SPECIAL FLASH EDITION

MERCURY RELEASED FROM DENTAL "SILVER" FILLINGS CAUSES PATHOLOGY IN THE KIDNEY AND IN ORAL AND GUT MICROFLORA

We consider the events so significant that we have decided to publish an abbreviated version of the Newsletter in order to provide you with this extremely important information in the most timely manner.

A new study by Vimy and Lorscheider validating the use of intra-oral mercury vapor readings as a predictor of mercury accumulation in human tissues has just been published. (copy attached) A major investigative report on the amalgam issue was published in the Chicago Tribune on August 15, 1990 (copy attached), and on the same date the following two abstracts demonstrating pathology were published in the current issue of "The Physiologists":

Vimy M.J., Boyd N.D., Hooper D.E. and Lorscheider F.L.

Glomerular filtration impairment by mercury released from dental "silver" fillings in sheep.
Departments of Medicine Pathology and Physiology, University of Calgary, Alberta, Canada.

In humans mercury (Hg) vapor is released from silver amalgam fillings which contain 50% Hg by wt. When such fillings are placed in sheep teeth, the kidneys will concentrate amalgam Hg at levels ranging from 5-10 ug Hg/g renal tissue 4-20 weeks after placement (FASEB J. 3:2641-2646, 1989; Am J. Physiol. 258:R939-945, 1990) In another report (publ. elsewhere) we demonstrate that the monkey kidney will likewise concentrate large amounts of amalgam Hg. For the present study occlusal fillings (12, total Hg 5100 mg) were placed in each of six adult female sheep under general anesthesia, using standard dental procedures. Glass ionomer occlusal fillings (12) were inserted in two control sheep. At several days prior to dental surgery, and at 30 and 60 days after placement of fillings, renal function was evaluated by glomerular filtration rate (GFR, inulin clearance) and by blood and urine electrolytes, urea and proteins. Average GFR of 69.5 ± 7.2 ml/min before amalgam placement was reduced to 32.3 ± 8.1 ml/min by 30 days and remained low at 27.9 ± 8.7 ml/min after 60 days. GFR did not change in controls. After amalgam replacement urine Na⁺ increased steadily from 24.8 ±7.7 to 82.2 ± 20.3 mmoles/L at 60 days. Urine K⁺ also increased. Levels of urea and total protein increased from 0-60 days after amalgam. Thus, amalgam Hg levels in kidney are sufficient to significantly reduce GFR, either by reducing renal blood flow or by alteration of the glomerular membrane. Electrolyte, urea and protein patterns in urine are also consistent with impaired renal tubular reabsorption.
Summers A.O., Wireman J. Microbiology Dept., University of Georgia, Athens, GA; Vimy M.J. and Lorschieder F.L. Depts of Medicine and Physiology, University of Calgary, Alberta, Canada.

Increased Mercury resistance in monkey gingival and intestinal bacterial flora after placement of dental "silver" fillings.

Mercury (Hg) vapor is continuously released from silver amalgam fillings in humans. However, the bioavailability and toxicological relevance of the Hg exposure is uncertain. Since an increase in Hg resistant bacteria in response to Hg contamination of soil or water is an indication of bioavailability of Hg in the environment, we examined whether the incidence of such bacteria in the gingival and fecal flora is altered following placement of amalgam tooth fillings. Occlusal fillings (16, total Hg 1500 mg) were inserted into two adult male cynomolgus monkeys under general anesthesia, using standard dental procedures. Duplicate samples (12) of fecal and gingival microbial flora were taken from each monkey during 10 days prior and 30 days after amalgam placement. Samples were cultured for Gram positive facultative oral bacteria and both Gram negative and Gram positive facultative fecal bacteria. Primary isolates were screened to determine the proportion resistant to Hg and to arsenate (As) and tetracycline (Tc), agents to which bacterial resistance is found in nature. While As and Tc resistance were detected continuously in all cultures, Hg resistance was undetectable until the 10th day after amalgam placement. Thereafter, levels of Hg resistance in gingival and fecal flora ranged from 1 to 100%, averaging 30% in both monkeys until termination. From the 3rd-30th day total fecal Hg excretion averaged 300 μg/animal/day. Thus, ingested Hg is sufficiently bio-available to select for a substantial increase in the proportion of Hg resistant bacteria in both the oral cavity and the intestine. Since Hg resistant bacteria convert Hg(II) or methyl-Hg(I) to volatile, lipid soluble Hg (0) (Summers, Ann Rev Microbiol 40:607-34, 1986), the increased incidence of such bacteria in flora may influence the pharmacodynamics and toxicity of ingested Hg from dental amalgam.

BIO-PROBE COMMENT: It is interesting to note that Swedish researchers have found high levels of mercury in the gut lining of patients with Crohn’s disease. A more complete study of Crohn’s patients is presently in progress. It would appear that the possibility exists that mercury from dental fillings may be an etiological factor in Crohn’s disease.

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Vimy M.J. and Lorschieder F.L.

Dental amalgam mercury daily dose estimated from intra-oral vapor measurements: A predictor of mercury accumulation in human tissues


ABSTRACT: Recent misconceptions regarding Hg exposure from dental amalgams have been based on several questionable assumptions. The present paper reexamines earlier estimations of Hg daily dose from dental amalgam in order to elaborate and refine the mechanical and volumetric parameters of open-mouth Hg vapor sampling. This facilitates a comparison with the physiological parameters of human respiration. Corrections for the sampling factors of flow rate and sampling dilution, and the respiratory factor of Hg accumulation in the closed mouth between oral inhalations, reduce our original daily dose estimates by approximately 50%. Application of a general pharmacokinetic model with our revised Hg daily dose estimates results in predictions for brain, kidney, blood, and urine which approximate tissue Hg measurements reported in subjects with dental amalgams. When tissue Hg predictions are made based upon alternate Hg daily dose estimates proposed by other investigators, the resultant error was as much as 11-fold lower than were actual tissue measurements in humans. It is concluded that intra-oral air Hg vapor measurements can be useful for estimating Hg daily dose and tissue Hg levels. (Address reprint requests to Dr. F.L. Lorschieder, Dept. Medical Physiology, Faculty of Medicine, University of Calgary, 3330 Hospital Drive N.W., Calgary, Alberta, Canada T2N 4N1.)

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OTHER REVIEWS/ABSTRACTS OF INTEREST

Weiner J.A., Nylander M. and Berglund F.

**Does mercury from amalgam restorations constitute a health hazard?**
The Science of the Total Environment, 1990 (In publication)

**ABSTRACT:** Amalgam is the most extensively used implant material in dentistry. There have been no clinical trials of this substance and there are no epidemiological studies that allow any conclusions on the safety of amalgam fillings. Amalgam restorations continuously emit mercury vapour, which is absorbed in considerable quantities via the lungs. A comparison with dose-effect relationships, obtained in occupational studies, for certain effects on the kidneys and central nervous system (CNS), suggests that individuals with unusually high emission of mercury from amalgam fillings are at risk. It is unclear whether or not clinically significant effects could be expected. The limited sensitivity of available occupational studies, together with insufficient knowledge of possible host factors affecting resistance to mercury, implies that other more severe effects in susceptible individuals cannot be excluded. Information on long-term effects on organs other than brain or kidney is sparse. Animal studies suggest the possibility of immune system reactions to mercury, i.e. development of autoimmunity, that are not primarily dose-dependent, but rather depend on genetic susceptibility. **From a toxicological point of view, amalgam is an unsuitable material for dental restorations.** BIO-PROBE NOTE: This review paper will be covered in more detail in a subsequent issue.

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The following three abstracts are from the 29th Annual Meeting of the Society of Toxicology as published in The Toxicologist, Vol. 10, No. 1, Feb. 1990:

**Abstract #1081, Page 271:**

**Oral 2,3-Dimercaptosuccinic acid (DMSA) for the management of moderately severe childhood lead poisoning.**

DMSA is a promising and relatively specific oral chelator for the treatment of Pb, Hg and As intoxication. We have completed a controlled clinical investigation of DMSA in 23 children with blood lead concentrations (BPb's) of 50-69 μg/dl to: a) compare the efficacy and safety of a 5-day course with DMSA (N=19) to that of iv CaNa2EDTA (N=4); and, b) establish an out-patient DMSA dose regimen capable of preventing a subsequent rebound in BPb. In-hospital, the mean BPb's declined by 61% in response to DMSA (1050 mg/m^2/d tid) and 46% with CaNa2EDTA (1000 mg/m^2/d bid) (P < 0.05). Red cell ALA-D and urinary Pb, ALA, and coproporphyrin also responded favorably. Upon discharge, those in the DMSA group received either 0, 350 or 700 mg/m^2/d (bid) for 14 days. The latter dose, but not less, was effective in preventing a rebound in BPb. DMSA was extremely well tolerated, even in 7 children who received oral iron and 2 who had severe G6PD deficiency. Thus, DMSA should ultimately simplify the clinical management of childhood lead poisoning.

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**Abstract #1083, Page 271.**
Zalups R.K., Gelein R.M.* and Cernichiari E. Mercer Univ. School of Med., Div. of Basic Medical Sciences, Macon GA and *Univ of Rochester Med. Ctr., Dept. of Biophysics, Rochester, NY.

**2,3-Dimercapto-1-Propanesulfonic Acid (DMPS) as a rescue agent for the nephropathy induced by mercuric chloride.**

The aim of the present study was to determine if DMPS can serve as a rescue agent for the acute nephropathy induced by mercuric chloride (HgCl₂). Uninephrectomized (NPX) and sham-operated (SO) male Sprague-Dawley rats were given a nephrotoxic dose of HgCl₂ (2.5 μmol/kg, i.v.) 11 days after surgery. One hour after the HgCl₂ was administered, both the NPX and SO rats received either 0, 10 or 100 mg/kg dose of DMPS (i.p.). The degree of rescue from the effects of HgCl₂ was determined by measuring the urinary excretion of several plasma solutes and five cellular enzymes (including LDH) for 24 hours before and 24 h after treatment with HgCl₂. Several renal functional tests were also performed. Moreover, a histopathological examination of the kidneys from all the animals was performed 24 h after the injection of HgCl₂. In the NPX and SO rats that received the 100 mg/kg dose of DMPS, there was no evidence of
any nephrotoxic effects of HgCl₂. However, there was evidence of some renal cellular injury in the NPX and SO rats that received the 10 mg/kg dose of DMPS, with more severe damage in the SO rats. These findings indicate that DMPS may be an effective rescue agent against the acute nephrotoxic effects of HgCl₂.

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Abstract #1272, page 318.
Jones D.P. and Hagen T.M. Dept. Biochem. and Winship Cancer Ctr., Emory Univ. Atlanta, GA.

Bioavailability of dietary glutathione (GSH).

Studies were performed with young adult male rats to determine whether GSH added to the semi-synthetic (GSH-free) AIN-76 diet is bio-available as intact GSH in the plasma. Plasma GSH was measured by rapidly derivatizing deproteinized plasma with iodoacetic acid and 1-fluoro-2,4-nitrobenzene to allow quantitation by high performance liquid chromatography. Added GSH (2.5 to 50 mg/g diet) resulted in increased plasma GSH concentration that reached a maximum after about 1 h and remained elevated above normal for at least 3 h. Addition of an equivalent dose of glutamate, cysteine and glycine did not result in an increase in plasma GSH. Rats treated with acivicin to inhibit GSH breakdown and L-histidinone-SR-sulfoximine to inhibit GSH synthesis also had increased plasma GSH concentration following eating of GSH-supplemented food. Studies of isolated, vascively perfused small intestinal segments showed that the intestine has a reductive mechanism to convert GSSG to GSH. Thus, supplementation of diet results in absorption of intact GSH and can be used to increase plasma GSH concentration. BIO-PROBE COMMENT: Some nutritionists are recommending use of the individual amino acids as a means of offsetting the high cost of Glutathione supplements. This research contradicts the use of individual amino acids to raise plasma GSH AND GSHs.

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Abstract #1405, Page 352.

Toxicology and quantitative risk assessment for mercury.

Mercury occurs in elemental, inorganic and organic forms and is known to induce a large array of toxic effects including renal toxicity, neurotoxicity, and gastrointestinal disorders. Exposure to mercury via inhalation, oral, dermal, and to a lesser extent iatrogenic routes, are all documented, but the inhalation and oral routes are environmentally more relevant. For exposure to elemental mercury, the major site of toxicity is the central nervous system. Studies addressing the toxic effects of mercury following inhalation exposure were evaluated for derivation of an inhalation reference dose (RfD) for use in quantitative risk assessment. Data from epidemiologic studies showed that long term occupational exposure to mercury levels of 0.18 mg/m³ resulted in an increased incidence of neuropsychiatric symptoms (insomnia, nervousness) but that a concentration of 0.10 mg/m³ represented a No-Observed-Adverse-Effect-Level (NOAEL). Animal studies indicated that inhalation exposure to 0.5 mg Hg/m³ throughout gestation produced evidence of developmental toxicity. Analysis of the data base and application of RfD methodologies provided a tentative life-time exposure value of 4 µg Hg/m³.

BIO-PROBE COMMENT: We have to assume that the epidemiologic studies referred to in this abstract are those conducted at chlor-alkali plants. Participants in these studies were exposed to chlorine as well as mercury vapor, a fact that was discounted by the researchers who conducted the studies. There is however scientific information demonstrating that when chlorine and mercury are present in the same breathing atmosphere, less mercury is absorbed and intoxication profiles result in gastroenteric disorders instead of the neurological symptoms normally caused by breathing mercury vapor. It would therefore seem plausible that the tentative life-time exposure value of 4 µg Hg/m³ arrived at by Young & Weil would be lower if the chlorine effect had been considered in the original epidemiological studies. Where does this leave the amalgam bearer inhaling an average daily dose of 9.0 µg/day as indicated by Vimy & Lorscheider?