

## Mercury Derived from Dental Amalgams and Neuropsychologic Function

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There is widespread concern regarding the safety of silver–mercury amalgam dental restorations, yet little evidence to support their harm or safety. We examined whether mercury dental amalgams are adversely associated with cognitive functioning in a cross-sectional sample of healthy working adults. We studied 550 adults, 30–49 years of age, who were not occupationally exposed to mercury. Participants were representative of employees at a major urban medical center. Each participant underwent a neuropsychologic test battery, a structured questionnaire, a modified dental examination, and collection of blood and urine samples. Mercury exposure was assessed using *a*) urinary mercury concentration (UHG); *b*) the total number of amalgam surfaces; and *c*) the number of occlusal amalgam surfaces. Linear regression analysis was used to estimate associations between each marker of mercury exposure and each neuropsychologic test, adjusting for potential confounding variables. Exposure levels were relatively low. The mean UHG was 1.7 µg/g creatinine (range, 0.09–17.8); the mean total number of amalgam surfaces was 10.6 (range, 0–46) and the mean number of occlusal amalgam surfaces was 6.1 (range, 0–19). No measure of exposure was significantly associated with the scores on any neuropsychologic test in analyses that adjusted for the sampling design and other covariates. In a sample of healthy working adults, mercury exposure derived from dental amalgam restorations was not associated with any detectable deficits in cognitive or fine motor functioning. **Key words:** attention, cognition, dental amalgams, memory, mercury exposure, neuropsychologic function. *Environ Health Perspect* 111:719–723 (2003). doi:10.1289/ehp.5879 available via <http://dx.doi.org/> [Online 13 November 2002]

Despite widespread concern about the safety of silver–mercury amalgam dental restorations (Skare and Engqvist 1994), there is little evidence regarding harm or safety in the general population. Dental amalgams have been used for over 150 years with no overt adverse effects. Nevertheless, a 1991 American Dental Association survey of 1,000 adults found that 50% thought amalgam restorations might have adverse effects (Gerbert et al. 1992). A similar survey of dentists found that although 89% of respondents believed that amalgams posed no risk, 52% reported that they would replace such restorations at a patient's request (Gerbert et al. 1992). Reviews in both the scientific and lay literature link amalgam restorations to severe psychiatric, neurologic, and immunologic effects (Anonymous 1991; Fung and Molvar 1992; Hanson and Pleva 1991; Weiner et al. 1990).

Severe chronic occupational exposure to elemental mercury (Hg<sup>0</sup>) vapor has been associated with a constellation of neuropsychologic symptoms, the “Mad Hatter Syndrome.” Amalgam restorations are approximately 50% inorganic mercury (Hg<sup>0</sup>), and systemic absorption of Hg<sup>0</sup> vapor from amalgams is well demonstrated (Berlin 1969; Berlin et al. 1975; Hurch et al 1980; Newton and Fry 1978; Takahata et al. 1970; Wantanbe 1969). Occupational exposure in dentists is associated with intentional tremor of muscles responsible

for fine motor tasks, personality changes, behavioral changes, memory loss, increased excitability, and severe depression (Echeverria et al. 1995; Ngim et al. 1992). No data are available to assess possible neurotoxic effects related to levels of amalgam-derived exposure found in the general population.

The present report draws on a cross-sectional sample of working adults, 30–49 years of age, that was designed to examine whether amalgam-derived mercury exposure is associated with cognitive functioning, including memory, attention and executive function, and visuomotor and visuospatial coordination. Exposure was assessed using the total number of visible amalgam surfaces and the number of visible occlusal amalgam surfaces, and by urinary mercury concentration (UHG).

### Materials and Methods

The Columbia-Presbyterian Institutional Review Board approved the protocol and informed consent documents for this study. Between September 1997 and December 1999, we invited a random sample of 1,966 employees at a university health center to participate in a study titled “Dental Health and General Well-Being.” We used a stratified random sampling of the personnel roster to select a sample with equal numbers in four strata defined by age (30–39 or 40–49 years) and employment status (professional or support

staff). Older employees were not studied because, on average, the total number of amalgam surfaces declines after 50 years of age because of the loss of teeth (National Institute of Dental Research 1987). After excluding 229 noneligible persons, 550 (32%) agreed to participate in a 90-min evaluation that included collection of urine and blood samples, a questionnaire, and a neuropsychologic battery. We excluded personnel no longer employed at the medical center, dental personnel, non-English speakers, and pregnant women.

**Participants.** Compared with nonparticipants, participants were less likely to be professional staff and less likely to be male (Table 1). One hundred nonparticipants agreed to complete a brief telephone interview to obtain basic demographic data (not the full questionnaire). They were similar to participants with regard to Hispanic origin and educational attainment, but were slightly more likely to be white and less likely to be Asian.

**Data collection.** Informed consent was obtained by one of four trained interviewers. Spot urine samples were obtained for the measurement of UHG and creatinine. A specially trained dentist performed a modified oral examination. An interview obtained information on demographic and social characteristics, occupational exposures, lifestyle behaviors (smoking, alcohol consumption, caffeine consumption, and gum-chewing behavior), bruxism, and health history. Each subject completed a neuropsychologic battery in the clinical research unit. The neuropsychologic tests were administered in a fixed order.

**Laboratory assays.** UHG was determined by flow-injection cold vapor atomic absorption spectrometry (Guo and Baasner 1993) by one technician. The laboratory participated in the quality control program for UHG

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run by Jean Philippe Weber of the Centre de Toxicologie du Quebec. Over the full range (i.e., 5–1,000 nmol/L) of standards analyzed, agreement was excellent [intraclass correlation coefficient (ICC) = 0.99]. Agreement was also excellent (ICC = 0.99) when data were reanalyzed over the low end of concentration (5–200 nmol/L). All UHGs were adjusted for urinary creatinine and measured using quantitative colorimetric determinations (Sigma Diagnostics Creatinine Kit; Sigma-Aldrich, St. Louis, MO), a modification of the Jaffe reaction (Heinegård and Tiderström 1973; Jaffe 1886).

**Modified dental examination.** Four specially trained dentists performed structured modified oral examinations to assess the number of teeth present and the number and location of all restorations. All examinations required only tongue depressors; teeth were not probed physically. Prior to the study, interobserver reliability was assessed in 49 clinic patients by having each examiner compared with an expert dentist. Overall agreement for amalgam counts, both total and occlusal, was excellent (ICCs from 0.93 to 0.99).

**Neuropsychologic battery.** Participants were evaluated on a neuropsychologic battery comprising widely used and well-standardized tests. Specific cognitive domains assessed and measures administered were based upon reports of neuropsychologic impairments in occupational studies (Albers et al. 1988; Echeverria et al. 1995; Langolf et al. 1978; Ngim et al. 1992; Ritchie et al. 1995; Roels et al. 1982; Smith et al. 1970, 1983). Specifically, verbal memory, nonverbal memory, attention, and fine motor coordination were assessed. We used the Selective Reminding Test (SRT)-total recall measure (Buschke and Fudd 1974), in which subjects have six trials to learn a 12-word list, to assess verbal memory. To assess nonverbal memory, we used the Benton Visual Retention Test-immediate recall condition (BVRT) (Benton 1974), in which subjects are given a 10-sec exposure to each of 10 designs, with immediate recall by drawing.

The Trail-Making Test (Reitan 1958) and the digit symbol subtest of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) (Wechsler 1981) assessed attention and psychomotor speed. The Trail-Making Test is given in two parts, and time to complete each task is measured. In part A, the participant is presented with a page of randomly organized numbers and is asked to draw a line connecting them in consecutive order. In part B, the participant is presented with a page containing both numbers and letters and is asked to connect them in order, but alternating between numbers and letters (i.e., 1-A, 2-B, etc.). The digit symbol subtest of the WAIS-R is considered a nonspecific yet sensitive indicator of subtle brain dysfunction. For

successful performance, participants must efficiently integrate attentional, executive, perceptual, and motor skills. The test consists of rows of blank squares, each paired with a random digit from 1 to 9. Above these rows is a printed key pairing each digit to a nonsense symbol. The participant fills in as many as possible blank spaces according to the key in 90 sec. The raw score represents the number of squares filled in correctly in the allotted time. We used age-corrected scores, with a mean of 10 and a standard deviation of 3, in analyses.

We used the Grooved Pegboard (Klove 1963; Matthews and Klove 1964) to assess fine motor coordination. This task was administered once with the dominant hand and once with the nondominant hand. The test is scored as time to completion of the placement of grooved pegs into a 25-hole board.

Four trained testers, blinded to the results of the UHG assay, administered all neuropsychologic assessments. A random sample of test sessions was observed by an expert neuropsychologist to ensure reliability of test administration. To ensure scoring accuracy, two examiners scored all batteries; the correlation measuring agreement was 99%.

**Statistical analysis.** Associations between each exposure measure (UHg, total number of amalgam restorations, number of occlusal amalgam restorations) and each neuropsychologic test were estimated using linear regression analysis. Analyses were adjusted for known predictors of neuropsychologic performance and

demographic characteristics associated with the exposure variables. All analyses were adjusted for sampling stratum as a four-category indicator variable (support staff 30–39 years of age, support staff 40–49 years of age, professional staff 30–39 years of age, and professional staff 40–49 years of age). Depending on the outcome, we controlled for age, sex, race/ethnicity, first language (English/other), U.S. born (yes/no), job description, and educational level (high school graduate, some college, college graduate, master's degree, doctoral degree) in the regression model.

We conducted confirmatory analyses that used number of total or occlusal amalgam restorations excluding restorations that were sized as “pinprick.” Analyses were repeated excluding the 43 subjects with more than four missing teeth not attributable to either orthodontic reasons or to removal of third molars. We also assumed that these teeth had a range of amalgam restorations. Results were essentially identical to the main analyses and are not presented.

## Results

**Mercury exposure.** Results for the characteristics of mercury exposure are shown in Table 2. The mean UHG was 1.7 µg/g creatinine and ranged between 0.09 and 17.8 µg/g creatinine. Fewer than 5% of participants had UHG > 5 µg/g creatinine. Mean UHG and mean numbers of total and occlusal amalgams varied by sampling strata, with older officers and support

**Table 1.** Characteristics of study participants and nonparticipants.

	Participants	Nonparticipants	
		Without telephone interviews <sup>a</sup>	Responded to the telephone interview
No. of subjects	550	1,087	100
Professional staff (%)	53	70	57
Male (%)	38	47	45
Mean age ± SD	38.8 ± 5.8	39.7 ± 5.8	39.4 ± 6.4
White (%)	40	— <sup>b</sup>	47
African American (%)	13	—	12
Asian (%)	21	—	9
Other/unknown (%)	26	—	32
Hispanic origin <sup>c</sup> (%)	21	—	22
Less than 4-year college degree (%)	26	—	24
4-year college degree (%)	12	—	22
Master's degree (%)	23	—	13
Doctoral degree (%)	39	—	38

<sup>a</sup>Nonparticipants were asked to answer a brief 5-min telephone questionnaire, which obtained data only on basic demographic characteristics. <sup>b</sup>Data were not obtained for nonparticipants who refused the telephone interview. <sup>c</sup>Asked independently from race.

**Table 2.** Elemental mercury exposure characteristics of healthy, working, nonoccupationally exposed adults.

	No. of participants	Mean ± SD	Median	Range
UHg (µg/g creatinine)	542	1.7 ± 1.7	1.3	0.09–17.8
No. of total amalgam surfaces <sup>a</sup>	511 <sup>b</sup>	10.6 ± 9.0	10	0–46
No. of occlusal amalgam surfaces	511	6.1 ± 4.5	6	0–19
No. of nonocclusal amalgam surfaces	511	4.5 ± 5.2	3	0–32

<sup>a</sup>Assessed during a noninvasive modified dental examination as described in “Materials and Methods.” <sup>b</sup>Dental assessments missing on 39 participants.

staff having higher UHg and more restorations. Approximately 14% of participants had no amalgam restorations. The numbers of total and occlusal amalgams were linearly related to UHg (Figure 1) ( $r = 0.46$ ,  $p < 0.0001$ ); mean UHg in those with 0 amalgam surfaces and those with  $> 15$  were 0.75 and 2.9  $\mu\text{g/g}$  creatinine, respectively.

**Neuropsychologic tests.** Results of the neuropsychologic battery are shown in Table 3. The mean scores of each neuropsychologic test were within the norms for the ages studied, and the scores followed the pattern expected by age. Professional staff performed better than support staff on the entire test battery in both age strata.

**Associations between other covariates and neuropsychologic battery.** Bivariate associations between potential confounders and neuropsychologic scores were as expected. Women performed better on tests of verbal and nonverbal memory (Lezak 1995) and on the digit symbol test (Kaufman et al. 1988; Snow and Weinstock 1990). Increasing education was associated with better scores on all tests (Lezak 1995).

**Associations between mercury exposure and neuropsychologic scores.** UHg was not associated with any measure of neuropsychologic performance (Table 4), either in analyses that adjusted only for sampling strata or in analyses that also adjusted for covariates. The results were essentially the same when UHg was replaced by its logarithmic transformation.

Mean scores, adjusted for covariates and sampling strata, on the SRT for subjects with

UHg above and below the median (1.29  $\mu\text{g/g}$  creatinine) were 53.0 and 52.1, respectively. Adjusted mean scores on the BVRT were 7.5 and 7.7, respectively. No differences were found for the WAIS-R digit symbol (11.4 vs. 11.3), Trail-Making B (68.0 vs. 69.7), and the Grooved Pegboard for the dominant (65.2 vs. 65.3) and nondominant (70.3 vs. 70.6) hands.

Similarly, no associations between counts of either total or occlusal amalgams and neuropsychologic performance were found (Table 4). Adjusted mean scores for subjects with more or less than the median numbers of total amalgams were 52.6 and 52.5, respectively, on the SRT and 7.4 and 7.8, respectively, on the BVRT. In addition, no differences were found for the WAIS-R digit symbol (11.4 vs. 11.3), Trail-Making B (68.6 vs. 69.1), and the Grooved Pegboard for the dominant (66.4 vs. 64.4) and nondominant (71.2 vs. 69.9) hands. Results were similar in parallel analyses of occlusal amalgams.

The results were unchanged in analyses that excluded all pinpoint amalgams, regardless of tooth surface. Results of the sensitivity analyses for the missing teeth also were unchanged.

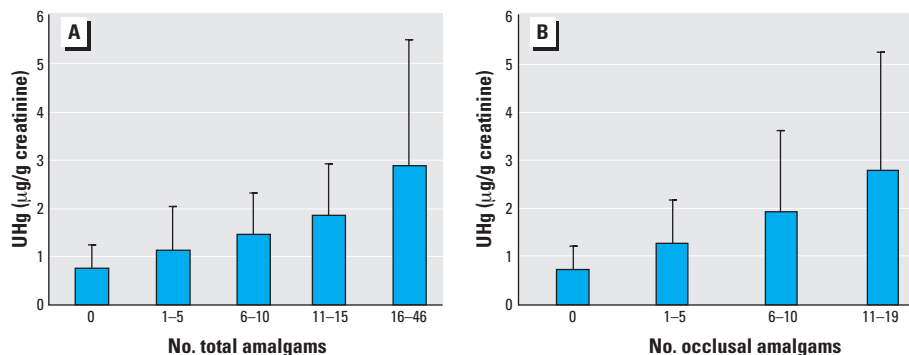
## Discussion

In our sample of working adults, exposure to mercury from dental amalgams was not associated with cognitive dysfunction. Specifically, performance on tests of verbal and nonverbal memory, attention and psychomotor speed, and fine motor coordination

were not associated with UHg. This sample excluded persons with occupational exposure to mercury; thus, our results should not be generalized to this group.

Exposure levels in our sample were low; mean UHg was 1.7  $\mu\text{g/g}$  creatinine. In comparison, UHg in persons occupationally exposed ranges between 2.0 and 60  $\mu\text{g/g}$  creatinine and varies with occupation. Dentists and dental workers have lower UHg (range, 2.0–45  $\mu\text{g/g}$  creatinine) (Bittner et al. 1998; Cianciola et al. 1997; Naleway et al. 1985, 1991; Ritchie et al. 1995; Steinberg et al. 1995; Woods et al. 1993) than workers in chloralkali or other factories that use mercury (range, 50–116  $\mu\text{g/g}$  creatinine) (Bernard et al. 1980; Buchet et al. 1980; Ellingsen et al. 2000, 2001; Hansteen et al. 1993; Lauwerys and Buchet 1973; Roels et al. 1985). Occupational studies that include unexposed employees as controls have found UHg similar to ours (range, 0.9–1.4  $\mu\text{g/g}$  creatinine) (Bernard et al. 1980; Buchet et al. 1980; Ellingsen et al. 2000; Hansteen et al. 1993; Lauwerys and Buchet 1973; Roels et al. 1985). In a healthy male military population with an average age of 53 years, UHg was also comparable (1.8  $\mu\text{g/g}$  creatinine) (Kingman et al. 1998). Some reports suggest that, in a minority of individuals, parafunctional behaviors (chewing and grinding) are associated with increased UHg (Barregard et al. 1995; Mackert 1987; Vimy et al. 1988). Our data do not confirm these reports, perhaps because the prevalence of these behaviors was very low. Nevertheless, our results may not be generalizable to such individuals because their exposure may be closer to that in occupational groups, where associations between exposure to mercury and neuropsychologic performance are reported.

Numbers of amalgam surfaces, total and occlusal, were lower than reported in previous U.S. samples. In the first National Health and Nutrition Examination Survey (NHANES I) performed between 1971 and 1974, the average numbers of decayed, missing, and filled surfaces were 25.7 and 55.5 in those 30–34 and 45–49 years of age, respectively (Brown and Swango 1993). Similar means were found in the 1985/1986 National Institute of Dental Research survey of employed adults and seniors (National Institute of Dental Research 1987). Our lower numbers likely reflect the



**Figure 1.** Relationships between UHg ( $\mu\text{g/g}$  creatinine) and the number of total mercury-containing amalgam surfaces (A) and the number of occlusal mercury-containing amalgam surfaces (B). Error bars represent 1 SD above the mean.

**Table 3.** Results (mean  $\pm$  SD) of neuropsychologic tests in 550 study participants 30–39 or 40–49 years of age.

Test	Overall sample ( $n = 547-549$ )	Support staff		Professional staff	
		30–39 years ( $n = 168-169$ )	40–49 years ( $n = 91-92$ )	30–39 years ( $n = 157-158$ )	40–49 years ( $n = 129-131$ )
SRT total recall (no. correct)	52.52 $\pm$ 8.37	52.28 $\pm$ 8.54	48.31 $\pm$ 8.78	54.90 $\pm$ 6.90	52.89 $\pm$ 8.41
BVRT (no. correct)	7.62 $\pm$ 1.84	7.55 $\pm$ 1.78	6.54 $\pm$ 2.15	8.30 $\pm$ 1.42	7.66 $\pm$ 1.77
WAIS digit symbol (age-scaled score)	11.38 $\pm$ 2.63	11.03 $\pm$ 2.92	10.01 $\pm$ 1.98	11.99 $\pm$ 2.40	12.06 $\pm$ 2.48
Trail-Making Test, condition A (time, seconds)	32.17 $\pm$ 13.11	31.86 $\pm$ 12.66	40.84 $\pm$ 17.11	27.80 $\pm$ 9.85	31.73 $\pm$ 10.90
Trail-Making test, condition B (time, seconds)	68.89 $\pm$ 29.60	70.80 $\pm$ 26.23	87.38 $\pm$ 40.96	58.25 $\pm$ 22.31	66.21 $\pm$ 25.89
Grooved Pegboard, dominant hand (time, seconds)	65.26 $\pm$ 13.63	63.05 $\pm$ 11.27	73.38 $\pm$ 20.74	60.80 $\pm$ 7.97	67.82 $\pm$ 12.61
Grooved Pegboard, nondominant hand (time, seconds)	70.46 $\pm$ 15.29	69.97 $\pm$ 14.76	78.12 $\pm$ 21.15	64.41 $\pm$ 9.52	73.02 $\pm$ 13.76

increased prevalence of water fluoridation and increased use of fluoride supplementation. Our results (Figure 1) confirm the previously observed linear association between number of amalgams and UHg (Kingman et al. 1998).

Our data show the expected relationships between several covariates, namely, employment strata, age, sex, and education, and performance on the neuropsychologic tests. These associations enhance our confidence in the data.

Unlike our study, where exposure levels were very low, occupational studies of workers in the thermometer and chloralkali industries find associations between UHg level and both neurologic and neuropsychologic deficits (Albers et al. 1988; Ehrenberg et al. 1991; Fawer et al. 1983; Herber et al. 1988; Langolf et al. 1978, 1981; Miller et al. 1975; Piikivi and Hanninen 1989; Ritchie et al. 1995; Roels et al. 1982; Smith and Langolf 1981; Smith et al. 1970, 1983). Neurologic deficits include increased intention and resting tremor (Albers et al. 1988; Ehrenberg et al. 1991; Fawer et al. 1983; Langolf et al. 1978, 1981; Roels et al. 1982; Smith et al. 1970), balance (Ehrenberg et al. 1991), and sensory and motor peripheral nerve dysfunction (Albers et al. 1982; Langolf et al. 1978; Levine et al. 1982; Miller et al. 1975; Singer et al. 1987). Current exposure was associated with decreased scores on the WAIS-R digit symbol subtest and the BVRT (Ellingsen et al. 2001). Two studies suggest long-lasting impairment of function 20–35 years after exposure ceased, indicating that cumulative, rather than recent, exposure is important (Fawer et al. 1983; Mathiesen et al. 1999). Studies evaluating neuropsychologic performance find associations between UHg and deficits in nonverbal memory, attention, and psychomotor coordination (Herber et al. 1988; Piikivi and Hanninen 1989; Ritchie et al. 1995; Smith and Langolf 1981; Smith et al. 1983).

Dentists and dental workers, who have exposure levels substantially lower than occupational workers, exhibit deficits in visuospatial

skills, verbal and nonverbal memory, attention, logical reasoning, response time and psychomotor coordination, and increases in tremor (Bittner et al. 1998; Ngim et al. 1992; Ritchie et al. 1995). These data suggest that dose–response relationships may begin at UHg levels found in U.S. dentists (4.6–8.1 µg/g creatinine) (Naleway et al. 1991). Echeverria et al. (1998) reported associations between mercury exposure and motor function, cognition, and self-reported symptoms and mood in their study of dental personnel receiving a challenge chelation test (which has not been validated as a measure of mercury exposure). Mean UHg in that study was 0.9 µg/L before and 9.1 µg/L after chelation (unadjusted for creatinine, although urine was collected for only 11 hr before and 6 hr after chelation).

Our power calculations indicated excellent power to detect small associations. Using a conservative significance level of 0.01, we had 80% power to detect 0.29 standard deviation units difference in neuropsychologic test score for those above the median exposure levels, and 90% power to detect 0.33 standard deviation units.

We considered the temporal relationship between placement of amalgams and neuropsychologic performance. Although cross-sectional studies are not able to derive temporal precedence, we may safely assume that the placement of amalgams and the resultant exposure to mercury preceded the outcomes. Most amalgams are first placed during the teenage years, and relatively few are placed after the age of 25 years.

We also considered the possibility of confounding by social class in childhood, because both dental care and neuropsychologic performance may be related to parental education and occupation. However, no associations between educational attainment and parental occupations up until the participant was 13 years of age and either the number of amalgams or neuropsychologic performance were found in the adult child. We also included these variables in the regression analysis; in no

case did their inclusion (either individually or together) change the regression coefficient relating mercury exposure to neuropsychologic test performance.

One limitation of this study is the absence of data on when the amalgams were placed, removed, or replaced. Most amalgam fillings were probably placed 10–20 years ago. Although it was possible to obtain the name of and permission to contact the participants' current family dentists, it was unlikely that participants would remember the name and addresses of all dentists seen over the 20-year period.

Finally, it is well known that exposure to high concentrations of organic mercury (notably methyl mercury) via fish and seafood consumption, such as those found in the Minimata Bay episode, is associated with neuropsychologic deficits in children (Igata 1991). Those findings, however, were not confirmed in more recent studies in the Faroe Islands (Grandjean et al. 1997) and Seychelles Islands (Palumbo et al. 2000) in the lowest exposure groups (which are likely to reflect levels found in U.S. children). We obtained data related to usual consumption of fish and other seafood, but we did not measure methyl mercury in the blood for two reasons. First, blood mercury represents relatively recent exposure and would yield little information regarding lifetime exposure history. Second, among participants, seafood consumption was distributed randomly across persons with few or many amalgams (data not shown). Our biological measure of exposure, UHg, also likely includes some organic mercury exposure.

The benefits of amalgams over other currently available restorative materials have been well described (Dodes 2001). Given the level of concern regarding amalgam safety among the public and dental profession, our results are reassuring in that exposure to amalgam-derived mercury is not associated with detectable subtle neuropsychologic deficits.

**Table 4.** Estimated adjusted regression coefficients of each exposure variable for each neuropsychologic test.

Test	UHg (µg/g creatinine)		Total number of amalgams		Number of occlusal amalgams	
	β <sup>a,b</sup>	SE(β)	β <sup>c</sup>	SE(β)	β <sup>d</sup>	SE(β)
SRT total recall (no. correct) <sup>e</sup>	-0.020	0.194	0.033	0.041	0.049	0.081
BVRT recall condition (no. correct) <sup>f</sup>	-0.040	0.040	-0.004	0.009	-0.018	0.017
WAIS-R digit symbol (age-adjusted scores) <sup>g</sup>	-0.038	0.056	-0.001	0.012	-0.016	0.023
Trail-Making test: A [time to completion (seconds)] <sup>h</sup>	0.120	0.320	-0.004	0.068	-0.052	0.135
Trail-Making test: B [time to completion (seconds)] <sup>i</sup>	-0.372	0.703	0.081	0.143	0.323	0.283
Grooved Pegboard: dominant hand [time to completion (seconds)] <sup>j</sup>	-0.428	0.339	0.085	0.071	0.189	0.140
Grooved Pegboard: nondominant hand [time to completion (seconds)] <sup>k</sup>	-0.323	0.380	-0.030	0.079	-0.044	0.155

<sup>a</sup>Estimated adjusted regression coefficient. <sup>b</sup>Change in test score per unit increase in UHg (µg/g creatinine). <sup>c</sup>Change in test score per unit increase in the total number of amalgams. <sup>d</sup>Change in test score per unit increase in the number of occlusal amalgams. <sup>e</sup>Adjusted for age, position (professional, support staff), sex, education, and English as a first language. <sup>f</sup>Adjusted for age, position (professional, support staff), job category (maintenance, facilities, security; clerks, receptionists, secretaries; engineers, research technicians; nurses, physicians' assistants, social workers, managers, attorneys; scientists, educators; physicians, psychologists, dentists), and English as a first language. <sup>g</sup>Adjusted for age, position, sex, education, ethnic group, U.S. born, and job category. <sup>h</sup>Adjusted for age, position, education, ethnic group, and U.S. born. <sup>i</sup>Adjusted for age, position, sex, education, ethnic group, and English as a first language. <sup>j</sup>Adjusted for age, position, sex, education, and ethnic group. <sup>k</sup>Adjusted for age, position, education, and ethnic group.

## REFERENCES

- Albers JW, Cavender GD, Levine SP, Langolf GD. 1982. Asymptomatic sensorimotor polyneuropathy in workers exposed to elemental mercury. *Neurology* 32:1168-1174.
- Albers JW, Kallenbach LR, Fine LJ, Langolf GD, Wolfe RA, Donofrio PD, et al. 1988. Neurological abnormalities associated with remote occupational mercury exposure. *Ann Neurol* 24:651-659.
- [Anonymous.] 1991. The Mercury in Your Mouth. Consumer Reports (May):316-319.
- Barregard L, Sallsten G, Jarvholm B. 1995. People with high mercury uptake from their own dental amalgam fillings. *Occup Environ Med* 52:124-128.
- Benton A. 1974. *The Revised Visual Retention Test*. 4th ed. New York:Psychological Corporation.
- Berlin M. 1969. The uptake of mercury in the brains of mammals exposed to mercury vapor and to mercuric salts. *Arch Environ Health* 18:719-729.
- Berlin M, Blomstrand C, Grant CA, Hamberger A, Trofast J. 1975. Tritiated methylmercury in the brain of squirrel monkeys. *Arch Environ Health* 30:591-597.
- Bernard A, Roels HA, Buchet J-P, Lauwerys RR. 1980. Comparison, by sodium dodecyl sulfate-polyacrylamide gel electrophoresis, of urinary proteins excreted by workers exposed to cadmium, mercury or lead. *Toxicol Lett* 5:219-222.
- Bittner AC, Echeverria D, Woods JS, Aposhian HV, Naleway C, Martin MD, et al. 1998. Behavioral effects of low-level exposure to Hg<sup>0</sup> among dental professionals: a cross-study evaluation of psychomotor effects. *Neurotoxicol Teratol* 20:429-439.
- Brown LJ, Swango PA. 1993. Trends in caries experience in US employed adults from 1971-74 to 1985: cross-sectional comparisons. *Adv Dent Res* 7:52-60.
- Buchet JP, Roels H, Bernard A, Lauwerys R. 1980. Assessment of renal function of workers exposed to inorganic lead, cadmium or mercury vapor. *J Occup Med* 22:741-750.
- Buschke H, Fudd PA. 1974. Evaluation of storage, retention and retrieval in disordered memory and learning. *Neurology* 11:1019-1025.
- Cianciola ME, Echeverria D, Martin MD, Aposhian HV, Woods JS. 1997. Epidemiologic assessment of measures used to indicate low-level exposure to mercury vapor (Hg<sup>0</sup>). *J Toxicol Environ Health* 52:19-33.
- Dodes JE. 2001. The amalgam controversy. An evidence-based analysis. *J Am Dent Assoc* 132:348-356.
- Echeverria D, Aposhian HV, Woods JS, Heyer NJ, Aposhian MM, Bittner AC, et al. 1998. Neurobehavioral effects from exposure to dental amalgam Hg<sup>0</sup>: new distinctions between recent exposure and Hg body burden. *FASEB J* 12:971-980.
- Echeverria D, Heyer NJ, Martin MD, Naleway CA, Woods JS, Bittner AC. 1995. Behavioral effects of low-level exposure to Hg<sup>0</sup> among dentists. *Neurotoxicol Teratol* 17:161-168.
- Ehrenberg RL, Vogt RL, Blair Smith A, Brondum J, Brightwell WS, Hudson PJ, et al. 1991. Effects of elemental mercury exposure at a thermometer plant. *Am J Ind Med* 19:495-507.
- Ellingsen DG, Bast-Pettersen R, Efskind J, Thomassen Y. 2001. Neuropsychological effects of low mercury vapor exposure in chloralkali workers. *Neurotoxicology* 22:249-258.
- Ellingsen DG, Efskind J, Haug E, Thomassen Y, Martinsen I, Gaarder PI. 2000. Effects of low mercury vapour exposure on the thyroid function in chloralkali workers. *J Appl Toxicol* 20:483-489.
- Fawer RF, DeRibaupierre Y, Guillemin MP, Berode M, Lob M. 1983. Measurement of hand tremor induced by industrial exposure to metallic mercury. *Br J Ind Med* 40:204-208.
- Fung YK, Molvar MP. 1992. Toxicity of mercury from dental environment and from amalgam restorations. *Clin Toxicol* 30:49-61.
- Gerbert B, Bernzweig J, Bleecker T, Bader J, Miyasaki C. 1992. Risks of the "big three": what dentists and patients believe about dental amalgam, fluoride and HIV. *J Am Dent Assoc* 123:82-88.
- Grandjean P, Weihe P, White R, Debes F, Araki S, Yokoyama K, et al. 1997. Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. *Neurotoxicol Teratol* 19:417-428.
- Guo T, Baasner J. 1993. Determination of mercury in urine by flame injection cold vapor atomic absorption spectrophotometry. *Anal Chim* 278:189-196.
- Hanson M, Pleva J. 1991. The dental amalgam issue. A review. *Experientia* 47:9-22.
- Hansteen I-L, Ellingsen DG, Clausen KO, Kjuus H. 1993. Chromosome aberrations in chloralkali workers previously exposed to mercury vapor. *Scand J Work Environ Health* 19:375-381.
- Heinegård D, Tiderström G. 1973. Determination of serum creatinine by a direct colorimetric method. *Clin Chim Acta* 43:305-310.
- Herber RFM, deGee AJ, Wibowo AAE. 1988. Exposure of dentists and assistants to mercury: mercury levels in urine and hair related to conditions of practice. *Community Dent Oral Epidemiol* 16:153-158.
- Hurch JB, Greenwood MR, Clarkson TW, Allen J, Demuth S. 1980. The effect of ethanol on the fate of mercury vapor inhaled by man. *J Pharmacol Exp Ther* 214:520-527.
- Igata A. 1991. Epidemiological and clinical features of Minamata Disease. In: *Advances in Mercury Toxicology* (Suzuki T, Imura N, Clarkson TW, eds). New York:Plenum Press, 439-458.
- Jaffe M. 1886. Über den Niederschlag, welchem Picrinsäure in normalen Harn erzeugt und über eine neue Reaction des Kreatinins. *Z Physiol Chem* 10:391.
- Kaufman AS, McLean JE, Reynolds CR. 1988. Sex, race, residence, region, and education differences on the 11 WAIS-R subtests. *J Clin Psychol* 44:231-248.
- Kingman A, Albertini T, Brown LJ. 1998. Mercury concentrations in urine and whole blood associated with amalgam exposure in a US military population. *J Dent Res* 77:461-471.
- Klove H. 1963. Clinical neuropsychology. In: *The Medical Clinics of North America* (Forster FM, ed). New York:Saunders, 1647-1658.
- Langolf GD, Chaffin DB, Henderson R, Whittle HP. 1978. Evaluation of workers exposed to elemental mercury using quantitative tests of tremor and neuromuscular function. *Am Ind Hyg J* 39: 976-984.
- Langolf GD, Smith PJ, Henderson R, Whittle H. 1981. Measurements of neurological functions in the evaluation of exposure to neurotoxic agents. *Ann Occup Hyg* 24:293-296.
- Lauwerys RR, Buchet JP. 1973. Occupational exposure to mercury vapors and biological action. *Arch Environ Health* 27:65-68.
- Levine SP, Cavender GD, Langolf GD, Albers JW. 1982. Elemental mercury exposure: peripheral neurotoxicity. *Br J Ind Med* 39:136-139.
- Lezak MD. 1995. *Neuropsychological Assessment*. 3rd ed. New York:Oxford University Press.
- Mackert JR. 1987. Factors affecting estimation of dental amalgam mercury exposure from measurements of mercury vapor levels in intra-oral and expired air. *J Dent Res* 66:1775-1780.
- Mathiesen T, Ellingsen DG, Kjuus H. 1999. Neuropsychological effects associated with exposure to mercury vapor among former chloralkali workers. *Scand J Work Environ Health* 25:342-350.
- Matthews CG, Klove H. 1964. *Instruction Manual for the Adult Neuropsychology Test Battery*. Madison, WI:University of Wisconsin Medical School.
- Miller JM, Chaffin DB, Smith RG. 1975. Subclinical psychomotor and neuromuscular changes in workers exposed to inorganic mercury. *Am Ind Hyg Assoc J* 10:725-734.
- Naleway C, Chou H-N, Muller T, Dabney J, Roxe D, Farrida S. 1991. On-site screening for urinary Hg concentrations and correlation with glomerular and renal tubular function. *J Public Health Dent* 51:12-17.
- Naleway C, Sakaguchi R, Mitchell E, Muller T, Ayer WA, Hefferen JJ. 1985. Urinary mercury levels in US dentists, 1975-1983: review of health assessment program. *J Am Dent Assoc* 111:37-42.
- National Institute of Dental Research. 1987. *Oral Health of United States Adults. The National Survey of Oral Health in US Employed Adults and Seniors: 1985-86*. NIH Publication no. 87-2868. Bethesda, MD:U.S. Department of Health and Human Services.
- Newton D, Fry FA. 1978. The retention and distribution of radioactive mercuric oxide following accidental inhalation. *Ann Occup Hyg* 21:21-32.
- Ngim CH, Foo SC, Boey KW, Jeyaratnam J. 1992. Chronic neurobehavioural effects of elemental mercury in dentists. *Br J Ind Med* 49:782-790.
- Palumbo DR, Cox C, Davidson PW, Myers GJ, Choi A, Shamlaye C, et al. 2000. Association between prenatal exposure to methyl mercury and cognitive function in Seychellois children: a reanalysis of the McCarthy Scales of Children's Ability from the main cohort study. *Environ Res* 84:81-88.
- Piikivi L, Hanninen H. 1989. Subjective symptoms and psychological performance of chlorine-alkali workers. *Scand J Work Environ Health* 15:69-74.
- Reitan RM. 1958. Validity of the Trail Making Test as an indicator of organic brain damage. *Percept Motor Skills* 8:271-276.
- Ritchie KA, Macdonald EB, Hammersley R, O'Neil JM, McGowan DA, Dale IM, et al. 1995. A pilot study of the effect of low level exposure to mercury on the health of dental surgeons. *Occup Environ Med* 52:813-817.
- Roels H, Gennart J-P, Lauwerys R, Buchet J-P, Malchaire J, Bernard A. 1985. Surveillance of workers exposed to mercury vapour: validation of a previously proposed biological threshold limit value for mercury concentration in urine. *Am J Ind Med* 7:45-71.
- Roels H, Lauwerys R, Buchet JP, Bernard A, Barthels A, Oversteyns M, et al. 1982. Comparison of renal function and psychomotor performance in workers exposed to elemental mercury. *Int Arch Occup Environ Health* 50:77-93.
- Singer R, Valciukas JA, Rosenman KD. 1987. Peripheral neurotoxicity in workers exposed to inorganic mercury compounds. *Arch Environ Health* 42:181-184.
- Skare I, Engqvist A. 1994. Human exposure to mercury and silver released from dental amalgam restorations. *Arch Environ Health* 49:384-394.
- Smith PJ, Langolf GD. 1981. The use of Sternberg's memory scanning paradigm in assessing effects of chemical exposures. *Hum Factors* 23:701-708.
- Smith PJ, Langolf GD, Goldberg J. 1983. Effects of occupational exposure to elemental mercury on short term memory. *Br J Ind Med* 40:413-419.
- Smith RG, Vorwald AJ, Path LS, Mooney TF Jr. 1970. Effects of exposure to mercury in the manufacture of chlorine. *Am Ind Hyg Assoc J* 31:687-699.
- Snow WG, Weinstock J. 1990. Sex differences among non-brain damaged adults on the Wechsler Adult Intelligence Scales: a review of the literature. *J Clin Exp Neuropsychol* 12:873-886.
- Steinberg D, Grauer F, Niv Y, Perlyte M, Kopolovic K. 1995. Mercury levels among dental personnel in Israel: a preliminary study. *Isr J Med Sci* 31:428-432.
- Takahata N, Hayashi H, Watanbe S, Anso T. 1970. Accumulation of mercury in the brains of two autopsy cases with chronic inorganic mercury poisoning. *Folia Psychiatr Neurol Jpn* 24:59-69.
- Vimy MJ, Luft AF, Lorscheider FL. 1988. Estimation of mercury body burden from dental amalgam: computer simulation of a metabolic compartmental model. *J Dent Res* 66:1235-1242.
- Watanbe S. 1969. Mercury in the body 10 years after long term exposure to mercury [Abstract]. In: *Proceedings of Sixteenth International Congress on Occupational Health, 22-27 September 1969, Tokyo, Japan*. Tokyo:Japan Organizing Committee of Sixteenth International Congress on Occupational Health, 553.
- Wechsler D. 1981. *WAIS-R Manual*. New York:Psychological Corporation.
- Weiner JA, Nylander M, Berglund F. 1990. Does mercury from amalgam restorations constitute a health hazard? *Sci Total Environ* 99:1-22.
- Woods JS, Martin MD, Naleway CA, Echeverria D. 1993. Urinary porphyrin profiles as a biomarker of mercury exposure: studies on dentists with occupational exposure to mercury vapor. *J Toxicol Environ Health* 40:235-246.