

Dentistry

Mercury and dentists

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Weighing new evidence against potential neurotoxicity

The new behavioural study among dentists by Ritchie *et al.*, reported in this issue of *Occupational and Environmental Medicine*, found no adverse effects associated with low exposure to mercury in urine, hair, or nails, that assess subjective symptoms as well as more objective measures of psychomotor performance. The new study laudably addresses the World Health Organisation's request for chronic Hg^o exposure studies that are useful in defining a threshold of effect below 25 µg/l and are not limited by insufficient statistical power and inconsistent measures of exposure and outcome.¹ The study highlights the potential for neurotoxicity from low exposure to Hg^o among dentists who work with amalgam restorations containing 50% Hg^o, and stimulates discussion on methodological issues in study design that might increase sensitivity to detect adverse effects.

Though few associations were noted, the negative results must be weighed with positive evidence for a lower threshold even applicable to the general population, because dentists incur exposures that are comparable to that in the general population. For example, in a US national sample of 6925 dentists participating in the American Dental Association Health Screen Program (1990–96), the distribution of urinary Hg was skewed; 90% had concentrations under 6.0 µg/l.² In a Washington State sample of 2196 dentists (1998–2000), the mean urinary concentration was 2.5 µg/l (range 0–67). The new study also reported mean urinary concentrations of 2.56 µg/l that agree with previous reports. It is noteworthy that two estimates among the general population are comparable to that of dentists with broad ranges (0–34 and 1–18 µg/l) and similar mean urinary concentrations of 3.1 and 9.0 µg/l respectively.

The study also undertook a more comprehensive evaluation of exposure than most studies in that measurement of total urinary mercury, summarising the contribution from working with amalgam and one's personal amalgam, was supplemented with the amount in hair and nails which is predominantly related to methyl mercury exposure from consumption of fish. Speciation of mercury in blood would have confirmed

expected correlations between total mercury in red blood cells and organic mercury in hair, which range between 0.66 and 0.71 in males and females. Exposure to methyl mercury (CH₃Hg⁺) is generally thought to be a more compelling problem because the methyl group increases solubility in blood and lipids, thereby increasing distribution and bioavailability. However, behavioural evaluations reflect potential effects from both forms of mercury on the central nervous system (CNS). Note that by interacting with thiols and lipids, Hg²⁺ promotes immediate damage to the cell while CH₃Hg⁺ crosses biomembranes easily and accumulates into the cytosol for later toxicological action. Once in the CNS, both forms are oxidised to Hg²⁺ where the distribution in the brain is similar, though the demethylation process is slow. Thus, observed differences between methyl and Hg^o health effects on the CNS are most likely attributable to differences in half life, distribution, and dose which the new study did not, but could have, readily addressed by examining the potential contribution from both forms of Hg simultaneously in regression analyses rather than assessing each measure alone.

“Exposures to 1–3 mg/m³ Hg trigger clinical CNS effects”

With respect to behavioural function, studies rely on observed deficits in clinical reports, coupled with the experimental and occupational evidence of impairment, to provide the basis for test selection on an anticipated continuum between clinical and preclinical effects. A preclinical deficit is defined as an adverse change in performance that is not usually detectable by clinical examination ranging between 3% and 18% when compared to a zero or a low exposure group. Exposures to 1–3 mg/m³ Hg^o trigger clinical CNS effects. Classic signs of mercurialism³ include: (1) psychosomatic symptoms; (2) alterations in affect or emotional lability; (3) insidious loss of mental capacity (progressively affecting memory and logical reasoning); and (4) motor effects (in the arms, progressing to incoordination, imbalance, and tremor

in muscles that perform fine motor control). Such diversity in effects indicates more than one mechanism of toxicity. Exposure to Hg^o may interfere with the limbic system associated with mood and memory, the motor strip associated with movement, and peripherally insult axons associated with vibration sensitivity or visual perception.

The new study correctly hypothesised that exposure may (1) increase symptoms; (2) deteriorate cognitive skills requiring prolonged attention, memory, and psychomotor skills; and (3) reduce motor speed, but did not hypothesise that effects were selective, leaving language and retrograde memory intact. Suggested hold tests were not used that estimate premorbid intelligence and can be readily measured by tests similar to the WRAT or Vocabulary. Perhaps because of constraints on a 20 minute assessment, the study focused on memory (with good redundancy in measures of attention) but omitted assessments of affect and manual dexterity. Note that dental studies^{4–8} have found associations between mood and urinary concentrations below 30 µg/l to as low as 4 µg/l with partial correlations as high as 0.50. Mood is also strongly associated with Hg body burden. Further, deficits in hand steadiness⁹ (known to be correlated with tremor), finger tapping, and manual dexterity have even been reported at <4 µg/l, comparable to exposures among the general population in the absence of slowed reaction time.

With respect to cognitive function, there is little debate regarding the potential for toxicity from high dose exposures to Hg^o consistent with urinary Hg concentrations exceeding 50 µg/l, but there is no consensus with respect to a lower threshold level of adverse effects. Exposures about 100 µg/l may result in mild but consistent cognitive deficits using tests of (1) short term memory (digit span, digit scanning, and visual memory); (2) verbal concept formation (WAIS similarities); and (3) visual-spatial function (block design, digit symbol, and the Raven Progressive Matrices test). Deficits in digit span and the WAIS Similarity test have also been detected in workers exposed to 30–50 µg/l. However, determination of a lower threshold is complicated by mixed results among chloralkali worker studies^{10–12} at exposures of 0.025–0.076 mg/m³ (10–19.9 µg/l in blood). In one study, symptoms, mood, and tremor were impaired among workers exposed for 14 years, but memory and psychomotor function were unaffected.¹⁰ In contrast, two studies found that subjective reports of fatigue, poor memory, and confusion were increased among workers exposed for 7¹¹ and 13.5¹² years, but tremor, coordination, and reaction time remained unaffected.

"A more uniform dental population needs to be evaluated"

As in the new study, these conflicts are best addressed by evaluating a more uniform dental population because they are homogeneous with respect to factors that alter performance—that is, uniform education and training, high academic achievement and motivation to succeed, excellent motor function skills, and similar socioeconomic status. However, the option to enhance detection of subtle CNS effects by using unexposed dentists as negative controls was not pursued by these investigators. This choice may partially explain differences in psychomotor performance (unrelated to mercury exposure) that distinguish dentists from the external control group of academics. The two groups were not comparable either demographically or on performance of psychomotor skills. Given this knowledge, it is unclear why the interaction between age, gender, and duration of employment (from as low as 6 months to more than 20 years) was excluded from the regression analyses. Another factor contributing to negative results may have been the proportion of volunteers (28%) among dentists that might introduce bias into the study. Behavioural scores are susceptible to motivation to perform well that may differ

between volunteers and randomly selected dentists. Inclusion of these subjects in the regression could explain resultant negative findings in the internal analyses among dentists. Lastly, the inclusion of 7% of dentists with kidney disorders is troublesome because the insult may alter urinary Hg concentrations, which in turn affects the shape of the exposure–effect curve.

Alternatively, the lack of Hg related deficits may well be attributable to the very low levels of exposure which challenge these and future researchers to pay very careful attention to the selection of subjects, choice of behavioural tests, sources of exposure, and more vigilant control for potential confounding not only from age and gender, but also vocabulary, alcohol consumption, use of medications, kidney function, and other neurotoxic exposures.

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Answers to multiple choice questions on Design of measurement strategies for workplace exposures by H Kromhout, on pages 349–354

- (1) (a) false; (b) true; (c) false; (d) false
- (2) (a) false; (b) false; (c) true; (d) true
- (3) (a) false; (b) false; (c) true; (d) false
- (4) (a) true; (b) true; (c) true; (d) false
- (5) (a) false; (b) true; (c) true; (d) false