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Literature Review

The Release of Mercury from Amalgam Restorations and Its Health Effects: A Review

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Clinical Relevance

Amalgam remains an important restorative material in dentistry. Because of continuing controversy concerning the material's safety and environmental friendliness, dentists should remain current in their knowledge of the effect of mercury and its release from amalgam. This will enable dentists to provide accurate, evidence-based information to their patients.

SUMMARY

Amalgam has successfully been used as a restorative material in dentistry for over a century. It has proven to be a cost-effective, wear-resistant material which, when properly placed, can provide many years of service. However, amalgam's popularity has decreased in recent years due, in part, to patient concerns about its potential for adversely affecting their health. Other reasons for its reduced use include the increased emphasis on more esthetic restorative materials and environmental concerns regarding the amount of mercury discharged into wastewater from dental offices. Controversy persists about amalgam's possible role in causing health problems due to its release of mercury. Although conclusive evidence is lacking that directly correlates amalgam with adverse health effects, clinicians should remain knowledgeable about mercury release from amalgam in order to intelligently address their patients' concerns. This article reviews the latest published scientific literature to provide this information.

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INTRODUCTION

Amalgam has been used in dentistry for more than 150 years,[1] and its excellent clinical track record is well known. Despite some shortcomings, amalgam has several positive characteristics compared with other restorative materials, including relatively low cost, good wear resistance, low technique sensitivity and high strength.[2-3] While amalgam's use has declined in recent years due to an increased emphasis on the use of esthetic restorative materials and concerns about potential environmental hazards related to its mercury (Hg) content, countless amalgam restorations remain in patients' mouths. Because of this fact and the plethora of misinformation about mercury in amal-

gam that is readily available on the Internet and in the lay press, it is important to periodically reassess the literature and the current state of knowledge about mercury release from dental amalgam and what, if any, hazards it presents to patients.

FORMS OF MERCURY

In order to better understand the issue of mercury in amalgam and its possible adverse effects, it is necessary to review the various forms of mercury. Three forms exist: inorganic, organic and elemental or metallic. Inorganic mercury exists in the form of salts of mercury, such as $HgCl_2$ and appears as a white powder or crystals.[4] Inorganic mercury can be highly toxic and cause renal failure and loss of the gastrointestinal tract lining. The most common form of an organic mercury compound is methylmercury, which forms when microscopic organisms convert inorganic mercury into methylmercury. Methylmercury is particularly damaging to embryos. It is water-soluble, accumulates in the food chain and, when ingested, is readily absorbed and slowly excreted.[5] Almost all human ingestion of methylmercury is from contaminated fish and wildlife. Because methylmercury accumulates in the food chain, periodic warnings have been issued about the possible dangers of consuming excessive amounts of certain fish.[6-9] Finally, elemental or metallic mercury is a silver/white liquid at room temperature and is used in such products as fluorescent bulbs, advertising signs, thermometers, barometers and, of course, dental amalgam. Mercury in its liquid form readily passes through the intestinal tract with little absorption[10-11] and has no known acute adverse physiologic effects.[12] Unfortunately, elemental mercury emits mercury vapor, which is readily absorbed into the blood through alveolar membranes and crosses the blood/brain barrier into the central nervous system.

MERCURY RELEASE FROM DENTAL AMALGAM RESTORATIONS

For many years, the consensus was that set amalgam did not release mercury. However, several studies in the late 1970s and early 1980s determined that this was not the case.[13-16]

A number of studies have attempted to quantify the amount of mercury vapor released from existing amalgam restorations.[16-19] The use of different methodologies in these studies, however, makes comparison of their results difficult, if not impossible. Interestingly, the studies found that patients without amalgam restorations had measurable amounts of intraoral mercury vapor, presumably from environmental exposure (see Table 1). A number of government and international agencies have established Recommended Exposure Limits or Threshold Limit Values for persons who are occupationally exposed to mercury vapor.[19-21] Determining whether the measured levels of intraoral mercury vapor exceed these limits is challenging, because different agencies have different threshold exposure limits. This is further complicated by the fact that governmental limits are usually presented as time-weighted-average values, and studies of intraoral mercury vapor levels generally do not present their results in these terms.

Studies quantifying intraoral mercury vapor levels due to amalgam restorations were followed by other investigations that attempted to determine a daily

Table 1: *Intraoral Mercury Vapor Levels*

Investigator	Chewing or Brushing	Patient Hg Vapor Levels		Units of Measure
		Amalgam Status		
		None	Present	
Svare and others (1981)[14]	Before	0.26	0.88	µg/m^3
	After	0.13	13.73	
Abraham and others (1984)[17]	Before	1.13	2.24	ng/15 sec
	After	1.06	18.97	
Ott and others (1984)[18]	Before	0.05	0.29	µg/m^3
	After	0.05	1.35	
Vimy and Lorscheider (1985)[16]	Before	0.54	4.91	µg/m^3
	After	0.72	29.1	
Patterson and others (1985)[15]	Before	0.06	3.81	ng/L
	After	not reported	8.2	

exposure amount (Table 2).[22-29] As with previous studies, these investigations used different collection methods, coupled with varying physiological assumptions that made comparison of the results difficult. Nonetheless, several of the studies concluded that daily human mercury exposure from amalgam is approximately 1 µg/day from inhalation of mercury vapor and 1 µg/day from the ingestion of ionic forms.[27,29-30] Despite these findings, it should be noted that even researchers who at times are critical of dentistry's use of amalgam, still conclude that no clear evidence exists to support the removal of existing amalgam restorations.[31]

Table 2: *Daily Mercury Vapor Exposure Relative to Number of Existing Amalgam Surfaces*

Author(s)	Amalgam Surfaces	Calculated Daily Hg Vapor (µg/day)
Vimy and Lorscheider[22]	>12	29
Snapp and others[23]	14	1.3
Lorscheider and Vimy[24]	12.6	10
Berglund[25]	12.6	1.7
Skare and Engqvist[26]	39	12
Clarkson and other[27]	NA*	1.2
Olsson and Bergman[28]	12.6	1.3
Halbach[29]	21	3.7

**NA=not applicable; is a review study.*

Because amalgam restorations do release mercury in measurable amounts, studies have been done to determine if having these restorations contributes to a patient's serum mercury levels. In 1999, Ahlqwist and others[32] reported the latest findings of a longstanding study of a cohort of 1,462 middle-aged and older Swedish women that began in 1968. Follow-up studies were conducted in 1974, 1975, 1980, 1981, 1992 and 1993. Serum mercury levels were positively correlated with the number of amalgam restorations present. Although the study also recorded different clusters of symptoms and the incidence of diabetes, myocardial infarction, stroke and cancer, no association was found between serum mercury levels and those diseases.

Berglund and Molin[33] performed a study to determine if removing amalgam restorations might significantly affect mercury levels in plasma and urine. Secondarily, they evaluated the effect of using a rubber dam or not using a rubber dam during the process. Operators removed all the amalgams from 18 patients with a rubber dam in place and from 10 patients without the use of a rubber dam. Measurement of the pre-removal and post-removal plasma and urine mercury levels indicated that only in the non-rubber dam group did the mercury levels increase significantly.

In 2005, a review of the scientific and medical literature concluded that evidence has consistently shown that mercury is released from dental amalgam restorations and is absorbed by the body.[34] The authors noted that many studies report positive correlations between the number of amalgam restorations (or surfaces) and urine mercury concentrations in non-occupationally-exposed individuals. The authors also reported, however, that these correlations do not prove that increased urine mercury concentrations cause adverse health effects. The review article, importantly, uncovered no convincing evidence indicating that adverse health effects are attributable to dental amalgam restorations, except for hypersensitivity reactions in susceptible individuals.

A study involving 73 schoolchildren (with a mean age of 12 years) attempted to determine if a correlation existed between the number and size of amalgam restorations and the prevalence of allergies or days absent from school due to illness. While the results indicated a positive correlation between the number and size of amalgam restorations and urine mercury levels, no significant correlations were found between the extent of amalgam restorations and diagnosed allergies or absence from school due to illness.[35]

MERCURY IN AMALGAM: EFFECTS ON SPECIFIC ORGANS AND SYSTEMS

A number of investigations have attempted to correlate the presence of amalgam restorations with diseases in certain organs and systems, specifically the kidneys, central nervous system and immune system.

Kidney Dysfunction

Several studies have investigated the effect of the presence of amalgam restorations on the levels of mercury in urine and other bodily fluids. A German study[36] measured 24-hour urinary mercury levels in 703 subjects with amalgam restorations. The mean urine Hg level was 0.75 µg/L and the mean level standardized for creatinine was 0.64 µg mercury/g of creatinine. The mean 24-hour mercury excretion rate was 0.48 micrograms in subjects younger than 18 years and 0.99 micrograms in subjects older than 18 years. The value standardized for creatinine reported in this study was lower than the minimum mean level (30 µg mercury/g of creatinine) reported by the World Health Organization to result in subtle effects in sensitive people.[37]

Another study investigated urinary mercury levels in German children age 3-15 years with and without amalgam restorations. The mean urinary mercury

concentration for the 93 children without amalgams was 0.17 µg/L, compared to 0.70 µg/L for the 86 children with amalgam restorations. A significant difference in urinary mercury levels was found between the two groups, as well as a positive correlation between the number of amalgam surfaces and urinary mercury levels.[38]

Dunn and others[39] randomly assigned 534 children age 6-10 years to either an amalgam or resin composite group and studied them over a five-year period during which they received amalgam or resin composite restorations. Among other things, the authors compared urinary mercury levels at various points with baseline values from the children when they had no amalgam restorations. They reported that the number of amalgam restorations had a significant dose-response relationship with urinary mercury levels. Interestingly, they also found that daily gum chewing in the presence of amalgam was associated with these elevated levels.

A study involving 1,100 military members suggested that the placement of 10 amalgam surfaces would result in a 1 µg/L increase in urinary mercury levels, which is equivalent to one part per billion.[40] To put this increase into perspective, the chronological equivalent of one part per billion is one second in 32 years.

A 1990 study involved the placement of amalgam restorations in eight physically healthy patients who did not have dental restorations.[41] A mean of 16 surfaces was restored with a calculated mean of 2.9 g of mercury inserted. Blood and urinary mercury levels were measured on seven occasions during a four-month period before and a three-month period after amalgam placement. Over the duration of the study, urinary mercury values increased continuously, with three-month values significantly higher than those seen prior to placement. However, no significant correlation was found between urinary mercury concentrations and the total number of amalgam surfaces. The results showed that the insertion of amalgam restorations contributed to urinary mercury concentrations. The effects of amalgam placement were negative during the three-month post-placement period, however, with regard to urinary selenium or erythrocyte glutathione peroxidase levels. Based on the results of this limited study, no kidney impairment and no difference in renal function was reported between patients with and without amalgam restorations.

Other studies have focused on the possibility that mercury exposure from amalgam restorations leads to impaired kidney function. Langworth and others[42] investigated a number of indicators of renal dysfunction (urinary excretion of albumin, orosomucoid, beta 2-microglobulin and N-acetyl-beta-glucosaminidase [NAG]; serum creatinine concentration and relative clearance of beta 2-microglobulin) in a group of 89 chloralkali workers exposed to mercury vapor and in 75 unexposed workers. Serum concentrations of immunoglobulins (IgA, IgG, IgM) and auto-antibodies towards glomeruli and other tissues were also measured, because their presence may indicate a humoral response induced by mercury. The values for the two groups were compared and evaluated based on different mercury vapor exposure conditions. Values for the mercury-exposed and the non-exposed groups can be seen in Table 3. None of the parameters of renal dysfunction differed significantly between the two groups, but there was a tendency toward increased excretion of NAG in the exposed group compared to the control. Also, a significant relationship existed between urinary mercury and urinary NAG. Both of these findings indicate slight tubular cell damage, probably as a result of mercury exposure. Serum immunoglobulin concentrations did not differ between the groups, and serum titers of auto-antibodies were low in both groups. Thus, the results gave no evidence of glomerular damage or of a tubular reabsorption defect. As mentioned, some of the findings indicated slight dose-related tubular cell damage in the mercury-exposed group; however, there were no overall signs of a mercury-induced effect on the immune system.

The association between the number of amalgam tooth surfaces, urinary mercury and proteinuria was investigated in a sample of 48 randomly selected, apparently healthy 17- to 22-year-old male students.[43] The presence of any of the following proteins in two separate urine samples was considered by the authors to be potentially indicative of a tubular and/or glomerular lesion: albumin; alpha-1-microglobulin (HC-protein); kappa and lambda light chains; and N-acetyl-beta-D-glucosaminidase. No significant relationship was found between any of the proteins and amalgam or urinary mercury. The results of this study did not suggest that amalgam restorations cause kidney dysfunction in humans.

In another study[44] of urinary mercury levels in indi-

Table 3: *Mercury Concentrations in Mercury-Exposed and Non-mercury-exposed Workers**

	Blood Mercury	Serum Mercury	Urine Mercury
Mercury-exposed (that is, chloralkali) workers	55 nmol/L	45 nmol/L	25.4 g/g of creatinine
Non mercury-exposed workers	15 nmol/L	4 nmol/L	1.9 g/g of creatinine

*Based on Langworth and others[42]

viduals with amalgam restorations, 100 healthy adults completed health questionnaires and voided urine samples. The urine mercury concentration and N-acetyl-beta-glucosaminidase (NAG) were then measured. The subjects were grouped into those having amalgam restorations (n=66) and those without (n=34) amalgam restorations. Data indicated that individuals with amalgam restorations were found to excrete slightly more mercury than people without them and demonstrated a very small increase in urinary NAG excretion. The amounts, however, were judged to be of no clinical significance and did not present a risk for renal damage.

A seven-year study involving 534 children ranging in age from 6 to 10 years without dental restorations and having two or more posterior teeth with caries was performed to assess their neuropsychological and renal functions.[45] The children were studied for five years during which their caries was treated with either amalgam (n=267) or resin composite (n=267) restorations. The neuropsychological outcomes measured were the five-year change in their full-scale intelligence (IQ) scores, tests of memory and tests of visuomotor ability. Renal glomerular function was evaluated by measuring creatinine-adjusted urinary albumin. The patients received a mean of 15 restored tooth surfaces. The results indicated that the amalgam group was associated with a significantly higher mean urinary mercury level at five years. No statistically significant differences were found in the changes in five-year full-scale IQ scores between children in the amalgam and resin composite groups. In addition, no statistically significant differences were found for the four-year change in general memory index, four-year change in visuomotor composite or five-year urinary albumin. The authors reported no significant differences in adverse neuropsychological or renal effects observed over the five-year period in children whose caries were restored using dental amalgam or composite materials. As a result of these findings, the authors concluded that the health effects of amalgam restorations in children need not be the basis for treatment decisions when choosing a dental restorative material.

Twenty-four patients were studied who had a history of long-term exposure to mercury vapor from mercury-containing amalgam restorations and exhibited adverse effects that were confirmed by a laboratory. Enzyme-linked immunosorbent assays (ELISAs) were used to evaluate the serum levels of antibodies to the antiglomerular basement membrane (anti-GBM-IgG). No evidence was found to indicate the presence of circulating anti-GBM antibodies in subjects suffering from adverse events of long-term exposure to dental amalgam. This finding was the same in individuals who presented with an allergy to mercury.[46]

The findings of these studies appear to indicate that the presence of amalgam restorations results in higher levels of urinary mercury. However, under the conditions of the these studies, no clinically significant signs of renal damage have been found as a result of tubular damage from the toxic effects of mercury or from mercury-induced immune system responses.

NEUROTOXICITY

The most well-known health hazard from mercury exposure is its adverse effect on neural tissue. The capability of mercury to readily cross the blood/brain barrier allows it access to the brain and central nervous system. Mercury's effects on neural tissue include demyelination, autonomic dysfunction, sensory nerve conduction delay, abnormal neuronal migration and abnormal central nervous system cell division. The resulting symptoms are many but include paresthesia, cerebellar ataxia, constriction of the visual fields and loss of hearing.[47]

One study of the effects of amalgam on mental health involves 587 subjects from an ongoing Swedish Adoption/Twin Study of Aging. This study employs controls for the genetic predisposition to the toxic effects of mercury when evaluating the role of amalgam restorations. The researchers analyze associations between the number of surfaces restored with dental amalgam and indices that estimate somatic health, mental health and memory functions. The most current results indicate no negative effects on physical or mental health due to the presence of dental amalgam.[48] Similarly, in a study of 129 Roman Catholic sisters age 75 years and older, no significant adverse effects from amalgam restorations were discovered using eight tests of cognitive function.[49] In a later study,[50] researchers measured Hg levels in multiple brain regions using trace element analysis and performed full neuropathologic examinations to assess the brain tissue status, including the presence/absence of Alzheimer's Disease (AD). No significant association of AD with the number, surface area or history of having dental amalgam restorations was found. Furthermore, no statistically significant differences were discovered in brain tissue Hg level between subjects with AD and control subjects.

A number of studies involving schoolchildren has been done in an attempt to determine whether the presence of amalgam restorations affects the schoolchildren's school performance and/or performance on psychological tests. A Greenland study involving 125 pupils age 12 to 17 years examined the relationship between the concentration of mercury in their hair and the pupils' scores in selected school subjects. The results indicated a weak but statistically insignificant relationship between the number of amalgam restorations and mercury concentration in hair samples. More

importantly, no correlation was found between hair mercury concentrations and poor results in school.[51] Three papers presented the results of a five-year study of 534 children ages 6 to 10 years, which attempted to determine if the presence of amalgam restorations had any effect on the primary or secondary outcomes of psychological tests administered to them.[52-54] The authors found no evidence that exposure to mercury from dental amalgam was associated with any adverse neuropsychological effects. Lastly, in a study of 507 children age 8 to 10 years who had at least one carious lesion on a permanent tooth and no previous exposure to amalgam, tests of memory, attention, visuomotor function or nerve conduction velocities were used to assess amalgam's effect.[55] One group of children (n=253) received amalgam restorations for posterior lesions and the other group (n=254) received non-mercury-containing resin composite restorations. During the seven-year study, the children in the amalgam group had a mean of 18.7 tooth surfaces restored and the children in the composite group had a mean of 21.3 tooth surfaces restored. There were no statistically significant differences in measures of the various neurobehavioral tests. The researchers concluded that the children who received amalgam restorations did not have statistically significant differences in neurobehavioral assessments compared with the children who received resin composite restorations.

Immune System

The possibility that amalgam restorations have an adverse effect on T-lymphocytes and, therefore, compromise the immune system, has been the subject of study for more than 20 years. The theory that dental amalgam negatively affects the number of T-lymphocytes was suggested by a pilot study in the 1980s.[56] A later study specifically investigated the potential for amalgam to reduce immunocompetence by measuring levels of the three major groups and six subgroups of T-lymphocytes in 37 subjects: 21 with amalgam restorations and 16 without. The authors found no evidence that amalgam restorations either affected lymphocytes or reduced immunocompetence.[57]

A 1992 paper[58] reported the results of a study involving 10 patients who claimed that their symptoms were caused and aggravated by amalgam placement. In this evaluation, one amalgam restoration was removed from each patient and replaced with a resin composite restoration. Clinical symptoms were recorded and laboratory tests were then performed. It was determined that six of the 10 patients were positive for contact allergies to metals, three of them to mercury ammonium chloride. A comparison of pre- and post-treatment laboratory tests showed significant reductions in plasma IgE and urinary albumin and significant increases in plasma C3d and urinary beta 2-microglobulin. However, there was no laboratory evidence of a direct toxic effect on the patients caused by mercury. Because of these findings, the authors concluded that a low, but acute dose of mercury from an amalgam restoration may activate the immune system. Although these results are noteworthy, no comparison with a control group was included in the study.

A 1994 study[59] of 41 healthy 15-year-old schoolchildren investigated a number of cellular and hormonal immune factors to determine whether a relationship existed between the factors, amalgam restorations and plasma mercury concentration (P-Hg). A low, but significant correlation ($r=0.40$, $p<0.05$) was found between the number of amalgam surfaces and the P-Hg values; however, no significant relationship was discovered between either the number of amalgam surfaces or P-Hg and the tested immune factors.

Cederbrant and others[60] studied the hypothesis that a susceptible immune system explains why some individuals with amalgam restorations present with psychologic, sensory or neurologic symptoms due to mercury exposure. Because the proliferation of lymphocytes had been used for a number of years as an indicator of hypersensitivity to metals and drugs,[61-62] Cederbrant and others used an *in vitro* lymphocyte proliferation assay to test for immune sensitivity to inorganic mercury. One objective was to determine if there was a difference between patients with amalgam restorations who claimed symptoms of amalgam-related disease versus those with amalgams who did not. The test subjects were 23 patients with amalgams who claimed amalgam-related disease symptoms, 30 healthy individuals with amalgam, 10 healthy subjects without amalgam and nine patients with oral lichen planus adjacent to amalgam. In addition to the lymphocyte proliferation assay, a wide range of immune parameters was also measured. No significant differences were found between the amalgam patients and the controls with regard to the parameters investigated, despite the fact that the *in vitro* assay was sensitive to the oral lichen planus control group.

AMALGAM ILLNESS

"Amalgam illness" is the term given to a condition, usually self-reported, that is attributed by patients to mercury vapor intake from their existing amalgam restorations. Symptoms are usually quite distinct from those observed as a result of classic Hg toxicity and can include fatigue, difficulty concentrating, muscular pain and immunologic disorders.[63] One source lists as many as 400 symptoms allegedly associated with amalgam illness.[64] Understandably, there is a great deal of confusion and debate regarding the actual existence of amalgam illness. Much of this is due to the lack of agreed-upon diagnostic criteria for the condition as well as the absence of an approved biologic test for its detection. Also complicating the clinical situation is the

fact that a number of psychiatric disorders exhibit symptoms similar to those purportedly due to amalgam restorations.[63] The role that psychological conditions play may be significant, as two studies found that 70% of patients claiming to have amalgam illness presented with a psychiatric diagnosis, compared with only 14% in a control group.[65-66]

The results from a number of studies suggest that psychological illness and not mercury from amalgam restorations is an important element in amalgam illness.[67-71] One study involved 218 patients with self-reported oral galvanism; no findings suggestive of either acute or chronic mercury intoxication were found.[72] Of these patients, 43% were diagnosed with a psychological disorder, often anxiety or panic disorders. Interestingly, the patients with an underlying psychological disorder demonstrated lower blood Hg levels than those without.

Another study evaluated 20 patients who demonstrated amalgam illness symptoms using the Defense Mechanism Test (DMT), which involves approximately 130 anxiety-provoking stimuli.[68] The results were compared to those of 37 controls. The authors reported that the amalgam illness group exhibited more inappropriate reactions to threats and used denial as a primary coping mechanism. They suggested that the test was a valuable tool in differentiating between people with amalgam disease and those without it, and that the DMT could be used to investigate the mechanisms behind amalgam illness.

In another study of amalgam illness, 67 patients with reported amalgam illness were evaluated and compared to 64 matched controls.[69] All the patients had medical and dental exams and had a psychological evaluation using a semi-structured interview. The medical examinations were unable to explain the patients' reported symptoms. The study did find, however, that more of the symptomatic patients exhibited alexithymic traits than the non-symptomatic controls. Alexithymic individuals are unable to talk about feelings due to a lack of emotional awareness. They typically show an inability to identify, understand or describe their own emotions. These individuals are at risk for other medical and psychiatric disorders and are less responsive to conventional treatments than individuals without the trait.[67] The researchers also found that 89% of the amalgam illness patients met criteria for psychiatric disorders as contrasted by 6% of the control group. A second study of the same individuals found that 55% of the amalgam illness patients and 73% of the controls showed no sign of somatic disease.[70] This was despite the fact that half of the patients reported feeling ill or very ill at the time of the examination, and they reported twice as many symptoms as the controls during a three-month period. These findings led the researchers to conclude that the patients' sense of ill health was more likely the result of psychiatric than somatic conditions.

Finally, a study investigated 10 patients with symptoms they believed were caused by their amalgam restorations and compared them to a control group of eight individuals without symptoms.[72] The intra-oral release of mercury vapor was measured following a standardized schedule, and mercury levels in plasma, erythrocytes and urine were determined. The calculated daily uptake of inhaled mercury vapor released from the amalgam restorations was found to be less than 5% of the daily uptake at the lower concentration range that the World Health Organization[37] states has been found to cause subtle symptoms in particularly sensitive individuals. Compared to the healthy group, the symptomatic group had neither a higher estimated daily uptake of inhaled mercury vapor nor a higher mercury concentration in blood and urine. The researchers concluded that the study provided no scientific support for the belief that the patients' symptoms were the result of mercury release from their amalgam restorations.

When evaluating patients who present with symptoms or claims of amalgam illness, dentists should be aware of the role that psychological conditions may play in the illness. Epidemiological studies indicate that dental amalgam is safe for the general population; however, one must always keep in mind that epidemiological studies are assumed to represent the general population and may not pertain to each and every individual. Overall patient health must remain the chief concern of every dentist; therefore, referrals should be made to appropriate health care providers when necessary to ensure that no underlying undiagnosed medical condition exists.

CONCLUSIONS

This review is not all-inclusive and presents only a small portion of the vast published literature on the subject of the health effects of mercury in amalgam restorations. It appears clear, however, that, despite a plethora of well-designed studies, no definitive evidence exists showing that amalgam is a hazard to patients. Despite this fact and amalgam's long history of reliable, cost-effective use in dentistry, debate continues regarding the wisdom of using it as a restorative material. Given these concerns and the pressures being brought to bear on the dental profession to reduce the discharge of mercury into the environment, amalgam faces an uncertain future. Continuing to educate the public with the true facts about amalgam and its use remains the profession's best defense against the elimination of amalgam as a viable treatment option.

Disclaimer

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or positions of the Department of the Navy, Department of the Air Force, Department of Defense or the US Government.

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References

1. Osborne JW (1992) Dental amalgam and mercury vapor release *Advances in Dental Research* **6(1)** 135-138.
2. Anusavice KJ (2003) *Phillips' Science of Dental Materials 11th Edition* WB Saunders, Philadelphia.
3. O'Brien WJ (2002) *Dental Materials and Their Selection 3rd Edition* Quintessence Publishing, Chicago.
4. US Environmental Protection Agency (2008) Frequent questions page; Retrieved online July 30, 2008 from: http://publicaccess.custhelp.com/cgi-bin/publicaccess.cfg/php/enduser/std_adp.php?p_faqid=1821.
5. US Geologic Survey (2000) Mercury in the environment, fact sheet 146-00; Retrieved online July 30, 2008 from: http://www.usgs.gov/themes/factsheet/146-00/.
6. Schober SE, Sinks TH, Jones RL, Bolger PM, McDowell M, Osterloh J, Garrett ES, Canady RA, Dillon CF, Sun Y, Joseph CB & Mahaffey KR (2003) Blood mercury levels in US children and women of childbearing age, 1999-2000 *Journal of the American Medical Association* **289(13)** 1667-1674.
7. Evans EC (2002) The FDA recommendations on fish intake during pregnancy *Journal of Obstetric, Gynecologic, and Neonatal Nursing* **31(6)** 715-720.
8. [No authors listed] (1992) Mercury toxicity. Agency for toxic substance and disease registry *American Family Physician* **46(6)** 1731-1741.
9. US Department of Health and Human Services and U.S. Environmental Protection Agency (2004) What you need to know about mercury in fish and shellfish. 2004 EPA and FDA advice for women who might become pregnant, women who are pregnant, nursing, young children; Retrieved online August 6, 2008 from: http://www.cfsan.fda.gov/~dms/admehg3.html.
10. Sandborgh-Englund G, Einarsson C, Sandström M & Ekstrand J (2004) Gastrointestinal absorption of metallic mercury *Archives of Environmental Health* **59(9)** 449-454.
11. Williams DF (1981) *Systemic Aspects of Biocompatibility, Vol 1* CRC Press, Boca Raton.
12. Clarkson TW & Magos L (2006) The toxicology of mercury and its chemical compounds *Critical Reviews in Toxicology* **36(8)** 609-662.
13. Gay DD, Cox RD & Reinhardt JW (1979) Chewing releases mercury from fillings *Lancet* **1(8123)** 985-986.
14. Svare CW, Peterson LC, Reinhardt JW, Boyer DB, Frank CW, Gay DD & Cox RD (1981) The effect of dental amalgams on mercury levels in expired air *Journal of Dental Research* **60(9)** 1668-1671.
15. Patterson JE, Weissberg BG & Dennison PJ (1985) Mercury in human breath from dental amalgams *Bulletin of Environmental Contamination and Toxicology* **34(4)** 459-468.
16. Vimy MJ & Lorscheider FL (1985) Intra-oral air mercury released from dental amalgam *Journal of Dental Research* **64(8)** 1069-1071.
17. Abraham JE, Svare CW & Frank CW (1984) The effect of dental amalgam restorations on blood mercury levels *Journal of Dental Research* **63(1)** 71-73.
18. Ott KH, Loh F, Kröncke A, Schaller KH, Valentin H & Weltle D (1984) [Mercury burden due to amalgam fillings] *Deutsche Zahnarztliche Zeitschrift* **39(3)** 199-205.
19. Occupational Safety and Health Standards. Code of Federal Regulations, 29 CFR§1910.z38;2000.
20. National Institute of Occupational Safety and Health (2000) *NIOSH Pocket Guide to Chemical Hazards* JJ Keller and Associates, Neenah, WI.
21. American Conference of Governmental Industrial Hygienists (1996) *Documentation of Threshold Limit Values (TLVs) and Biological Exposure Indices ACGIH*, Cincinnati, OH.
22. Vimy MJ & Lorscheider FL (1985) Serial measurements of intra-oral air mercury: Estimation of daily dose from dental amalgam *Journal of Dental Research* **64(8)** 1072-1075.
23. Snapp KR, Boyer DB, Peterson LC & Svare CW (1989) The contribution of dental amalgam to mercury in blood *Journal of Dental Research* **68(5)** 780-785.
24. Lorscheider FL & Vimy MJ (1990) Mercury from dental amalgam *Lancet* **336(8730)** 1578-1579.
25. Berglund A (1990) Estimation by a 24-hour study of the daily dose of intra-oral mercury vapor inhaled after release from dental amalgam *Journal of Dental Research* **69(10)** 1646-1651.
26. Skare I & Engqvist A (1994) Human exposure to mercury and silver released from dental amalgam restorations *Archives of Environmental Health* **49(5)** 384-394.
27. Clarkson TW, Hursh JB, Sager PR & Syversen TLM (1988) Mercury In: Clarkson TW, Hursh JB, Sager PR, Syversen TLM *Biological Monitoring of Toxic Metals* Plenum Press, New York 199-246.
28. Olsson S & Bergman M (1992) Daily dose calculations from measurements of intra-oral mercury vapor *Journal of Dental Research* **71(2)** 414-423.
29. Halbach S (1995) Combined estimation of mercury species released from amalgam *Journal of Dental Research* **74(4)** 1103-1109.
30. Mackert JR Jr (1987) Factors affecting estimation of dental amalgam mercury exposure from measurements of mercury vapor levels in intra-oral and expired air *Journal of Dental Research* **66(12)** 1775-1780.
31. Clarkson TW, Magos L & Myers GJ (2003) The toxicology of mercury—current exposures and clinical manifestations *New England Journal of Medicine* **349(18)** 1731-1737.
32. Ahlqwist M, Bengtsson C, Lapidus L, Gergdahl IA & Schütz A (1999) Serum mercury concentration in relation to survival, symptoms, and diseases: Results from the prospective population study of women in Gothenburg, Sweden *Acta Odontologica Scandinavica* **57(3)** 168–174.
33. Berglund A & Molin M (1997) Mercury levels in plasma and urine after removal of all amalgam restorations: The effect of using rubber dams *Dental Materials* **13(5)** 297-304.

34. Brownawell AM, Berent S, Brent RL, Bruckner JV, Doull J, Gershwin EM, Hood RD, Matanoski GM, Rubin R, Weiss B & Karol MH (2005) The potential adverse health effects of dental amalgam *Toxicological Reviews* **24(1)** 1-10.
35. Olstad ML, Holland RI, Wandel N & Pettersen AH (1987) Correlation between amalgam restorations and mercury concentrations in urine *Journal of Dental Research* **66(6)** 1179-1182.
36. Zander D, Ewers U, Freier I, Jermann E, Westerweller S & Brockhaus A (1990) Exposure to mercury in the population I. Mercury concentrations in the urine of normal subjects *Zentralblatt fur Hygiene und Umweltmedizin* **190(4)** 315-324.
37. World Health Organization (1991) Environmental Health Criteria 118 Inorganic Mercury World Health Organization, Geneva.
38. Schulte A, Stoll R, Wittich M, Pieper K & Stachniss V (1994) Mercury concentrations in the urine of children with and without amalgam fillings *Schweizer Monatsschrift fur Zahnmedizin* **104(11)** 1336-1340.
39. Dunn JE, Trachtenberg FL, Barregard L, Bellinger D & McKinlay S (2008) Scalp hair and urine mercury content of children in the Northeast United States *The New England Children's Amalgam Trial Environmental Research* **107(1)** 79-88.
40. Kingman A, Albertini T & Brown LJ (1998) Mercury concentrations in urine and whole blood associated with amalgam exposure in a US military population *Journal of Dental Research* **77(3)** 461-471.
41. Molin M, Bergman B, Marklund SL, Schutz A & Skerfving S (1990) The influence of dental amalgam placement on mercury, selenium, and glutathione peroxidase in man *Acta Odontologica Scandinavica* **48(4)** 287-295.
42. Langworth S, Elinder CG, Sundquist KG & Vesterberg O (1992) Renal and immunological effects of occupational exposure to inorganic mercury *British Journal of Industrial Medicine* **49(6)** 394-401.
43. Herrström P, Schütz A, Raihle G, Holthuis N, Högstedt B & Råstam L (1995) Dental amalgam, low-dose exposure to mercury, and urinary proteins in young Swedish men *Archives of Environmental Health* **50(2)** 103-107.
44. Eti S, Weisman R, Hoffman R & Reidenberg MM (1995) Slight renal effect of mercury from amalgam fillings *Pharmacology & Toxicology* **76(1)** 47-49.
45. Bellinger DC, Trachtenberg F, Barregard L, Tavares M, Cernichiari E, Daniel D & McKinlay S (2006) Neuropsychological and renal effects of dental amalgam in children: A randomized clinical trial *Journal of the American Medical Association* **295(15)** 1775-1783.
46. Guzzi G, Fogazzi GB, Cantù M, Minoia C, Ronchi A, Pigatto PD & Severi G (2008) Dental amalgam, mercury toxicity, and renal autoimmunity *Journal of Environmental Pathology, Toxicology And Oncology* **27(2)** 147-155.
47. Clarkson TW (2002) The three modern faces of mercury *Environmental Health Perspectives* **110(Supplement 1)** 11-23.
48. Björkman L, Pedersen NL & Lichtenstein P (1996) Physical and mental health related to dental amalgam fillings in Swedish twins *Community Dentistry and Oral Epidemiology* **24(4)** 260–267.
49. Saxe SR, Snowdon DA, Wekstein MW, Henry RG, Grant FT, Donegan SJ & Wekstein DR (1995) Dental amalgam and cognitive function in older women: Findings from the nun study *Journal of the American Dental Association* **126(11)** 1495-1501.
50. Saxe SR, Wekstein MW, Kryscio RJ, Henry RG, Cornett CR, Snowdon DA, Grant FT, Schmitt FA, Donegan SJ, Wekstein DR, Ehmann WD & Markesbery WR (1999) Alzheimer's disease, dental amalgam and mercury *Journal of the American Dental Association* **130(2)** 191-199.
51. Tulinius AV (1995) Mercury, dental amalgam fillings and intellectual abilities in Inuit school children in Greenland *Arctic Medical Research* **54(2)** 78-81.
52. Bellinger DC, Trachtenberg F, Daniel D, Zhang A, Tavares MA & McKinlay S (2007) A dose-effect analysis of children's exposure to dental amalgam and neuropsychological function: The New England Children's Amalgam Trial *Journal of the American Dental Association* **138(9)** 1210-1216.
53. Bellinger DC, Daniel D, Trachtenberg F, Tavares M & McKinlay S (2007) Dental amalgam restorations and children's neuropsychological function *The New England Children's Amalgam Trial Environmental Health Perspectives* **115(3)** 440-446.
54. Bellinger DC, Trachtenberg F, Zhang A, Tavares M, Daniel D & McKinlay S (2008) Dental amalgam and psychosocial status: The New England Children's Amalgam Trial *Journal of Dental Research* **87(5)** 470-474.
55. DeRouen TA, Martin MD, Leroux BG, Townes BD, Woods JS, Leitão J, Castro-Caldas A, Luis H, Bernardo M, Rosenbaum G & Martins IP (2006) Neurobehavioral effects of dental amalgam in children: A randomized clinical trial *Journal of the American Medical Association* **295(15)** 1784-1792.
56. Eggleston DW & Nylander M (1987) Correlation of dental amalgam with mercury in brain tissue *Journal of Prosthetic Dentistry* **58(6)** 704-707.
57. Mackert JR Jr, Leffell MS, Wagner DA & Powell BJ (1991) Lymphocyte levels in subjects with and without amalgam restorations *Journal of the American Dental Association* **122(3)** 49-53.
58. Anneroth G, Ericson T, Johansson I, Mörnstad H, Ryberg M, Skoglund A & Stegmayr B (1992) Comprehensive medical examination of a group of patients with alleged adverse effects from dental amalgams *Acta Odontologica Scandinavica* **50(2)** 101-111.
59. Herrström P, Holmén A, Karlsson A, Raihle G, Schütz A & Högstedt B (1994) Immune factors, dental amalgam, and low-dose exposure to mercury in Swedish adolescents *Archives of Environmental Health* **49(3)** 160-164.
60. Cederbrant K, Gunnarsson LG, Hultman P, Norda R & Tibbling-Grahn L (1999) *In vitro* lymphoproliferative assays with $HgCl_2$ cannot identify patients with systemic symptoms attributed to dental amalgam *Journal of Dental Research* **78(8)** 1450–1458.
61. Nyfeler B & Pichler WJ (1997) The lymphocyte transformation test for the diagnosis of drug allergy: Sensitivity and specificity *Clinical and Experimental Allergy* **27(2)** 175-181.

62. von Blomberg-van der Flier BM, Bruynzeel DP & Scheper RJ (1989) Impact of 25 years of *in vitro* testing in allergic contact dermatitis In: Frosch PJ, Dooms-Goossens A, Lachapelle J-M, Rycroft RJG, Scheper RJ (eds) *Current Topics in Dermatitis* Springer-Verlag, Heidelberg 569-577.

63. Malt UF, Nerdrum P, Oppedal B, Gundersen R, Holte M & Löne J (1997) Physical and mental problems attributed to dental amalgam fillings: A descriptive study of 99 self-referred patients compared with 272 controls *Psychosomatic Medicine* **59(1)** 32-41.

64. Foundation for Toxic Free Dentistry (1992) *System Analysis of Patient Adverse Reaction Reports* submitted to the US Food and Drug Administration.

65. Bratel J, Haraldson T, Meding B, Yontchev E, Ohman SC & Ottosson JO (1997) Potential side effects of dental amalgam restorations (I) An oral and medical investigation *European Journal of Oral Sciences* **105(3)** 234-243.

66. Bratel J, Haraldson T & Ottosson JO (1997) Potential side effects of dental amalgam restorations. (II). No relation between mercury levels in the body and mental disorders *European Journal of Oral Sciences* **105(3)** 244-250.

67. Taylor GJ, Bagby RM & Parker JDA (1997) *Disorders of Affect Regulation: Alexithymia in Medical and Psychiatric Illness* Cambridge University Press, Cambridge, UK.

68. Henningsson M & Sundbom E (1996) Defensive characteristics in individuals with amalgam illness as measured by the percept-genetic method Defense Mechanism Test *Acta Odontologica Scandinavica* **54(3)** 176-181.

69. Bågedahl-Strindlund M, Ilie M, Furhoff AK, Tomson Y, Larsson KS, Sandborgh-Englund G, Torstenson B & Wretlind K (1997) A multidisciplinary clinical study of patients suffering from illness associated with mercury release from dental restorations: Psychiatric aspects *Acta Psychiatrica Scandinavica* **96(6)** 475-482.

70. Furhoff AK, Tomson Y, Ilie M, Bågedahl-Strindlund M, Larsson KS, Sandborgh-Englund G, Torstenson B & Wretlind K (1998) A multidisciplinary clinical study of patients suffering from illness associated with release of mercury from dental restorations Medical and odontological aspects *Scandinavian Journal of Primary Health Care* **16(4)** 247-252.

71. Berglund A & Molin M (1996) Mercury vapor release from dental amalgam in patients with symptoms allegedly caused by amalgam fillings *European Journal of Oral Sciences* **104(1)** 56-63.

72. Herrström P & Högstedt B (1993) Clinical study of oral galvanism: No evidence of toxic mercury exposure but anxiety disorder an important background factor *Scandinavian Journal of Dental Research* **101(4)** 232-237.