Dental "silver" tooth fillings: a source of mercury exposure revealed by whole-body image scan and tissue analysis

LESZEK J. HAHN, REINHARD KLOIBER, MURRAY J. VIMY,* YOSHIMI TAKAHASHI,† AND FRITZ L. LORSCHEIDER[1]

*Departments of Radiology, *Medicine, and †Medical Physiology, University of Calgary, Faculty of Medicine, Calgary, Alberta, T2N 4N1, Canada*

ABSTRACT

Mercury (Hg) vapor is released from dental "silver" tooth fillings into human mouth air after chewing, but its possible uptake routes and distribution among body tissues are unknown. This investigation demonstrates that when radioactive ^{203}Hg is mixed with dental Hg/silver fillings (amalgam) and placed in teeth of adult sheep, the isotope will appear in various organs and tissues within 29 days. Evidence of Hg uptake, as determined by whole-body scanning and measurement of isotope in specific tissues, revealed three uptake sites: lung, gastrointestinal, and jaw tissue absorption. Once absorbed, high concentrations of dental amalgam Hg rapidly localize in kidneys and liver. Results are discussed in view of potential health consequences from long-term exposure to Hg from this dental material. — HAHN, L. J.; KLOIBER, R.; VIMY, M. J.; TAKAHASHI, Y.; LORSCHEIDER, F. L. Dental "silver" tooth fillings: a source of mercury exposure revealed by whole-body image scan and tissue analysis. *FASEB J.* 3: 2641–2646; 1989.

Key Words: dental amalgam · mercury · tooth fillings · mercury vapor · mercury exposure

MERCURY (HG) HAS BEEN THE major component of tooth filling materials for the past 150 years (1) and its use has met with continuing controversy, as clear experimental evidence regarding its safety has not been demonstrated (2). Dental "silver" tooth fillings typically have a weight composition that is approximately 50% pure elemental Hg, 35% silver, 13% tin, 2% copper, and a trace amount of zinc when mixed as an amalgam (3). A newly placed multisurface dental silver filling involving an occlusal (grinding) surface of a molar tooth contains between 750–1000 mg of Hg and has an average serviceable life span in the human mouth of 7–9 years (4, 5). Approximately 80% of all tooth restorations employ this Hg/silver dental amalgam (6).

The traditional view in dentistry maintains that the Hg component of dental amalgam becomes inert once the fillings have been allowed to set for several days, and that long-term danger to the patient from Hg vapor is therefore remote (7). However, more recent clinical studies in subjects with amalgam fillings who chewed gum for 10 min have demonstrated that quite substantial amounts of Hg vapor are released into intra-oral air from dental amalgam, being sixfold higher than prechewing levels (8). The intra-oral Hg vapor concentration remained elevated during 30 min of continuous gum chewing; and after cessation of chewing, the mouth Hg vapor concentration declined slowly to prechewing levels over a period of 90 min (9). Control subjects with no amalgams had insignificant intra-oral air Hg vapor levels that did not change as a function of chewing (8). Brushing the teeth with commercial toothpaste will also stimulate the release of Hg vapor from amalgam surfaces (10). Although a positive correlation has been demonstrated between the number of dental amalgams and the levels of Hg vapor in the mouth (8, 9), it remains uncertain how much of this Hg is absorbed into body tissues. A current review, addressing whether Hg usage in dentistry constitutes a potential public health hazard, has concluded that further experimental evidence is needed, particularly regarding the metabolic fate of Hg vapor (2). The objective of this investigation was to determine possible sites of uptake and patterns of tissue distribution for Hg released from in situ dental amalgams. Qualitative information by whole-body scanning and quantitative tissue measurements by scintillation detection were determined using radioactive ^{203}Hg in a sheep experimental model.

[1]To whom correspondence should be addressed, at: Department of Medical Physiology, Faculty of Medicine, Health Sciences Centre, University of Calgary, 3330 Hospital Dr. N.W., Calgary, Alberta T2N 4N1, Canada.

0892-6638/89/0003-2641/$01.50.

METHODS

In the present study a 4-year-old ewe that weighed 61 kg was anesthetized with halothane administered through an endotracheal tube fitted to a Narkovet-2 gas anesthetic machine. Dental surgery was performed with the preparation and placement of occlusal amalgam fillings according to standard procedure (11) into 12 molar teeth (3 molars on each side of the upper and lower jaws). This particular number of teeth was chosen because previous attempts to estimate the daily dose of Hg and body burden in humans had focused on subjects having 12 or more teeth with occlusal amalgam fillings (9, 12). The amalgam mass placed in each finished molar tooth of this ewe was approximately 850 mg, of which 50% was elemental Hg. **Figure 1** shows the placement of nonradioactive dental amalgam fillings in teeth of a sheep from a preliminary study with a lateral view of the skull (*A*), an occlusal view of amalgam restorations in the right lower jaw (*B*), and radiograph images of the upper and lower right jaws before (*C*) and after (*D*) amalgam placement. Before mixing the amalgam, 7.5 mCi of radioactive ^{203}Hg (New England Nuclear, Boston, Mass.), which had a specific activity of 12 mCi/g, was diluted 11-fold with nonradioactive Hg. At the conclusion of the dental surgery, the oral cavity was flushed with H_2O and rinsed several times by vacuum aspiration to remove any amalgam particle trimmings.

After surgery the ewe was provided free access to water and fed fresh hay twice daily for 29 days. During the course of the study intra-oral Hg vapor measurements were taken intermittently after chewing as previously described (8). On day 29, the animal was killed with sodium pentobarbital/saturated KCl. The tooth structure above the gum line containing the entire amalgam filling was individually sectioned and removed intact from each of the 12 molars to reduce the high background from ^{203}Hg remaining in the fillings. The animal was then imaged using a Technicare Omega-500 large-field-of-view gamma camera equipped with a medium energy collimator (13, 14). An image of the sheep was obtained in the right lateral projection, using the 279 ± 28 KeV gamma rays of ^{203}Hg. In addition, transmission images were obtained using a flat 30-cm diameter ^{57}Co source that outlined the contour of the sheep's body. A posterior projection image was repeated after removal of the gastrointestinal tract. Tissue and fluid specimens were weighed at autopsy and analyzed for radioactivity. Isotope measurements were taken for

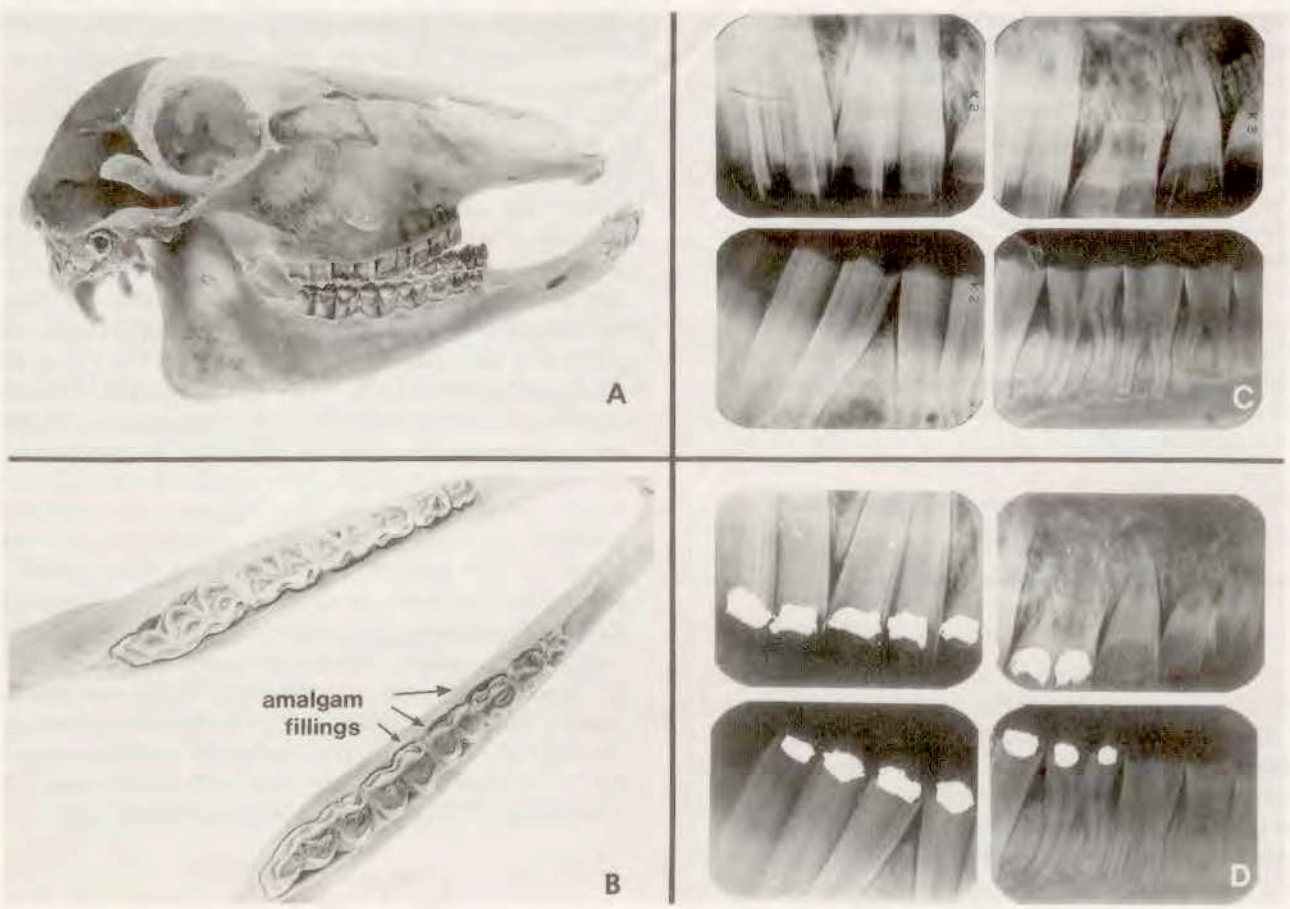

Figure 1. Placement of dental amalgam fillings in sheep teeth: *A*) lateral view of sheep skull; *B*) occlusal view of sheep mandible showing occlusal amalgam restorations in the mandibular right quadrant; *C*) periapical radiographs of the upper and lower right quadrants before amalgam placement; *D*) periapical radiographs of the upper and lower right quadrants after amalgam placement. The x-ray views indicate that anchorage of these fillings has been achieved with appropriate undercuts.

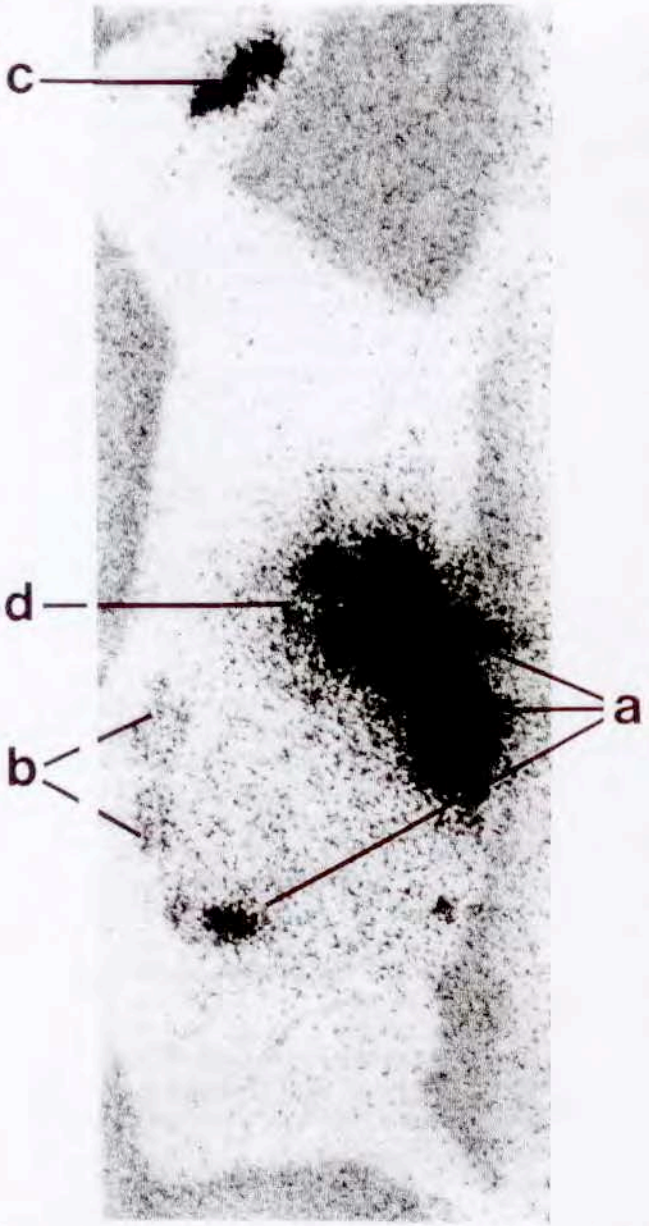

Figure 2. Right lateral image of amalgam ^{203}Hg distribution in the intact sheep, after removal of the dental amalgams, with superimposed transmission scan showing the body contour. The greatest concentrations of ^{203}Hg are in the gastrointestinal tract (*a*), kidneys (*b*), and in the gum and alveolar bone of the jaws (*c*). Liver activity (*d*) is obscured by large quantities of Hg in the gut on this image.

10 min per specimen (approximately 2% SD counting error) or 100 min per specimen for tissues with low counts (<10% SD counting error) in a Picker gamma well-counter calibrated to an energy range window of 249–309 KeV. Background counts +15% were set automatically for subtraction after a blank reading was taken for 100 min. This instrument subtraction level was sufficiently high so that no net counts were detectable during a repeat 100-min background measurement. At an 80% instrument counting efficiency, 1 μCi equals 1,776,000 cpm. Data, initially expressed as net radioactive cpm, were corrected for the physical half-life (47 days) of ^{203}Hg decayed to 29 days (65% remaining), for the specific activity of ^{203}Hg (83,300 ng/μCi), and for the dilution of ^{203}Hg with nonradioactive Hg (11-fold). The final calculation represented the total amalgam Hg (ng) per g (wet wt) of tissue or fluid as follows: (cpm/65%) × (83,300 ng/μCi × 11)/1,776,000 cpm/μCi/g.

RESULTS

Figure 2 demonstrates the ^{203}Hg distribution from amalgam within the body of the sheep as viewed from the right side. The transmission image obtained without moving the animal is superimposed to facilitate orientation. Primary sites of Hg concentration are in the abdominal cavity, specifically in the gastrointestinal tract, liver, and kidneys. A second major site is in the upper and lower jaws, even though the tooth structure containing the radioactive amalgam has been removed in its entirety.

Figure 3 is the posterior image of ^{203}Hg distribution from amalgam in the sheep's abdomen after removal of the gastrointestinal tract. The left kidney is clearly identified. The larger area of activity on the right side of the animal represents the liver and the right kidney, from which some tissue had been removed for well-counting.

Table 1 lists the total concentration of amalgam Hg in various tissues at autopsy 29 days after placement of dental amalgam fillings. Whole blood and urine contained 9.0 and 4.7 ng Hg/g, respectively. Muscle concentration of Hg was similar to blood, but concentration in fat remained low. In the oral/nasal tissues, Hg was concentrated primarily in gum mucosa (323 ng/g) and tooth alveolar bone (318 ng/g). In the gastrointestinal tract the washed stomach lining (929 ng/g) and

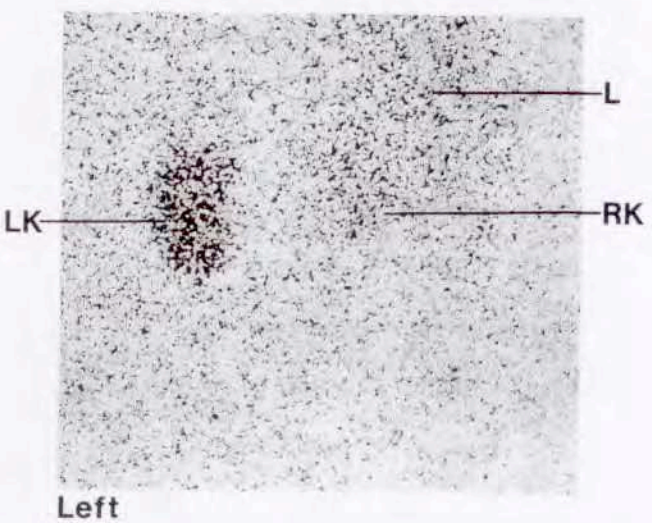

Figure 3. Posterior image of amalgam ^{203}Hg distribution in the abdomen after removal of the gastrointestinal tract which demonstrates Hg within the kidneys and liver. The left kidney (LK) is clearly identified. The large area of Hg deposition on the right side of the animal represents a combination of liver (L) and right kidney (RK). Some tissue had been removed from the right kidney, which had been mobilized and placed further from the detector, explaining the lower intensity compared with the left.

TABLE 1. *Concentration of amalgam Hg in sheep tissues 29 days after placement of dental amalgam fillings*

Tissue	ng Hg/g
Whole blood	9.0
Urine	4.7
Skeletal muscle (gluteus)	10.1
Fat (mesentery)	0.9
Cortical maxillary bone	3.6
Tooth alveolar bone	318.2
Gum mucosa	323.7
Mouth papilla	19.7
Tongue	13.0
Parotid gland	7.8
Ethmoturbinal (nasal) bone	10.7
Stomach	929.0
Small intestine	28.0
Large intestine	63.1
Colon	43.1
Bile	19.3
Feces	4489.3
Heart muscle (ventricle)	13.1
Lung	30.8
Tracheal lining	121.8
Kidney	7438.0
Liver	772.1
Spleen	48.3
Frontal cortex	18.9
Occipital cortex	3.5
Thalamus	14.9
Cerebrospinal fluid	2.3
Pituitary gland	44.4
Thyroid	44.2
Adrenal	37.8
Pancreas	45.7
Ovary	26.7

feces (4489 ng/g) contained the most Hg, although Hg concentration in other washed intestinal tract tissues was three- to sixfold higher than in blood, and bile concentration was more than twice that of blood. Heart muscle contained Hg levels that were similar to skeletal muscle. However, lung concentration of Hg (30 ng/g) was threefold higher than blood, and tracheal lining was much higher at 121 ng/g. Abdominal organs demonstrating the greatest concentration of Hg were kidney (7438 ng/g) and liver (772 ng/g). Spleen contained 48 ng Hg/g, which was fivefold higher than blood content. In the central nervous system the brain frontal cortex and thalamus concentrations of Hg were higher than in either blood or cerebrospinal fluid. Endocrine gland concentrations of Hg were three- to fivefold higher than blood. There is not a direct correlation between the intensity of Hg-203 localization on the whole-body scan and absolute radioactivity counts in autopsied tissues because of attenuation and geometry factors that affect the image.

DISCUSSION

The results of this study clearly demonstrate that substantial quantities of Hg from amalgam will appear in various body tissues as early as 29 days after placement of amalgam fillings in teeth. This Hg can be readily visualized by scintigraphy and can be easily quantified by analysis of tissue radioactivity. The experimental design of this in vivo isotope study has the advantage that all of the Hg measured originates only from dental amalgam and cannot be attributed to food, water, or background environmental sources.

Our findings indicate at least three principal sites for absorption of Hg from amalgam. First, the lungs absorbed Hg as did the cilia lining the trachea because of continual breathing of intra-oral air that had a Hg vapor concentration ranging from 19–50 $\mu g/m^3$ throughout this study. In humans, approximately 80% of inhaled elemental Hg vapor is absorbed into blood and becomes available for tissue retention (15). Second, the gastrointestinal tract contained a large amount of Hg likely due to mixing of intra-oral Hg vapor, amalgam microparticles, and dissolved mercuric ions with saliva and food before swallowing. About 10% of the elemental Hg in the human gastrointestinal tract can be absorbed into blood (16). Even though the efficiency of Hg absorption in the gut is low, large amounts of Hg in feces seen in the present study may signify a substantial pathway for uptake of Hg in its elemental or vapor forms. Amalgam microparticles containing Hg would not likely be susceptible to gut absorption. Third, some tissues in the jaw such as gum mucosa and the tooth root and surrounding bone also absorbed Hg. The Hg absorbed into the jaw could be transported from bone marrow directly into blood by venous routes radiographically demonstrated for human circulation (17). The highly vascularized oral mucosa may likewise afford a route for some Hg vapor transport directly into the systemic circulation.

We are confident that the Hg uptake observed in this animal was not the result of procedural contamination during dental surgery because serial blood measurements taken for 24 h after surgery had no measurable radioactivity. This indicates that the endotracheal tube prevented inhalation of Hg vapor. Any amalgam particles not removed from the mouth by surgical rinsing would have passed through the gastrointestinal tract well before 29 days when the imaging was performed.

After the Hg released from dental amalgam is absorbed into blood, the two principal target organs of rapid accumulation are kidney and liver. Based on organ weights for kidneys (250 g) and liver (1000 g) in the adult ewe, the total Hg concentrated in the kidney in this animal was 1.86 mg, and in the liver it was 0.77 mg, after only 29 days. Even during this relatively short time, the brain and several endocrine glands (pituitary, thyroid, adrenal, pancreas, and ovary) also showed evidence of Hg accumulation from the dental amalgams.

Since Hg/silver fillings remain in human teeth for 8–10 years, this would allow an extended opportunity for body tissues to be continuously exposed to Hg. Other investigators have recently reported that Hg concentrations in autopsied human brain and kidney are significantly higher in those subjects with dental amalgams than in subjects with no amalgams (18).

Each molar tooth of this sheep contained approximately 425 mg Hg, only one-half the amount of Hg used in the average human occlusally involved molar filling. In humans, occlusally involved Hg/silver dental fillings frequently encompass additional tooth surfaces such as buccal, lingual, mesial, and distal aspects. Thus, such complex human tooth restorations have a greater surface area exposed to grinding forces from which Hg may vaporize. This is in contrast to occlusal restorations in this sheep that are limited only to the occlusal surface and are totally supported circumferentially by solid tooth structure. The natural ovine molar is multiridged for forage grinding. Technical reproduction of these ridges to their original exact functional occlusal level in the amalgam fillings was not possible. Therefore, the restorations were purposely overcarved, which created a concave occlusal surface, ensuring that the amalgams would not be functionally too high and thus subject to abnormally rapid wear. None of the Hg/silver fillings were lost from the mouth during the course of this study.

We believe the sheep is a suitable experimental model for the purpose of our investigations because it exhibits molar chewing mechanics that are similar to those of humans. Moreover, intra-oral air Hg vapor levels in the sheep are very similar to those reported in humans with the same number of amalgams (9). Although sheep may chew more than the average human does, it is likely that humans who are chronic gum chewers or who exhibit bruxism (chronic grinding of teeth) would have daily periods of chewing that are comparable to sheep fed two meals per day. The sheep body weight also compares favorably with humans, and the sheep is the most widely used obstetrical model in research today.

In other studies of sheep that were not imaged (19), we have established that Hg vaporized from dental amalgam fillings will progressively accumulate in both maternal and fetal tissues as a function of time, and tissue Hg levels will remain elevated in experiments run for as long as 140 days. Exposure of newborn lambs to milk suckled from ewes with dental amalgams results in Hg uptake into tissues of the young.

In North America 5.4% of the population display contact hypersensitivity to Hg (20). The pathogenesis of a variety of immediate or delayed Hg-induced hypersensitivity responses by the immune system resulting in glomerulonephritis has been postulated (21). Experimental evidence supports this contention because Hg is capable of inducing autoreactive T lymphocytes and specific autoantibodies resulting in Hg-induced autoimmunity (22, 23), indicating a potential for Hg to precipitate antibody-mediated tissue injury and autoimmune disease. The kidney and endocrine glands are known sites of autoimmune disorders, which brings into question the long-term implications of Hg concentration in these tissues from dental amalgams as demonstrated by the present study.

Our laboratory findings in this investigation are at variance with the anecdotal opinion of the dental profession, which claims that amalgam tooth fillings are safe. Experimental evidence in support of amalgam safety is at best tenuous (2). From our results we conclude that dental amalgams can be a major source of chronic Hg exposure. As it has been estimated that in North America 100,000 kg of Hg are used each year in dentistry (7), continuing research in this area is essential and may have an effect on public health. FJ

The authors thank J. E. Fewell, Director of the Reproductive Medicine Research Group, and the Christie Unit for the Study of Human Reproduction, for providing facilities and assistance with materials to conduct this investigation. Nuclear medicine facilities were kindly supplied by the Foothills Provincial Hospital Department of Nuclear Medicine, Calgary. Partial support was provided by a grant from the International Academy of Oral Medicine and Toxicology. The authors are also grateful to S. Naatz and M. Satchwell for their assistance with the dental surgery, S. Kelly for assistance with animal management, and C. McKay and K. Wise for assistance with the nuclear medicine imaging procedures.

REFERENCES

1. American Academy of Dental Science (1876) *History of Dental and Oral Science in America*, Samuel S. White Publ., Philadelphia
2. Enwonwu, C. O. (1987) Potential health hazard of the use of mercury in dentistry: critical review of the literature. *Environ. Res.* **42**, 257–274
3. Skinner, E. W., and Phillips, R. W. (1969) Dental amalgam alloys. Metallography of amalgam. (Chapt. 20, p. 303); Dental amalgam: technical considerations (Chapt. 22, p. 332) In *The Science of Dental Materials*, 6th Ed. W. B. Saunders Co., Philadelphia
4. Paterson, N. (1984) The longevity of restorations. *Br. Dent. J.* **157**, 23–25
5. Phillips, R. W., Hamilton, A. I., Jendresen, M. D., McHorris, W. H., and Schallhorn, R. G. (1986) Report of committee on scientific investigation of the American Academy of Restorative Dentistry. *J. Prosthet. Dent.* **55**, 736–772
6. Bauer, J. G., and First, H. A. (1982) The toxicity of mercury in dental amalgam. *Calif. Dent. Assoc. J.* **10**, 47–61
7. Rupp, N. W., and Paffenbarger, G. O. (1971) Significance to health of mercury used in dentistry: a review. *J. Am. Dent. Assoc.* **82**, 1401–1407
8. Vimy, M. J., and Lorscheider, F. L. (1985) Intra-oral air mercury released from dental amalgam. *J. Dent. Res.* **64**, 1069–1071
9. Vimy, M. J., and Lorscheider, F. L. (1985) Serial measurements of intra-oral air mercury: estimation of daily dose from dental amalgam. *J. Dent. Res.* **64**, 1072–1075
10. Patterson, J. E., Weissberg, B., and Dennison, P. J. (1985) Mercury in human breath from dental amalgam. *Bull. Environ. Contam. Toxicol.* **34**, 459–468
11. Hampson, E. L. (1980) Amalgam restorations. In *Textbook of Operative Dentistry*, 4th Ed., pp. 39–63, Wm. Heineman Medical Books Ltd., London
12. Vimy, M. J., Luft, A. J., and Lorscheider, F. L. (1986) Estimation of mercury body burden from dental amalgam: computer simulation of a metabolic compartmental model. *J. Dent. Res.* **65**, 1415–1419
13. Anger, H. O. (1967) Radioisotope cameras. In *Instrumentation in Nuclear Medicine* (Hine, G. J., ed) Vol. I, pp. 485–552, Academic Press, New York

14. Sorenson, J. A., and Phelps, M. E. (1987) The Anger camera: basic principles. In *Physics in Nuclear Medicine,* 2nd Ed., pp. 298–317, Grune & Stratton Inc., Orlando, Florida
15. Nielsen-Kudsk, F. (1965) Absorption of mercury vapor from the respiratory tract in man. *Acta Pharmacol. Toxicol.* **23,** 250–262
16. Task Group on Metal Accumulation (1973) Accumulation of toxic metals with specific reference to their absorption, excretion and biological half-times. *Environ. Physiol. Biochem.* **3,** 65–107
17. Stortebecker, P. (1967) Dental significance of pathways for dissemination from infectious foci. *J. Can. Dent. Assoc.* **33,** 301–311
18. Nylander, M., Friberg, L., and Lind, B. (1987) Mercury concentrations in the human brain and kidneys in relation to exposure from dental amalgam fillings. *Swed. Dent. J.* **11,** 179–187
19. Vimy, M. J., Takahashi, Y., and Lorscheider, F. L. (1990) Maternal-fetal distribution of mercury (^{203}Hg) released from dental amalgam fillings. *Am. J. Physiol.* In press.
20. North American Contact Dermatitis Group (1973) Epidemiology of contact dermatitis in North America: 1972. *Arch. Dermatol.* **108,** 537–540
21. Druet, P., Bernard, A., Hirsch, F., Weening, J. J., Gengoux, P., Mahieu, P., and Berkeland, S. (1982) Immunologically mediated glomerulonephritis induced by heavy metals. *Arch. Toxicol.* **50,** 187–194
22. Hirsch, F., Kuhn, J., Ventura, M., Vial, M-C., Fournie, G., and Druet, P. (1986) Autoimmunity induced by $HgCl_2$ in Brown-Norway rats. 1. Production of monoclonal antibodies. *J. Immunol.* **136,** 3272–3276
23. Pelletier, L., Pasquier, R., Hirsch, F., Sapin, C., and Druet, P. (1986) Autoreactive T cells in mercury-induced autoimmune disease: in vitro demonstration. *J. Immunol.* **137,** 2548–2554

Received for publication June 23, 1989.
Accepted for publication August 28, 1989.