

2015 Update of the LSRO Report on the Health Effects of Dental Amalgam

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Literature Search

To update the extent to which the research gaps identified in the Life Science Research Office (LSRO) report have been addressed, a search of the literature published between June 16th, 2010 (the end point of the last ADA update) and December 31st, 2014 was conducted. A search of the MEDLINE database using PubMed identified 133 articles on the topic of dental amalgam. The search was limited to *in vivo* studies on humans published in English. The abstracts of the 133 articles were reviewed to identify all studies relevant to amalgam and biochemical, behavioral and/or toxicological effects. Nineteen relevant articles were identified and summarized. Several other searches using key terms from the research gap topics for the same time period were also conducted using PubMed to capture the insight from additional relevant work.

Search terms: dental amalgam and health

Initial Search: 133 articles total, 19 retrieved

Literature was considered if it reported dental amalgam exposure and measured impact on a health outcome that related to a research gap previously identified by the LSRO in 2010 (1). For each research area, insights from the studies and a rating of evidence quality is provided. The ADA Center for Evidence Based Dentistry's criteria system was used to assess the quantity and quality of the updated literature. Evidence quality is rated as "good" when it is characterized by generally high quality studies with similar conclusions; "limited," when based on generally lower-quality studies or inconsistent results across studies; or "poor," in which the evidence is solely expert opinion or case reports.

Update of Research Gaps Previously Identified in the LSRO Report

Research gaps identified in the LSRO report for which relevant literature was identified are listed below with brief summaries evaluating the impact of the new research. A brief synopsis of each individual study with insight about its quality follows.

Neurotoxic and/or Neuropsychological Effects of Mercury Exposure

Summary: Studies evaluating amalgam exposure and neurological effects consistently found no association, but the new evidence in this area remains limited, since only one study used a standardized, validated measurement of exposure.

Low-level mercury exposure and peripheral nerve function. Franzblau A, et al. (2012)(2)

This study examined the effect of occupational mercury exposure on peripheral nerve function in a convenience sample of 2,656 dentists, who attended the American Dental Association's annual meeting from 1997 through 2006. A questionnaire was distributed, and urinary mercury measurements and sensory nerve conduction in the median and ulnar nerves were performed. No consistent effect of urinary mercury concentration on sensory nerve conduction was found. The quality of this study was high: nerve conduction was measured using established techniques with high inter-examiner and intra-examiner reliability, mercury exposure was measured using a standard and validated biomarker assay, the sample size was adequate, and analyses controlled for likely confounders.

Hospital admissions for neurological and renal diseases among dentists and dental assistants occupationally exposed to mercury. Thygesen LC, et al. (2011) (3)

Records from 1964 to 2006 were used in this study of a Danish cohort of 122,481 workers. This cohort included 5,371 dentists and 33,858 dental assistants, whose hospital admissions for neurological and renal diseases were compared to those of general physicians/lawyers (comparison group for dentists), and medical secretaries/nurses and legal secretaries (comparison group for dental assistants). Inverse associations were found in dentists and dental assistants compared to controls, where periods of low mercury exposure increased risk of neurological disease or renal disease, respectively. Occupational mercury exposure did not increase the risk of hospital admissions for neurological, Parkinson's or renal diseases in this cohort. The quality of this study was medium: the sample size was adequate, the sample was generalizable, the health outcomes were based on clinical diagnoses, and the comparison groups were appropriate. However, mercury exposure was based on averages based on Norwegian urine samples and period of employment; actual mercury exposure was not measured for members of the cohort.

Cognitive status in persons with amalgam-related complaints. Sundström A, et al. (2010) (4)

This case-control study examined whether those with amalgam-related health complaints had more cognitive deficit symptoms than their matched controls. The study drew its sample from a Swedish population-based longitudinal study, of 342 participants who had amalgam-related health complaints and were matched by age, gender, education, test sample, and test wave to 342 participants without health complaints. Participants completed a self-reported health questionnaire. The measured outcome

was composed of 14 cognitive tests, where their z-scores were summed and grouped into three broader categories: episodic memory, semantic memory, and visuo-spatial ability. Although the cases reported more musculoskeletal and neuropsychological symptoms compared to controls in their questionnaire, there were no statistical differences in measured symptoms between cases and controls for any of the cognitive tests. The quality of this study as evidence of health outcomes of amalgam exposure was low: health outcomes were evaluated prospectively and the comparison group was demographically similar, but there was no measurement of exposure to amalgams or mercury, and all health outcomes except cognitive function were based on self-report and evaluated cross-sectionally.

Co-Exposure to Two Chemical Forms of Mercury (i.e. Organic (methylmercury) and Elemental Mercury)

Summary: The evidence for this research area remains limited, due to the low number of studies and the small and purposive sample of the single study in this area. The new study does not evaluate health effects. In the Seychelles studies, methylmercury was considered a covariate because the number of subjects was too low to consider an interaction.

New insight into biomarkers of human mercury exposure using naturally occurring mercury stable isotopes. Sherman LS, et al. (2013) (5)

This study investigated whether mercury stable isotopes could be used to better distinguish between exposure to elemental mercury versus organic mercury. North American dental professionals' (n=12) hair and urine was characterized through mercury stable isotopes analysis. They found that hair mercury samples were an accurate measure for organic mercury, however, the mercury found in urine was highly variable. The authors hypothesized that organic mercury is able to demethylate within the body and contribute to urinary mercury concentration. These data suggest that the majority (>70%) of mercury in urine from individuals with <10 dental amalgams is derived from ingestion of methylmercury in fish. In which case, previous estimates of mercury exposure from dental amalgams using urinary mercury are overestimates and should be corrected for in future studies to account for this common dietary source of mercury. The quality of this study is medium: the exposure and outcome measures are based on standard and valid methods, but the small sample size precluded control for moderating or confounding factors beyond fish consumption and amalgam contacts, and the sample was purposive, such that selection bias may affect the internal or external validity of the study.

In-Utero Effects of Low-Level Exposure to Elemental Mercury

Summary: Studies found no evidence that *in utero* exposure to maternal amalgam restorations are associated with adverse health outcomes. The level of evidence for this research area is rated as good, since the studies have consistent findings and individually are of high quality.

The Seychelles Child Development Study (SCDS) includes well-defined cohorts of adequate size to detect associations with covariates known to influence neurodevelopment, precise biological markers of exposure, and the use of standard neurodevelopmental assessments.

Prenatal exposure to dental amalgam: evidence from the Seychelles Child Development Study main cohort. Watson GE, et al. (2011) (6)

The Seychelles Child Development Study (SCDS) Main Cohort is a prospective, double-blind, longitudinal cohort study designed to evaluate the association between prenatal methylmercury exposure from maternal diet and child neurodevelopmental outcomes. This study combined SCDS Main Cohort data with retrospective chart review to analyze the association between maternal dental amalgam exposure levels during gestation and neurodevelopment of children at 66 months. The study enrolled 587 mother-child pairs. Dental amalgam status was determined retrospectively using dental records, and six age-appropriate, neurodevelopmental tests were performed. Total number of amalgam surfaces as well as occlusal point scores were used as exposure metrics for mercury in dental amalgams. Occlusal point scores were calculated by scoring the size of occlusal amalgams in premolars and molars and summing occlusal scores for a total occlusal point score. The associations of amalgam occlusal point scores on neurodevelopmental outcomes differed by sex, where boys scored low on a letter and word identification test with increasing exposure, however given the number of models fit (48), this could be a chance finding; the authors concluded that their findings required confirmation from additional studies. No significant associations of elemental mercury exposure from dental amalgams on any neurodevelopmental outcomes were found. The quality of this study is high: the sample size is adequate, the sample was controlled for moderators and confounders (including methylmercury from maternal fish consumption), and neurobehavioral outcomes were measured using standard, validated measures; one limitation is that maternal amalgam exposure is based on retrospective chart review and thus, may not be entirely accurate.

Prenatal exposure to dental amalgam in the Seychelles Child Development Nutrition Study: associations with neurodevelopmental outcomes at 9 and 30 months. Watson GE, et al. (2012) (7)

This prospective, double-blind, longitudinal study used the Seychelles Child Development Nutrition Study (SCDNS), to evaluate the association between maternal dental amalgam status during gestation and neurodevelopment of children at 9 and 30 months. Unlike the first study, this study prospectively determined dental amalgam status (number of amalgams and occlusal point scores), using 242 mother-child pairs and used mental (MDI) and psychomotor (PDI) developmental indices of the Bayley Scales of Infant Development-II (BSID-II) as outcome measurements. They also adjusted for methylmercury and fatty acids via high fish consumption of the population. There was a transient association at one time point between occlusal point score and adverse MDI outcome for girls only. There was no statistical association observed between elemental mercury exposure, the number of maternal amalgam surfaces, and neurodevelopmental endpoints measured, and the non-significant effect of maternal amalgam status on BSID II score was not clinically significant. The quality of this study is high: the sample size is adequate; the relationship between maternal amalgam and child development was evaluated prospectively; the exposures and outcomes were measured using standard, reliable, validated tools; and the statistical analysis adjusted for moderators and confounders. However, although the BSID II is a widely used and validated measure of child development with adequate predictive validity for future cognitive and motor functioning (8), it lacks validity for future IQ (7), indicating that further evaluation of children at later ages is necessary.

Neurodevelopmental outcomes at 5 years in children exposed prenatally to maternal dental amalgam: the Seychelles Child Development Nutrition Study. Watson GE, et al. (2013) (9)

This study extended The Seychelles Child Development Nutrition Study (SCDNS) to five years and evaluated the association between maternal dental amalgam status during gestation and neurodevelopment of children. The study enrolled 236 mother-child pairs, where maternal amalgam status (number of amalgams and occlusal points) was determined prospectively, and outcomes for children were age-appropriate tests of cognitive, language, perceptual functions and scholastic achievement. Authors adjusted for several covariates, including methylmercury and maternal fatty acid status. The authors found no associations for either exposure measurement on any outcomes and concluded that their findings do not support evidence that elemental mercury in utero exposure from maternal dental amalgam adversely affects children's neurocognitive development. The quality of this study is high: the sample size is adequate; the relationship between maternal amalgam and child development was evaluated prospectively; the exposures and outcomes were measured using standard, reliable, validated tools; and the statistical analysis adjusted for moderators and confounders.

Cognitive function among sons of women who worked in dentistry. Naimi-Akbar A, et al. (2012) (10)

This Swedish study linked national registries to match 17-18-year-old boys born between 1960-1978 of mothers whose occupation was a dentist or dental nurse with boys whose mothers worked as physicians or assistant nurses. The mother-child pair's ages were matched within one year. Outcome measures were four cognitive tests of linguistic understanding and the ability to use oral and written language. After adjustment, the authors found no associations between neurocognitive detriment and being a son of a mother who was assumed to be occupationally exposed to elemental mercury, compared to being a son of a non-dental professional. The quality of this study was medium: the sample size was adequate, there was adjustment for confounders, and the outcome was measured using a validated standard measurement tool, but exposure to mercury was identified purely by recorded occupation.

Mercury in Breast Milk and Effects on Brain Development

Summary: Studies have inconsistently shown that maternal amalgam restorations lead to mercury in breast milk; only one new study was identified on this topic, which found that the number of amalgams was statistically associated with increased mercury concentration in breast milk, but since the study was of lower quality, the level of evidence in this area remains limited. No new studies evaluated the effect of mercury in breast milk on the developing brain.

Effect of teeth amalgam on mercury levels in the colostrums human milk in Lenjan. Norouzi E, et al. (2012) (11)

In a small sample of Iranian women with low fish consumption (n=38), the authors found that mercury concentrations in breast milk samples were correlated with the number of amalgams in the mother's mouth ($p < 0.05$; $r = 0.76$). The mean mercury concentrations in breast milk of mothers without dental fillings (n =13), with one to three dental teeth fillings (n =10), and four to eight dental fillings (n =15) were 2.87, 5.47, and 13.33 $\mu\text{g/l}$, respectively. Mercury concentrations were not found to be significantly different based on age, mother's weight or newborn's birth weight. The quality of this study was rated as low: both the number of amalgam restorations and level of mercury in milk were measured using standard methods, but there was no control of potential confounders such as maternal diet, age, or socioeconomic status, the sample size was small, and the sample selection rationale was not reported, such that the sample may not be representative of the Iranian population.

Genetic Variability in Mercury Pharmacokinetics or Sensitivity

Summary: Studies have identified several genes that may modify the health effects of mercury exposure, but few studies seek to replicate the results of another. The studies of polymorphisms of genes relating to glutathione synthesis and degradation pathways have found inconsistent results. Therefore, although the studies in this area are generally of medium quality, the lack of consistency means that research in this area remains limited. Additionally, all new studies identified in this area were based on either a single cohort of Portuguese children, or a single convenience sample of primarily (>90%) Caucasian attendees of a US-based dental convention, which may limit the generalizability of the results. In regards to gender differences, there is evidence that there are differences in mercury excretion and the effect of mercury on blood pressure, but more studies are needed; the evidence in this area is limited.

Modification of neurobehavioral effects of mercury by a genetic polymorphism of coproporphyrinogen oxidase in children. Woods JS, et al. (2012) (12)

This study evaluated whether the effect of mercury exposure on neurobehavioral tests could be modified by a single nucleotide polymorphism (SNP) of a coproporphyrinogen oxidase gene in children that is known to affect adults. The study was comprised of participants from the Casa Pia Dental Amalgam Trial from 1996-2006 in Portugal. Originally, 507 children, ages 8-12 years, were followed for 7 years after having dental amalgam or resin composite restorations. These children had similar socioeconomic status, home environment, and no preexisting psychological, behavioral, neurodevelopmental, immunosuppressive, or renal disorders. Twenty three neurobehavioral tests were conducted annually during the study; these served as the outcomes. Urinary mercury was measured yearly during the study, and was relatively high at baseline, meaning that mercury exposures other than dental amalgams were already present. Associations were evaluated using the maximum and cumulative mercury measure. In this current study, 330 children's allelic status of CPOX4 was genotyped after the 7 years follow-up of the original study. Covariates adjusted for in regression analyses were age at assessment, race and non-verbal IQ. The authors found several mercury-gene interactions across neurobehavioral test categories, where the presence of the gene mutation (combined homo and heterozygous mutant type) modified the adverse effect of chronic mercury exposure on decreased test scores, particularly among boys. The authors do not mention the clinical relevance of the point decrease of the test scores, only that they were statistically significant. The quality of this study is medium: the sample size is adequate, the study data is prospective, and the exposure and outcome variables were measured using standard and valid methods, but there is no control for numerous potential confounders or modifiers, and with the number of statistical tests done (and no adjustment in p -value to account for multiple comparisons), at least some of them would appear to reject the null hypothesis purely by chance. Although the authors had dental amalgam exposure date (i.e. cumulative surface exposure), they did not report on whether associations with amalgam and the polymorphisms were observed.

Modification of neurobehavioral effects of mercury by genetic polymorphisms of metallothionein in children. Woods JS, et al. (2013) (13)

This study evaluated whether the effect of mercury exposure on neurobehavioral tests could be modified by two other single nucleotide polymorphisms (SNPs) of a metallothionein gene in children that is known to affect adults. The study was also comprised of participants from the Casa Pia Dental Amalgam Trial from 1996-2006. Originally, 507 children, ages 8-12 years, were followed for 7 years after

having dental amalgam or resin composite restorations. A battery of neurobehavioral tests throughout the study served as the outcome. Urinary mercury exposure was measured yearly during the study, and associations were evaluated using the maximum and cumulative mercury measure. In this study, 330 children's allelic status of MT1M and MT2A were genotyped after 7 years follow-up. Covariates adjusted for in regression analyses were age at assessment, race and non-verbal IQ. The authors found that the presence of either gene mutation modified the adverse effect of chronic mercury exposure on decreased neurobehavioral test scores, only among boys. The authors note that these results should be interpreted with caution until verified with a larger study. Again, the authors do not mention the clinical relevance of the point decrease of the test scores, only that they were statistically significant. The quality of this study is medium: the sample size is adequate, the study data is prospective, and the exposure and outcome variables were measured using standard and valid methods, but there is no control for numerous potential confounders or modifiers, and with the number of statistical tests done (and no adjustment in p -value to account for multiple comparisons), at least some of them would appear to reject the null hypothesis purely by chance.

Genetic polymorphisms of catechol-O-methyltransferase modify the neurobehavioral effects of mercury in children. Woods JS, et al. (2014) (14)

This study evaluated whether the effect of mercury exposure on neurobehavioral tests could be modified by several single nucleotide polymorphisms (SNPs) of a catechol-O-methyltransferase gene in children that is known to affect adults. The study was comprised of participants from the Casa Pia Dental Amalgam Trial from 1996-2006. Originally, 507 children, ages 8-12 years, were followed for 7 years after having dental amalgam or resin composite restorations. A battery of neurobehavioral tests throughout the study provided results for the outcome. Urinary mercury exposure was measured yearly during the study, and associations were evaluated using acute (urinary mercury at 2nd year follow up) and chronic (cumulative mercury at year 7) mercury measures. In this study, 330 children's allelic status of *COMT* rs4680, rs4633, rs4818, and rs6269 were genotyped after a 7-year follow-up. Covariates adjusted for in regression analyses were age at assessment, race and non-verbal IQ. These data may suggest a modifying effect of *COMT* genotype on the neurobehavioral test score response to Hg exposure in boys. The analysis did not appear to correct for multiple comparisons and the observed effects were not consistent between acute and chronic exposure. The quality of this study is medium: the sample size is adequate, the study data is prospective, and the exposure and outcome variables were measured using standard and valid methods, but there is no control for numerous potential confounders or modifiers, and with the number of statistical tests done (and no adjustment in p -value to account for multiple comparisons), at least some of them would appear to reject the null hypothesis purely by chance.

An investigation of modifying effects of metallothionein single-nucleotide polymorphisms on the association between mercury exposure and biomarker levels. Wang Y, et al. (2012) (15)

This study investigated whether single-nucleotide polymorphisms (SNPs) in metallothionein (MT) genes influenced individual differences in mercury biomarker concentrations. The study was comprised of 515 dental professionals, whose occupational and environmental mercury exposure was assessed, using urine and hair samples as well as a questionnaire. Dental professionals' mercury concentrations were similar to those of the U.S. population. The presence of 13 MT SNPs was determined for each individual and regression analyses were used to evaluate whether the presence of any of these SNPs increased urinary or hair mercury concentrations. These data may suggest some MT SNPs may influence mercury concentrations though as the authors point out – the underlying mechanism(s) for the observed exposure-biomarker relationship is unclear. The quality of this study is medium: the sample size was

adequate, but there was no control for possible modifying or confounding variables beyond gender, and with the number of statistical tests done (and no adjustment in *p*-value to account for multiple comparisons), at least some of them would appear to reject the null hypothesis purely by chance.

Glutathione enzyme and selenoprotein polymorphisms associate with mercury biomarker levels in Michigan dental professionals. Goodrich, JM, et al. (2011) (16)

Using the same convenience sample of 515 dental professionals as Wang, et al (15), this study used urine samples to measure elemental mercury exposure, hair samples to measure methylmercury exposure, and Taqman assays of buccal swab samples to genotype sample members' DNA at 15 polymorphic sites. A self-administered questionnaire provided information on subject demographics, occupational practices such as number of amalgams removed or placed per week, and personal exposures to mercury, such as number of amalgams in subject's mouth and detailed information on fish consumption. The aim of this study was to investigate whether polymorphisms in selenoproteins and glutathione-related genes influence mercury retention, and if retention is differential by exposure type. In all, 15 polymorphisms of glutathione-related (*GSTT1*, *GSTM1*, *GSTP1*, *GSTM3*, *GGT1*, *GSS*, *GSR*, *GCLC*, *GCLM*) and selenoprotein (*SEPP1*, *GPX1*, *GPX4*) genes were investigated. The study found that dentists had significantly higher urine and hair mercury levels compared to non-dentists and that, fish consumption was the most significant predictor of hair mercury level. Linear regressions of mercury levels predicted by mercury exposure and polymorphisms found that: urine mercury levels were significantly predicted by double deletion of *GSTT1* compared to the intact gene, the T allele for *SEPP1* 3'UTR, while hair mercury levels differed by *GSTP1*-105 (rs1695) genotype. Sample members with the T allele of *SEPP1* 3'UTR accumulated less mercury in the hair from fish consumption, whereas those with the minor allele of *GSS* 5' allele accumulated more mercury in the hair from fish consumption compared to those without the allele. No other polymorphism showed significant results as either a main effect or as an interaction term for hair or urine mercury. The quality of this study's evidence is medium: standard techniques were used to assess mercury exposure, the sample size was adequate for many of the tests but underpowered for several polymorphisms due to low allele frequency, and regression analyses included adjustment for potential modifiers and confounders, but there was no adjustment for multiple statistical comparisons.

Methylmercury and elemental mercury differentially associate with blood pressure among dental professionals. Goodrich, JM, et al. (2012) (17)

The purpose of this study was to assess whether exposure to methylmercury increases cardiovascular risk in humans. A subset (n=284) of the convenience sample of dental professionals from the previous two studies (15, 16) was surveyed on their demographics, occupational practices (including number of amalgams handled per week in dental practice), medical history (including number of mercury-containing dental amalgams in their own mouths), and alcohol and fish consumption patterns. A direct mercury analyzer was used to assess mercury levels in sample members' urine and hair. A commercially available blood pressure device was used to repeatedly measure pulse, diastolic (DBP) and systolic blood pressure (SBP) for each participant; average readings were used. Hair and mercury levels were significantly higher among males. Urine mercury levels were associated with decreased SBP, although only statistically significantly for males, but not associated with DBP. Higher levels of mercury in hair were associated with increases in SBP and DBP, although the effect was larger among males and only statistically significant for males. The quality of this study is high: the sample size is adequate, there was

statistical adjustment for potential confounders, and standard, validated methods were used to measure mercury exposure, levels, and blood pressure.

Additional Areas of Interest

Hypersensitivity to Amalgam

Summary: Two studies in this area demonstrated a temporal association between amalgam exposure and negative health, however both study designs were of low quality. Evidence in this area is limited.

Metal-induced inflammation triggers fibromyalgia in metal-allergic patients. Stejskal V, et al. (2013) (18)

This study examined the frequency and type of metal allergy from personal exposure in 15 female patients diagnosed with fibromyalgia (FM) and in 10 healthy controls. Any metal exposure able to be removed was replaced with non-metal alternatives, for dental amalgams, gold restorations, and titanium dioxide coated medication. Patient inflammation was measured by a lymphocyte transformation test (MELISA) in vitro at baseline and after 5 years. Patient health was evaluated at baseline and over a span of 5-10 years by a rheumatologist and self-reported questionnaire. Authors found at least one metal allergy in all FM patients, in particular to nickel, inorganic mercury, gold, tin and palladium. Baseline measurements showed 58% lymphocyte reactivity to one or more metals, and after 5 years, only 10% of patients had a lymphocyte reaction to one or more of the metals. For the health assessment, 50% of patients no longer had FM, 20% had improved symptoms, 30% had no change, and all patients reported improved health. The authors conclude that reduction in metal exposures may reduce inflammation in patients with chronic inflammatory diseases. However, the quality of the study is low: the sample size was very small, there was no mention of how patients were selected or if the in vitro portion of the study was blind to case/control status, there was only one medical examiner, and there was no control group used to compare changes in FM status or subjective health that may occur over time.

Health-related quality of life and symptoms in patients with experiences of health problems related to dental restorative materials. Naimi-Akbar A, et al. (2013) (19)

This study evaluated the change in perceived health of Swedish individuals who applied for subsidized replacement of their dental amalgams because of perceived health impairment after initial placement. Researchers mailed a questionnaire measuring perceived health changes over time and health-related quality of life (HRQoL) since dental amalgam replacement to 515 people ; Of the 280 respondents (57%), 161 (93%) had had their amalgams replaced and 13 (5%) had not. After replacement of dental amalgams, more than half of the respondents indicated persistence of musculoskeletal pain, sleep disturbances, and experienced fatigue. Replacement of dental amalgams did not appear sufficient to resolve symptoms attributed to the presence of dental amalgams. The quality of this study as evidence is low: the outcomes are purely subjective and subject to recall bias due to the long recall period (13 years), the sample size is inadequate, there is indication of nonresponse bias, and there was no adjustment for multiple comparisons although more than 30 statistical tests were conducted.

Population Prevalence of Mercury

Dental amalgam and urinary mercury concentrations: a descriptive study. Nicolae A, et al. (2013) (20)

This study examined urinary mercury (Hg) concentrations stratifying by gender, age and number of dental amalgams in the Canadian population. The study used the 2007/2009 Canadian Health Measures Survey (CHMS), which is a nationally representative sample, of 5,418 Canadians aged 6-79 years. The overall mean urinary mercury concentration varied between 0.12 µg Hg/L and 0.31 µg Hg/L. Urinary mercury concentrations increased with the number of dental amalgam surfaces. However, many of these measurements were urged to be taken with caution because of high sample variability. The quality of this study is high: the sample size is adequate, the sample population is representative of the Canadian population rather than being restricted to just one occupational group or area, and exposure to mercury was assessed using a validated and standard method. As evidence of the relationship between dental amalgam and mercury biomarker levels the evidence is medium, since although there was control for age and gender there was no detailed information on amalgams and no control for body mass index (BMI), fish consumption, or other potential moderators or confounders.

Mercury and the Oral Mucosa

Oral lichenoid contact lesions to mercury and dental amalgam--a review. McParland H. and Warnakulasuriya S. (2012) (21)

This is a clinical review of the effects of amalgam and mercury from dental restorations on human oral mucosa. The authors conclude that evidence does not show that exposure to mercury from amalgam restorations poses a serious health risk in humans, except for a small number of hypersensitivity reactions.

Environmental Impact

The National Institute of Environmental Health Sciences (NIEHS) strategic plan for 2012-2017 (22) includes research in combined exposures as a top research priority. It recognizes the need to evaluate how chemicals interact with each other and how their combined effect may impact human health, especially in sensitive populations like children (23). For example, Yorifuji et al. 2011 (24), using the Faroe Island study, found that methylmercury in cord blood modified the effect of prenatal lead (Pb) on neurocognitive tests. Ongoing examination of the combined effect of exposure from dental amalgams and other environmental factors will continue to increase understanding of dental material safety profile.

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