Correlation of dental amalgam with mercury in brain tissue

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Since the 1800s, dental amalgam has been the most commonly used restorative material in dentistry. The mecury content of dental amalgam (approximately 50%) has created an ebb and tide of controversy regarding its safety for patients and dental personnel. Organic mercury compounds and elemental mercury vapor can cause central nervous system damage,[1,2] and long-term exposure to inorganic (metallic) mercury vapor from dental amalgam may increase the brain tissue concentration of this neurotoxic metal.

In 1957, Frykholm[3] used radioactive isotopes of mercury in dental amalgam to demonstrate that systemic mercury levels in patients returned to baseline measurements 2 weeks after placement of dental amalgam restorations. However, Frykholm's study did not address long-term accumulation of mercury in brain tissue. More recently, Svare et al.[4] demonstrated that minute amounts of mercury vapor are continuously released from dental amalgam restorations in humans and that the release is accelerated 15-fold in expired air immediately after mastication. Abraham et al.[5] reported a correlation of inorganic mercury levels in the blood of humans to the total surface area of occlusal dental amalgam and that the amount of inorganic mercury was enhanced eightfold immediately after mastication. Schiele et al.[6] and Friberg et al.[7] reported a positive correlation between the number and surfaces of dental amalgam and mercury levels in human brain tissue.

This project was conducted to determine whether a positive correlation exists between the number of dental amalgam occlusal surfaces in the oral cavity and the mercury content of brain tissue.

METHOD

Examination of the cadaver dentition and collection of brain tissue specimens from nonrandomized, sudden, unexpected death subjects was conducted as part of routine autopsy procedures at the Los Angeles Count Coroner's Office.

All of the brain tissue samples were collected i Evergreen (Evergreen Scientific International, Inc., L Angeles, Calif.) polystyrene 17 mm by 100 mm steri specimen tubes (single lot number No. 0228-27, catalo number No. 222-2094-050) and immediately placed i an ice chest with dry ice. The specimens were kept at temperature between 0° C and minus 75° C until th time of analysis.

Prior to laboratory analysis, subjects were defined a cadavers with a minimum of five occlusal surfaces dental amalgam and a minimum of 10 posterior (premo lars and first and second molars) teeth, and controls wer defined as cadavers with 0 to 1 occlusal surface of dent amalgam and a minimum of 14 posterior teeth. Th requirement of 14 posterior teeth was necessary t eliminate the possibility of recent extractions of teet with dental amalgam leading to incorrect classification o the cadaver. Only the occlusal surfaces were considere because of the effect of mastication on the release o mercury from dental amalgam. No dental amalgam wa present on the anterior teeth of the controls.

The brain specimens, identified only by cadaver nam and Coroner's Office number, were analyzed at th National Medical Services (NMS) by using the metho of Hatch and Ott[8] for total mercury content by col vapor atomic absorption spectrophotometry, and at th Swedish Environmental Research Institute (IVL) b radio chemical neutron activation analysis after blin preparation at the Karolinska Institute (KI).

RESULTS

Atomic absorption

Three to five grams of white matter from the mid frontal plane were collected from 38 adult cadavers and 6 to 9 grams of gray mater (cortex) and white matter from the occipital lobe were collected from an additional 39 adult cadavers. These specimens were analyzed by NMS using atomic absorption spectrophotometry with a detection limit of 1 to 4 ng Hg/gm wet weight dependent on the size of the sample tested. Of the 77 samples, only 28 were above the detectable limit and no correlation between mercury content and occlusal surfaces of dental

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amalgam, age, sex, or race could be established on the basis of the results obtained by CVAAS.

Neutron activation analysis

Six to nine grams of gray matter (cortex) and white matter from the occipital lobe were collected from 83 adult cadavers. These specimens were analyzed blindly by IVL using RNAA.[9,10] The detection limit was approximately 0.2 ng absolute (that is, a 0.5 to 0.9 g sample gave 0.4 to 0.2 ng/gm ww). Standard reference material from the International Atomic Energy Agency (IAEA) was used to establish accuracy.

Results obtained by RNAA are presented in Tables I and II.

ASSUMPTIONS

1. The mercury level of cadaver brain tissue remains constant from the time of death to the time it is analyzed.
2. With a sample size of 83 cadavers, the exposure of nondental environmental mercury to subjects with dental amalgam is similar to the exposure of nondental environmental mercury to subjects without dental amalgam.

LIMITATIONS

1. An elevation in the level of mercury in the brain could occur from mercury exposure including food, paint, cosmetics, medications, thermometers, electronic components, and environmental pollution.
2. Exposure to dental amalgam in primary teeth was not determined. A control with no, or one, current dental amalgam filling could have had an elevation in the level of mercury in the brain based upon the presence of dental amalgam in exfoliated primary teeth.

DISCUSSION

Data from this project demonstrate a positive correlation between the number of occlusal surfaces of dental amalgam and mercury levels in the brain. This indirect evidence suggests that additional experimental research is necessary to determine to what extent mercury from dental amalgam fillings contributes to the body burden of mercury in the brain. The relationship between mercury levels in the brain and incipient clinical signs and symptoms of mercury toxicity needs to be established.

Fukuda[11] was able to elicit a "fine" tremor in the fore and hind limbs of two of six rabbits exposed intermittently to mercury vapor; the brain concentrations ranged from 0.8 to 3.7 μg Hg/g wet weight. Kishi et al.[12] found a decline in conditioned avoidance response in rats after exposure to 3 mm Hg/m³ for 3 hr/day, 5 days/week.

Table I. Analysis of mercury in gray matter

	Controls	Intermediates	Subjects
Number	16	16	51
Amalgam surfaces	0 - 1	1.5 - 4	5 - 14.5
Age range	17 - 40	13 - 48	14 - 59
Age mean	27.7	25.7	30
Ng/g Hg mean	6.70	10.57	15.21
Ng/g Hg range	1.9 - 22.1	2.1 - 27.6	3 - 121.4
Standard deviation	5.08	6.32	18.26

Comparison of controls to intermediates
Mann-Whitney u test (one-tail): $u = 69$; $z = 2.22$; $p < .0132$

Comparison of controls to subjects
Mann-Whitney u test (one-tail): $u = 252$; $z = 2.29$; $p < .011$

Table II. Analysis of mercury in white matter

	Controls	Intermediates	Subjects
Number	13	12	35
Amalgam surfaces	0 - 1	1.5 - 4	5 - 14.5
Age range	17 - 40	13 - 48	14 - 59
Age mean	27.1	27	31.8
Ng/g Hg mean	3.80	6.58	11.22
Ng/g Hg range	1.4 - 7.1	1.3 - 13.9	1.7 - 110.1
Standard deviation	1.90	3.50	18.41

Comparisons of controls to intermediates
Mann-Whitney u test (one-tail): $u = 42$; $z = 1.96$; $p < .025$

Comparison of controls to subjects
Mann-Whitney u test (one-tail): $u = 105$; $z = 2.84$; $p < .0025$

The time of onset of effects varied from 12 to 39 weeks. All rats recovered to preexposure baseline levels of performance within 12 weeks after the termination of exposure. Significantly, poor performance was noted at brain concentrations of 20 μg Hg/gm wet weight and recovery to normal behavior was observed when the brain levels fell to 10 μg Hg/gm wet weight. No pathologic changes in brain tissue were observed. Unfortunately, the levels of mercury in the human brain sufficient to cause early symptoms of erethism in the most susceptible persons is not known.

Our data demonstrate a 35% higher level of total mercury mean value in the gray matter (cortex) than in the total mercury mean value in the white matter.

Dental amalgam contains inorganic mercury. In this study, however, total mercury was measured because of the bi-directional conversion between inorganic and organic mercury in humans.

The overall results from neutron activation analysis averaged more than 3.7 times higher than the overall results from atomic absorption. Direct comparison

between RNAA and CVAAS was made by collecting two duplicate specimens of 35 cadavers. In this population, the CVAAS range was <1 to 14 ng Hg/gm, mean = 2.81 ng Hg/gm; the RNAA range was 3 to 28.7 ng Hg/gm, mean = 10.5 ng Hg/gm. Our data suggest that neutron activation analysis may be a more sensitive method of measuring the mercury content in brain tissue.

The exposure of a 7-month-old fetus to mercury was documented by the analysis of brain tissue from a gravid cadaver. The cadaver dentition contained 14 total surfaces of dental amalgam with nine occlusal surfaces. A brain tissue sample was obtained from the fetus immediately upon the removal from the womb. Analysis of the mother's brain tissue revealed 6.7 ng/gm in white matter and 9.9 ng/gm in gray matter (cortex); analysis of the fetal brain tissue revealed 2.8 ng/gm in white matter and 6.7 ng/gm in gray matter (cortex).

The mercury in fetal brain tissue most likely arrives through the placenta from maternal blood. The temporary high levels of mercury in the blood immediately following the removal and placement of dental amalgam has been documented.[3] Although the toxic or teratogenic levels of mercury in human fetal brain tissue have not been established, the removal and insertion of dental amalgam for gravid patients, or women of child-bearing age with the possibility of pregnancy, should be avoided whenever practical.[13]

Of interest was the extremely high mercury measurement of one automobile accident victim that was not included in the statistical data. A 53 year-old, well-nourished, slightly obese white woman, whose weight was 55.8 kg and height 135 cm, suffered multiple blunt-force traumas including a maxillary fracture and laceration of the mouth as the driver of an automobile that ran head-on into a cement pole at an estimated speed of 50 kph. A total of 30 surfaces (12.5 occlusal surfaces) of dental amalgam were present in the teeth. The victim survived approximately 1 hour after the accident.

Duplicate samples measured 13.6 and 19.5 μg Hg/gm wet weight of gray matter from the occipital lobe cortex and 6.38 and 11.75 μg Hg/gm wet weight of white matter from the occipital lobe cortex. This level of mercury is approximately 1000 times the mean level of subjects in the cadaver study.

Had this person survived the automobile accident, the level of mercury in the brain probably would have contributed to symptoms of erethism. Emergency room physicians should be advised to check the blood levels of mercury in survivors of major trauma to the oral cavity associated with the presence of dental amalgam.

Because of the high level of mercury in the brain, samples of the kidney and liver were subsequently analyzed. Measurements showed 1.22 μg Hg/gm wet weight of kidney and 294 ng Hg/gm wet weight of liver, indicating a general systemic contamination of mercury.

SUMMARY

Data from this project demonstrate a positive correlation between the number of occlusal surfaces of dental amalgam and mercury levels in the brain ($p < .0025$ in white matter). This is indirect evidence suggesting that mercury from dental amalgam fillings may contribute to the body burden of mercury in the brain. The toxic levels of mercury in human tissues have not been sufficiently investigated and the amount of mercury in human brain tissue from dental amalgam may or may not be clinically significant. Nevertheless, dental amalgam exposure should be considered in monitoring sources of mercury accumulation in human brain tissue.

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