health effects, environmental pollution, and aesthetics.^[2] The metallic colour of amalgam does not blend with the



natural tooth colour so patients and professionals preferred tooth-coloured restorative material for cavity filling in carious teeth for better aesthetics. Researchers agree that amalgam restorations leach mercury into the mouth, but consistent findings are not available to report whether it has any significant health risk.^[3] In this review, an attempt has been made to summarize that there is no convincing evidences pointed out to adverse health effects due to dental amalgam restorations and can be used as a preferred restorative material where aesthetics is not a concern.

Amalgam composition and historical background

Amalgam consists of an alloy of silver, copper, tin, and zinc combined with mercury. Unreacted alloy particles of silver-tin are considered as gamma phase. These particles combine with mercury and form a matrix consisting of gamma- $1(Ag_2Hg_3)$ and gamma-2 phases. (Sn₇₋₈Hg). The

Address for correspondence: Dr. Vandana A. Pant, BBD College of Dental Sciences, 1, Akhilesh Das Nagar, Faizabad Road, Lucknow-227 105, Uttar Pradesh, India. E-mail: drvandanapant@rediffmail.com

gamma-2 phase is responsible for early fracture and failure of amalgam restorations. Hence, copper was introduced to avoid gamma-2 phase, replacing the tin-mercury phase with a copper-tin phase (Cu₅Sn₅).^[4] Louis Regnart, known as the 'Father of Amalgam', improved on boiled mineral cement by adding mercury, which greatly reduced the high temperature originally needed to pour the cement on to a tooth. In 1890s GV Black gave a formula for dental amalgam that provided clinically acceptable performance and remained unchanged virtually for 70 years. In 1959, Dr Wilmer Eames^[5] promoted low mercury-to-alloy mixing ratio. The mercury-to-amalgam ratio, dropped from 8:5 to 1:1. The formula was again changed in 1963, when amalgam consisting of a high-copper dispersion alloy was introduced.^[6] It was later discovered that the improved strength of the amalgam was a result of the additional copper forming a copper-tin phase that was less susceptible to corrosion than the tin-mercury phase in the earlier amalgam.^[7]

Modern amalgams are produced from precapsulated (preproportioned) alloy consisting of 42% to 45% mercury by weight. These are convenient to use and provide some degree of assurance that the material has not been not contaminated before use or spilled before mixing.^[8]

Amalgam controversy and amalgam war

In the year 1843, the American Society of Dental Surgeons (ASDS), founded in New York City, declared use of amalgam to be malpractice because of the fear of mercury poisoning in patients and dentists and forced all its members to sign a pledge to abstain from using it.^[9] It was the beginning of the amalgam war.^[10] Because of its stance against amalgam, membership in the American Society of Dental Surgeons declined, and due to the loss of members, the organization was disbanded in 1856 thus resulting in the end of the amalgam war. In 1859, the American Dental Association (ADA) was founded and it did not forbid use of amalgam.^[11] The ADA position on the safety of amalgam has remained consistent since its foundation. In 1920s inferences were made that mercury was not tightly bound in amalgam so its use was discouraged. In 1991, National Institute of Health-National Institute for Dental Research (NIH-NIDR) and FDA concluded that there was no basis for claims that amalgam was a significant health hazard,^[12] but claims of amalgam hazards continued to be published in non-scientific journals, and occasionally in scientific journals.

Mercury exposure from amalgam restorations

Mercury is ubiquitous in environment and humans are routinely exposed via air, water, and food.^[8] Exposure to mercury in human individuals with amalgam restoration occurs during the placement or removal of dental restorations. Once the reaction is complete, less amount of mercury is released, that is far below the current health standard.^[8] The exposure to mercury from restoration depends on the number and size of restoration, composition, chewing habits, food texture, grinding, brushing of teeth, and many other physiological factors. As a vapour, metallic mercury could be inhaled and absorbed through the alveoli in the lungs at 80% efficiency. It is the main route of entry of mercury into the human body, whereas the absorption of metallic mercury through skin or via the gastrointestinal tract is very poor.^[8] The organic compounds of mercury such as methyl mercury are readily absorbed by many organisms and accumulate as it passes into food chain. Research on monkeys had shown that mercury released from amalgam restorations is absorbed and accumulated in various organs such as kidney, brain, lung, liver, gastro-intestinal tract, and the exocrine glands.^[13] The organic form of mercury was also found to have crossed the placental barrier in pregnant rats^[14] and proven to cross the gastrointestinal mucosa when amalgam particles are swallowed at the time of amalgam insertion or during removal of old amalgam fillings,^[15] whereas the inorganic form of Mercury ions (Hg^{+2}) circulate into the blood stream but hardly cross the blood-brain barrier and placental barrier.

Mercury does not collect irreversibly in human tissues. The average half life of mercury is 55 days for transport through the body to the point of excretion. Thus mercury that came into the body years ago may no longer be present in the body.^[8]

Diagnostic methods to detect levels of mercury in body

Toxicity from mercury could occur through exposure to organic, inorganic, and elemental forms of mercury. According to decreasing toxicity of mercury it is classified as organomercury (methyl and ethyl mercury), mercury vapour, and inorganic mercury. Various diagnostic methods exist to detect the level of mercury in body, including tests for blood, urine, stool, saliva, hair analysis, and others. These tests may determine if mercury is in the body and/or if it is being excreted. A study^[16] conducted by measuring the intraoral vapour levels over a 24-h period in patients with at least nine amalgam restorations showed that the average daily dose of inhaled mercury vapour was $1.7 \,\mu g$ (range from 0.4 to 4.4 μ g), which is approximately 1% of the threshold limit value of 300 to 500 μ g/day established by WHO, based on a maximum allowable environmental level of $50 \mu g/day$ in the workplace. According to Berdouses et al.^[17] mercury exposure from amalgam can be greatly increased by personal habits such as, chewing and brushing.

Berglund,^[18] in 1993, determined the daily release of mercury vapour from amalgam restorations made of alloys of the same types and batches as those used in the *in vitro* part of the study. He carried out a series of measurements

on each of eight subjects before and after amalgam therapy and found that none of the subjects were occupationally exposed to mercury. The amalgam therapy, that is, from 3 to 6 occlusal amalgam surfaces and from 3 to 10 surfaces in total-had very little influence on the intraoral release of mercury vapour, regardless of amalgam type used, effects was not found on mercury levels in urine and saliva. Rapid and reliable detection of mercury in blood and urine resulting from environmental and occupational exposure may be carried out by using atomic fluorescence spectrophotometry.^[19] Measurements of total mercury in the urine tend to reflect inorganic mercury exposure and total mercury levels in whole blood are more indicative of methyl mercury exposure. Commonly two types of urine tests have been used in which one is the unprovoked mercury test that does not use a pharmaceutical mercury chelator and only reflects the amount of mercury the body naturally removes via the urine. The other is the urine mercury challenge (provoked) test, which uses a pharmaceutical chelator to remove the mercury captured via the kidneys/urine pathway. Both methylmercury and inorganic mercury can also be measured in breast milk. The relative proportions of these species depend on the frequency of fish consumption, dental amalgam status, and occupational exposures. In a study for comparison of hair, nails, and urine for biological monitoring of low level inorganic mercury exposure in dental workers, the data suggested that urine mercury remains the most practical and sensitive means of monitoring low level occupational exposure to inorganic mercury.^[20]

Various related studies

In this review electronic databases and PubMed have been used for data sources and articles from peer reviewed journals and various organizations including WHO (1991), the Agency for Toxic Substances and Disease Registry (ATSDR) (1999), US Environmental Protection Agency (EPA,1997), the National Research Council (NRC) (2000), the Institute of Medicine (2001; 2004) and Life Science Research Office (LSRO) (2004) have been evaluated to investigate the biochemical, behavioural, and/ or toxicological effects resulting from exposure to amalgam, mercury vapour (HgO), inorganic mercury (Hg²⁺), or organic mercury (methyl and ethyl mercury). The LSRO search was limited to in vivo studies on humans relevant to amalgam and biochemical, behavioural and/or toxicological effects as health effects in laboratory animals do not reliably predict health effects in humans.

Effects of prenatal mercury exposure

Nonionized mercury is capable of crossing through lipid layers at membrane barriers of the brain and placenta, is oxidised within these tissues and is slowly removed. This fact has become the basis for claims of neuromuscular problems in patients with amalgam restorations.^[8] Removing these restorations do not eliminate exposure to mercury. Maternal amalgam restoration results in in utero exposure to low levels of elemental mercury. There is no evidence that exposure to mercury has been associated with any adverse pregnancy outcomes or health effects in the newborn and infants. In a prospective study consisting of 72 pregnant women, it was found that the number and surface areas of amalgam restorations positively influenced the concentration of mercury in amniotic fluid. The levels of mercury detected in amniotic fluid were low and no adverse outcomes were observed during the pregnancy or in the newborns.^[21] Blood samples obtained from umbilical cord had no significant mercury levels considered to be hazardous for neurodevelopmental effects in children using the EPA reference dose (5.8 μ g/L in cord blood).^[22] To find co-relation between mercury exposure from amalgam restorations placed during pregnancy and low-birth weight 1,117 women with low birth weight infants were compared with random sample of 4,468 women who gave birth to infants with normal birth weight. Women (4.9%) had at least one amalgam restoration placed during pregnancy. These women were not at greater risk for a low birth weight infant and neither were women who had 4 to 11 amalgam restorations placed.^[23] In a study conducted by Daniels^[24] 90% of the women received dental care during pregnancy. Having more restorations placed at time of conception did not negatively affect pregnancy or birth outcome. Mean umbilical cord mercury concentration was slightly higher in women who had dental care. However, cord mercury concentrations did not differ significantly among mothers in relation to amalgam restoration during pregnancy or by the number of amalgams in place prior to pregnancy. Overall, amalgam restorations were not associated with negative birth outcomes or delayed language development. They stated that amalgam restorations in girls and women of reproductive age should be used with caution to avoid prenatal mercury exposure, although there were no adverse effects seen.

Health effects of amalgam in children

The Children's Amalgam Trial is a randomized trial, to address potential impact of mercury from amalgam restorations on neuropsychological and renal function in children. Bellinger *et al.*^[25] conducted a study on 534 New England children, aged 6–10 years for 5 years. All subjects were in need of at least two posterior occlusal restorations. Participants were randomized to receive either amalgam or composite restoration at baseline and at subsequent visits. The primary endpoint was to assess the 5-year change in IQ scores. Secondary endpoints included measures of other neuropsychological assessments and renal functioning. In the 5-year follow-up period the investigators conducted multiple assessments of IQ score, memory index, and urinary albumin. No statistically significant differences were reported in neuropsychological or renal effects observed in

the children who had amalgam restorations compared to those with composite restorations.

In another study, authors have concluded that there was no difference in the neuropsychological function of the children who received amalgam restorations compared to the children with composite restorations.^[26] A doseeffect analysis of children's exposure to amalgam and neuropsychological function was also evaluated in the children's amalgam trial. The authors examined a sample of children with substantial unmet dental needs using a dose-effect analysis. There was no significant association between neuropsychological outcomes and mercury exposure. The authors concluded that there appeared to be no detectable adverse neuropsychological outcomes in children attributable to the use of amalgam restorations.^[27] The relation between amalgam and the psychosocial status of children was also assessed as a part of the New England Children's Amalgam Trial (NECAT). The two groups of children were examined for psychosocial outcomes. It was carried out using both a parent-completed "Child Behaviour Checklist" and children's self-reports and concluded that there was no evidence associated with adverse psychosocial outcomes in the 5-year period following amalgam placement.^[28]

Kingman *et al.*^[29] studied correlation between exposure to amalgam and neurological functions. No significant associations between amalgam exposure and clinical neurological signs of abnormal tremor, coordination, gait, strength, sensation or muscle stretch reflexes or for any level of peripheral neuropathy in the subjects have been observed. A significant association was detected between amalgam exposure and the continuous vibro-tactile sensation response. The study reported that this association was a subclinical finding that was not associated with symptoms, clinically evident signs of neuropathy or any functional impairment.

In the Children's Amalgam Trial, one of the secondary endpoints included renal functioning. The investigators assessed changes on markers of glomerular and tubular kidney function and urinary mercury levels. They found no significant differences between the treatment groups and no significant effects related to the number of dental amalgam restorations on the markers. Children in both treatment groups experienced micro albuminuria, but the prevalence was higher in amalgam group. The authors concluded that the increase in micro albuminuria may be random, but should be further evaluated.^[30] The other safety trial was conducted in Lisbon, Portugal^[27] in which a randomized controlled clinical trial carried out in 507 children 8- to 10-years old at baseline. They were evaluated for several years thereafter to determine if any health changes occurred following restorations with amalgam or composites. On carrying out annual standardized tests of memory, attention,

physical coordination, and velocity of nerve conduction, the scientists did not detect a pattern of decline in the test scores of individual children who received amalgam restorations. They found a trend of higher treatment need in children receiving composite, thus suggesting that amalgam should remain a viable dental restorative option for children. The investigators performed annual clinical neurological examinations to assess neurobehavioral and neurological effects. The authors concluded that amalgam exposure had no adverse neurological outcomes.^[31]

The 7 years of longitudinal data provide extensive evidence about relative safety of amalgam in dental treatment. Substantial amalgam exposure did lead to creatinine adjusted urinary mercury levels that were higher in the amalgam group. Children with amalgam restorations had slightly elevated levels of mercury in their urine, measuring on average 1.5 μ g/L of urine for the first two years and levelling off to $1.0 \,\mu\text{g/L}$ or less thereafter. However, these values fall within the background level of $0-4 \mu g/L$, which is usual for an average person not exposed to industrial or other known sources of mercury.^[32] Thus, the longitudinal studies on the use of amalgam in children did not suggest any negative effects on neuropsychological function or renal function within the 5-year follow-up period. It was reported that urinary mercury concentrations were highly correlated with both the number of amalgam restorations and the time since placement in children. The finding suggested that there may be sex-related differences in mercury excretion. They found that females have significant increase in the rate of mercury excreted in urine than males. Thus, this association might confer a lower mercury toxicity risks in females.^[33] Dunn et al.^[34] evaluated scalp, hair, and urine mercury content of children collected over the 5-year period, mean hair mercury level was $0.3-0.4 \mu g/g$ and mean urinary mercury level was 0.7–0.9 μ g/g creatinine. The authors reported that use of chewing gum in the presence of amalgam restoration was a predictor of higher urinary mercury levels. Data suggested that amalgam-associated mercury exposure might be reduced by avoidance of gumchewing in the presence of amalgam restorations.

Sixty children were studied to assess urinary mercury excretion and its relation to amalgam restoration and fish consumption. Children with amalgam restorations had significantly higher urinary mercury levels compared to children with non-amalgam restorations. The urinary mercury levels in the amalgam group were well below levels that are known to cause adverse health effects.^[35]

Health effects related to mercury exposure in adults

An investigation on 20,000 people in the New Zealand Defence Force between years 1977–1997 was done to find out association between amalgam restorations and disorders

related with nervous system and kidney. No significant correlation between amalgam restorations and chronic fatigue syndrome or kidney disease was observed. A slightly elevated risk for multiple sclerosis was reported, but may have been due to confounding variables.[36] In another study, where few patients believed that their amalgam restoration made them ill, medical examination including physical examination, electrocardiogram, abdominal sonography, and blood chemistry was done. The study concluded that symptoms of the patients were due to psychological factors. There was no connection between the mercury levels in the patient's blood, urine, and saliva and their symptoms.[37] The association between amalgam and multiple sclerosis was assessed via a systematic review and meta-analysis. Three case control studies and one cohort study met their inclusion criteria. The meta-analysis revealed a slight nonstatistically significant increase between the presence of amalgam restorations and multiple sclerosis. The study does not provide evidence for or against an association.^[38]

Halbach *et al.*^[39] evaluated the internal exposure to amalgam-related mercury and estimated the amalgam-related absorbed dose of mercury. The integrated mercury absorbed from amalgam restorations was estimated at up to 3 μ g per day for an average number of restorations and 7.4 μ g per day for a high amalgam load. The authors concluded that these estimates are below the tolerable dose of 30 μ g per day established by WHO.

Hypersensitivity reactions by amalgam restorations

Amalgam is capable of producing delayed hypersensitivity reactions in some individuals. These reactions usually present with dermatological or oral symptoms. The constant exposure to mercury in amalgam restorations may sensitize some individuals, making them more susceptible to oral lichenoid lesions. These oral lesions are rarely noticed by the affected individuals and cause no discomfort. There is evidence that a certain percentage of lichenoid lesions are caused by amalgam restorations,^[40] but other restorative materials can also cause lichenoid lesions. It was also noted that the restorations associated with lichenoid lesions are poorly contoured, corroded and old. Hence corrosion of amalgam restoration or perhaps the biofilm present on such restorations may contribute to the development of hypersensitive reaction rather than material itself.^[41] Symptoms of an amalgam allergy include skin rashes in the oral, head and neck area, itching, swollen lips, localized eczema-like lesions in the oral cavity. These clinical signs usually require no treatment and will disappear on their own within a few days of exposure. However, in some instances, an amalgam restoration will have to be removed and replaced with alternate restorative material. The replacements have led to significant improvements.^[42] Although mercury allergy is rare but sometimes hypersensitivity to it may lead

to dermatitis or type IV delayed hypersensitivity reactions most often affecting the skin as a rash.^[43]

Mercury exposure in dental professionals

Dentists and dental nurses are at risk of potential exposure to inorganic mercury through their handling of amalgam, although now days their exposure has reduced due to low mercury to alloy ratio and through mercury management. One hundred and eighty dentists were evaluated in West Scotland for mercury exposure and its effects on their health and cognitive function. Dentists were found to have, on an average, over four times the level of urinary mercury compared to age and education-matched control subjects. The authors reported that based on their questionnaire, dentists were more likely to report having a disorder of the kidney, although the effect was not significantly associated with their urinary mercury level. An age effect was found for memory disturbances in dentists but not in the control subjects. There was no significant association between urinary mercury concentrations and self-reported memory disturbance.[44] A study on 43 dental nurses, with an average age of 52, were exposed to copper amalgam with a 30-year follow-up; were compared with 32 matched controls. It was concluded that the dental nurses did not appear to be neurobehavioraly compromised. Seven symptoms of mercury poisoning that were reported at a higher rate by exposed group than by the control group (arthritis, bloating, dry skin, headache, metallic taste, sleep disturbances, and unsteadiness). It did not appear that the investigators performed post-hoc testing to compensate for multiple comparisons.^[45] The possible health risk of occupational exposure to mercury vapour in the dental office was assessed by evaluating the cytogenetic examination of leukocytes and blood mercury levels of dentists.[46] Genotoxicity of occupational exposure to mercury vapour in ten dentists was evaluated. The authors concluded that mercury vapour concentration in blood was below 0.1 mg/m³ and did not exhibit cytogenetic damage to leukocytes.

Mercury management in dental operatory

In 1999, the ADA Council on Scientific Affairs adopted mercury hygiene recommendations to provide guidance to dentists and their staff members for safe handling of mercury and minimizing the release of mercury into the dental office environment. These were updated in 2003 and are as follows: work in well-ventilated areas, remove professional clothing before leaving the workplace, periodically check the dental operatory atmosphere for mercury vapour, (use dosimeter badges or use of mercury vapour analysers for rapid assessment after any mercury spill or clean-up procedure). The current Occupational Safety and Health Administration (OSHA), standard for mercury is 0.1 mg per cubic meter of air averaged over 8-h work shift. The National Institute for Occupational Safety and Health has recommended the permissible exposure limit to be changed to 0.05 mg/m³ averaged over 8-h work shift over a 40-h workweek.^[47] During preparation and placement of amalgam only precapsulated amalgam alloys should be used. If possible, recap single-use capsules after use, store them in a closed container and recycle them. Avoid skin contact with mercury or freshly mixed amalgam. Use high-volume evacuation systems when finishing or removing amalgam. Floor coverings should be non absorbent, seamless and easy to clean. Use of carpet in operatory is not recommended where an accidental mercury spill might occur. Chemical decontamination of carpeting may not be effective, as mercury droplets can seep through the carpet and remain inaccessible to the decontaminant. In case of accidental mercury spill a vacuum cleaner should never be used to clean up the mercury. Small spills (less than 10 g of mercury present) can be cleaned safely using commercially available mercury cleanup kits.

Amalgam substitutes

In the recent year's composites, glass ionomer cements and a variety of hybrid structures have been used due to increased demand for aesthetic restorations. Composite serves better than amalgam when conservative preparation is recommended like small occlusal restorations, in which amalgam require removal of more sound tooth structure.^[48] Composites have different setting reaction mechanisms and it interacts with the patient's tissues in different ways. The small organic molecules (monomers) react to form polymers. Some of the monomers may not have reacted during placement and therefore low levels remain in the set restoration, which are known to be toxic to cells and others may cause allergic reactions. The effects they cause vary depending on the substance and on the type of body tissue with which they come into contact. Concerns have been raised about the endocrine disrupting (in particular, oestrogen-mimicking) effects of plastic chemicals such as "Bisphenol A" used in composite resins.^[49]

Amalgam possesses greater longevity than composite.^[50] However, this difference has decreased with continued development of composite resins.[51] Amalgam is moderately tolerant to the presence of moisture during placement. In contrast, technique for composite resin placement is more sensitive and require "extreme care" and "considerably greater number of steps".^[51] Mercury acts as bacteriostatic agent whereas TEGMA (constituting some older resin-based composites) "encourages the growth of microorganisms".[51] The New England Children's Amalgam Trial suggested that the longevity of amalgam is higher than that of resin-based compomer placed in primary teeth and composites in permanent teeth.^[50,52] Compomers and composites were seven times likely to require replacement than amalgam.^[52] "Recurrent marginal decay" is the main reason for failure in both, amalgam and composite restorations, accounting for 66% (32/48) and 88% (113/129), respectively.^[53] "Christensen^[50] quoted Amalgam restorations are and will continue to be the mainstay of posterior tooth restorations for many years to come." Though use of amalgam has decreased during the past few years, more studies on safety of composites or other aesthetic materials with long-term follow-up of are necessary before they can be considered a definitive alternative for amalgam.

CONCLUSION

The current use of amalgam has not posed a health risk apart from allergic reactions in few patients. Clinical justifications have not been available for removing clinically satisfactory amalgam restorations, except in patients allergic to amalgam constituents. Mercury hypersensitivity is an immune response to very low levels of mercury. There is no evidence that mercury released from amalgams results in adverse health effects in the general population. If the recommended mercury hygiene procedures are followed, the risks of adverse health effects in the dental office could be minimized. Amalgam is safe and effective restorative material and its replacement by nonamalgam restorations is not indicated. Also a recent review by the American Dental Association Council on Scientific Affairs states that: "Studies continue to support the position that dental amalgam is a safe restorative option for both children and adults. When responding to safety concerns it is important to make the distinction between known and hypothetical risks."

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