NIDR/NIH PANEL VIOLATES MANDATE!
NATIONAL INSTITUTES OF HEALTH
TECHNOLOGY ASSESSMENT CONFERENCE STATEMENT
EFFECTS AND SIDE EFFECTS OF DENTAL RESTORATIVE MATERIALS
26-28 AUGUST 1991

THE PANEL'S STATEMENT

After announcing its "consensus opinion" at a press conference on 28 August 1991, the very first question a reporter asked of the NIDR/NIH Technology Assessment Panel on dental materials was: "How can you give dental amalgam a clean bill of health in one breath and in the very next breath admit that you have no scientific evidence to support that position?"

THE PANEL'S OWN CONTRADICTIONS

The Panel was unable to provide a satisfactory answer to that question- with good reason! At the opening session on the morning of 26 August the chairman of the panel, Dr. William D. McHugh of the Eastman Dental Center, instructed the Panel to base its findings solely on scientific evidence. The very same William D. McHugh, D.D.S., announced the Panel's conclusion at the press conference. It was: "Although mercury vapor is released from dental amalgam, the quantities released are very small and DO NOT CAUSE VERIFIABLE ADVERSE EFFECTS ON HUMAN BEINGS." (pg 19, lines 12-14 of the NIH document distributed to the press and attenders.)

Dr. McHugh also read a statement added after that conclusion: "While current evidence supports the concept that existing dental restorative materials are safe, it must be recognized that the supporting data are incomplete." [BIO-PROBE NOTE: The qualifying statement was added to the conclusion after this writer pointed out the contradictions to the conclusion in the Panel's document.]

"Recognized" by whom- certainly not by the NIH Panel, since their second statement contradicts their conclusion! By specific direction, the conclusions were to be made on the basis of science, not unsubstantiated opinions.

Prior to announcing the conclusion, Dr. McHugh also made a number of other conflicting statements at the press conference (not placed in quotes as my notes do not contain the full, specific wording contained in the written document):

- Dental amalgam releases very small amounts of mercury over many years.
- Data on amalgam contribution to total body burden is still unclear. The relative importance of this is still not determined to their (the Panel's) satisfaction.
- There is a paucity of data. This may be due to various factors, such as the inability of dentists to recognize the adverse effects of mercury.
- Under certain conditions, mercury exposure from dental amalgam fillings can cause systemic reactions.
- The risk/benefit ratio can not be calculated, due to the lack of data.
- Dr. Michael Kashgarian, a non-dentist member of the Panel, stated that we have assumed that dental materials...
materials are safe, because of their long use. He also stated that dental materials should be subjected to the same scrutiny as are medical devices.

It is going to be very difficult for the Panel to reconcile their "conclusion" to these stated conditions. If that isn't enough to deal with, the following are statements in their own written document.

**FURTHER WRITTEN CONTRACTIONS FROM THE PANEL**

The following quote is taken directly from the Panel's comments on risk/benefit ratios (page 16, lines 14-17): "Lack of reliable quantitative estimates of the risks and benefits of the various dental materials discussed at this conference preclude calculation of benefit/risk ratios. The paucity of data concerning predictable risks associated with restorative dental materials was striking."

The benefits of various dental restorative materials were clearly stated during the conference and in the Panel's document. As indicated in the second sentence of the above statement, the risks have not been fully investigated, which precludes conclusions on risk/benefit statements. The choice of the word "preclude" in this statement is interesting. By definition it means: "To make impossible by necessary consequence" (Webster's New Collegiate Dictionary). The Panel obviously violated their position by arriving at a conclusion that, in their own words, was unjustified.

If that isn't bad enough, the Panel provided further evidence of their misrepresentation. In presenting the future directions for research on materials for tooth restorations (page 18), the Panel made five recommendations:

1. "Carry out long-term epidemiological and multidisciplinary studies to determine whether there is a link between restorative materials and the incidence of local and/or systemic effects, and establish benefit/risk ratios of these materials."

2. "Determine the long-term effects of dental restorative materials on the developing organism."

3. "Develop new methods and materials for restoring teeth such as utilizing bonding agents with improved composites, amalgams, and new biocompatible materials that minimize removal of healthy tooth structure, release cariostatic agents, and reduce the risk of side effects."

4. "Determine the composition, degradation, release pattern, and pharmokinetics of all restorative materials and their components under a variety of conditions. The effects of such materials and their components on cells, tissues, and organs should be established."

5. "Investigate the cellular and molecular mechanisms by which mercury at different concentrations damages different types of cells (e.g. CNS, kidney, oral epithelium, etc.)."

It is clearly obvious that these recommendations contradict a conclusion that the amounts of mercury vapor released from dental amalgam fillings "do not cause verifiable adverse effects on human beings", which is a concise statement indicating confirmation based on scientific evidence.

**EXPERT TESTIMONY**

The fourteen members (3 physicians, 3 Ph.D.'s, 2 with other degrees, and 6 dentists, including the chairman) of the National Institutes of Health Technology Assessment Panel on the Effects and Side Effects of Dental Restorative Materials heard expert testimony from twenty-two speakers. Of these, five speakers addressed side effects specifically related to dental amalgam.

One of these five addressed only oral mucosa and skin reactions related to dental amalgam, particularly from an allergic perspective. Another addressed only the potential teratogenic effect on unborn babies. A third speaker addressed only the mercury vapor release from dental amalgam.

Only two speakers addressed the potential toxic effects of mercury exposure from dental amalgam. One of these, Dr. John W. Reinhardt, presented the documented human autopsy studies demonstrating a correlation between the amount of amalgam fillings present and levels of mercury in human brain and kidney tissues. He also presented documented studies connecting mercury exposure to Alzheimer's Disease and Parkinson's Disease.

Dr. Michael F. Ziff presented nine studies demonstrating the pathologic effect of dental amalgam on periodontal structures, including the transfer of amalgam mercury into these tissues, as well as confirmation that such damage is a classic feature of mercury exposure. He also presented three studies connecting dental amalgam mercury to the occurrence of Oral Lichen Planus, including the transfer of amalgam mercury into these lesions, as well as three studies demonstrating the relation between the presence of amalgam fillings and an increased occurrence of allergic responses to mercury.
Dr. Ziff also presented three epidemiologic studies (all of which included age-matched controls without amalgams) showing an influence of dental amalgam on various disease states, oral and systemic, and two Swedish epidemiologic studies (neither of which included any controls without amalgams) showing no influence on certain clinical symptoms.

All of these studies were published in standard dental and medical journals.

Dr. Ziff continued with reports of the rapidly increasing numbers of case histories related to adverse health effects from dental amalgam fillings, including those published in journals and a large number that have recently been filed with the Food and Drug Administration as Amalgam Adverse Reaction Reports (recently confirmed with Dr. Singleton of the F.D.A. by a reporter). [BIO-PROBE NOTE: Dr. Gregory Singleton, Chief Dental Officer of the F.D.A. was a member of the planning committee for this NIH conference.]

In spite of the fact that all of the evidence provided by Dr. Ziff and Dr. Reinhardt was derived from reputable and "verifiable" sources, none of this information was included in the Panel’s report or, more to the point, considered in their formal conclusion.

DISCUSSION

It is clear from the information provided herein, that the NIH Panel did not develop their "consensus opinion" on scientific information and therefore violated their mandate from the NIH, to say nothing of their obligation to the public health. There is absolutely no question that their conclusion on the safety of dental amalgam, and their statements to the press and public, are misleading and constitute misrepresentation.

At the conference, the Panel was informed that mercury toxicology experts (W.H.O. and U.S.E.P.A.) have concluded that no amount of exposure to mercury vapor can be considered totally harmless. They were also informed that these experts have concluded that subjects with dental amalgam fillings absorb more mercury from these fillings than from all other non-occupational sources combined, including fish in the diet. They were also informed that current occupational mercury exposure standards utilized to defend the use of dental amalgam are based only on the appearance of clinically observable signs and symptoms, and do not consider mercury damage up to that point; nor do they consider susceptible population sub-groups, such as the elderly, children, or unborn babies.

If an ultra-conservative position was desired, the panel should have concluded that the health effects of the now proven chronic mercury exposure from dental amalgam fillings are uncertain at this time. In view of the scientific evidence provided to the Panel, and now on record with the National Institutes of Health, even that conclusion is open to challenge. But to flatly conclude that this mercury exposure does not cause adverse effects on human beings is patently inexcusable!

WHAT TO DO?

This writer, Michael F. Ziff, D.D.S., has already written a letter to Dr. John H. Ferguson, the Director of the NIH Office of Medical Applications of Research, outlining in one page the above information and requesting that the NIH reject the findings of the Panel and appoint another panel that will base its findings on scientific evidence as directed. Copies of this letter were sent to Dr. Bernadine Healy, the Director of the National Institutes of Health, and Secretary Louis W. Sullivan of the U.S. Department of Health and Human Services. [Addresses below.]

It is fervently hoped that others will do the same and also voice their feelings, along with the documentation contained herein, to their elected representatives in the U.S. Congress. Our responsibility to the public health demands no less.

If the National Institutes of Health fails to correct this matter, we will have no choice but to demand a congressional investigation of the issue!!!

WHO TO CONTACT:

John H. Ferguson, M.D.
Director, Office of Medical Applications of Research
National Institutes of Health
Building 1, Room 260.
Rockville Pike
Bethesda, MD. 20892-0001
Dr. Bernadine Healy  
Director. National Institutes of Health  
Building 1, Room 126  
Rockville Pike  
Bethesda, MD. 20892-0001  

Secretary Louis W. Sullivan  
Health and Human Services  
200 Independence Ave. S.W.  
Washington, DC 20201

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EFFECTS AND SIDE EFFECTS OF DENTAL RESTORATIVE MATERIALS  
NIDR/NIH-OFFICE OF MEDICAL APPLICATIONS OF RESEARCH  
TECHNOLOGY ASSESSMENT CONFERENCE  
MICHAEL F. ZIFF, D.D.S.

DOCUMENTED CLINICAL SIDE EFFECTS TO DENTAL AMALGAM

INTRODUCTION

As all dental restorative materials are foreign substances, their potential for producing adverse health effects is determined by their relative toxicity and bioavailability, as well as host susceptibility. Adverse health effects to dental restoratives may be local in the oral cavity or systemic, depending on the ability of released components to enter the body and, if so, their rate of absorption.

The medical scientific community is now in general agreement that patients with dental amalgam fillings are chronically exposed to mercury, that the average daily absorption of mercury from dental amalgam is 3-17 micrograms per day, and that the amalgam mercury absorption averages 1.25-6.5 times the average mercury absorption from dietary sources (Environmental Health Criteria 118: Inorganic Mercury. World Health Organization. Geneva. 1991). The health significance of this chronic mercury exposure is now being investigated by a number of medical research groups.

ORAL ADVERSE EFFECTS TO DENTAL AMALGAM

There are a number of published investigations of oral side effects to dental amalgam.

Investigations have documented the harmful effects of various dental materials, including amalgam, on dental pulp tissue. This topic will not be addressed as proper handling and pulpal protection have minimized this problem.

It has been well documented in the dental literature that electrical currents are generated when amalgam fillings are placed in teeth. Investigations conducted in Sweden failed to find a correlation between the degree of electrical current generated by dental amalgams and the occurrence of general oral and systemic symptoms thought to be attributed to "oral galvanism". There have been no investigations of the potential impact of these vagrant currents on oro-facial neuromuscular function.

EFFECTS OF DENTAL AMALGAM ON PERIODONTAL DISEASE

It has been well documented and referenced that classic signs of chronic mercury exposure include gingivitis, alveolar bone loss, loosening and loss of teeth, bruxism, metallic taste, oral ulceration, and excessive salivation. (Shafer, W.G.; Hine, M.K.; and Levy, B.M. 1958.)

A number of early reports attributed periodontal pathology to electrogalvanism resulting from dissimilar metals. Phillips has stated: "When contacting dissimilar base metal alloys are present in the oral cavity, spectacular examples of corrosion and soft and hard tissue destruction have been reported." This position was affirmed by Lemons at the 1984 NIDR Workshop on the Biocompatibility of Metals in Dentistry.

The first formal investigation of the effect of dental amalgam on the periodontal structures was by Zander (1957). Clinical and histologic examination confirmed inflammatory response in gingival tissue adjacent to amalgam fillings. The author concluded: "Clinical observations of a chronic inflammatory reaction of the gingival tissues around restorations are confirmed by the present investigation"; "There is no doubt that not only dental calculus but also the materials used in restorative dentistry may be a contributing factor in
gingival disease"; and "In patients in whom such clinical symptoms as chronic gingivitis, recurrent necrotizing ulcerative gingivitis and periodontal pockets do appear, such conditions can sometimes be treated successfully only by removal of gingival tissues to below the margin of dental restorations."

These findings were confirmed by App (1961), who concluded: "The amalgam restoration produced a chronic inflammation of the adjacent gingival tissues. The tissue response to amalgam is the same as the tissue response to calculus. Since calculus is an etiological factor in periodontal disease and the sulcus epithelium responds to amalgam as it does to calculus, these restorative materials must also be considered etiologic factors in periodontal disease."

At this point it was not certain if the adverse effects were a result of plaque accumulation on the amalgam fillings or from materials in the fillings themselves. Trott and Sherkat (1964) conducted a controlled clinical study on 82 medical and dental students. Oral hygiene was strictly monitored and the study criteria ruled out a number of factors which can cause gingival disease, either alone or in combination. Thirty-five of the 82 subjects had significant gingival disease. Results showed a correlation between gingival disease and amalgam fillings as compared to contralateral amalgam-free sites in the same subjects.

These findings were confirmed by Sanchez Sotres and associates (1969), who conducted a histologic analysis of gingival tissue adjacent to amalgam fillings and of control tissues. The inflammation intensities were 1.6 for control tissues, 1.8 for tissues adjacent to polished amalgam, and 2.5 for tissues adjacent to unpolished amalgam. The authors concluded that the inflammation resulted from chemical factors, rather than the mechanical characteristics or texture of the restorations.

Trivedi and Talim (1973) also conducted a histologic analysis of gingival tissue adjacent to dental restoratives, including amalgam. An inflammatory reaction occurred at 62.5% of the tissue sites in contact with amalgam and proliferation of epithelium occurred in 68.7% of the sites adjacent to amalgam.

Turgeon and associates (1972) conducted a clinical investigation on sixteen children between the ages of 11 and 17. Thirty amalgam Class II fillings provided 32 experimental papilae and 44 proximal surfaces. Corresponding contralateral sites without amalgam fillings served as controls. Their findings were: "Clinical procedures involved in restoring posterior teeth with Class II amalgam restorations caused an immediate gingival inflammation characterized by erythema and increased crevicular depth, but without significant migration of the epithelial attachment." After eight months the experimental areas showed significantly more erythema than the control areas.

Freden and associates (1974) biopsied gingival tissue adjacent to dental amalgam fillings and control tissue in contact with intact tooth structure. The tissues were analyzed for mercury content by flameless atomic absorption spectrophotometry. All of the biopsies which had been in contact with amalgam fillings showed markedly higher mercury contents than did the control biopsies. Mercury content in subject sites was 19-380 mcg/gm (mean=147) and 1-10 mcg/gm (mean=3) in control sites.

Using three independent criteria, Goldschmidt and associates (1976) confirmed that 10(-4) to 10(-6) molar concentrations of corrosion product ions liberated from dental amalgam produce injurious effects on human gingival fibroblasts. Inhibition of amino acid incorporation into protein-like material was seen with eluates of amalgam and with ionic solutions of most metals comprising dental amalgam. Mercury, silver, copper, and zinc ions in 10(-5) molar concentrations caused damage. Compound cytotoxic effects occurred at 10(-6) molar concentration.

Fisher and associates (1984) confirmed several earlier reports in finding alveolar bone resorption to be significantly higher under Class II amalgam fillings than in control sites after four years. Fifty-four paired interproximal amalgam fillings, extended subgingivally versus unextended, were placed in 43 subjects and compared to control sites. The rate of alveolar crest resorption for the unextended fillings was similar to that of controls but was significantly higher for those amalgams extended subgingivally.

Siblerud (1990) compared oral health parameters of 50 subjects with amalgam fillings to 51 subjects without amalgams. Amalgam subjects displayed more gingival bleeding, periodontal disease, metallic taste and foul breath than did the amalgam-free group. An additional 86 subjects were surveyed before and after amalgam removal. In this group, 86% of the oral cavity symptoms were either eliminated or improved after amalgam removal.

**DENTAL AMALGAM AND ORAL LICHER PLANUS**

Finne and associates (1982) tested 29 patients with oral lichen planus for contact allergy to dental materials and found 62% of the subjects to be allergic to mercury. All of the subjects had amalgam fillings.
The amalgams were removed in four of the subjects, with total remission of the lesions occurring in three of these and considerable improvement in the fourth.

Mockaven and associates (1984) found 16% of 67 subjects with oral lichen planus to be allergic to mercury. Of the 67 subjects, 64 had amalgam fillings.

Boleska and associates (1990) found high levels of mercury in lichen planus lesions adjacent to amalgam fillings.

**DENTAL AMALGAM AND MERCURY ALLERGY**

Djerassi and Berova (1969) investigated the incidence of allergy to dental amalgam and its components in 180 subjects with amalgam fillings and 60 controls with no amalgams. None of the controls exhibited positive reactions to amalgam or its components. Of the subjects, 16.1% exhibited an allergic response to amalgam and 11.0% were allergic to mercury. Of subjects with amalgam fillings for up to five years, 5.8% showed positive reactions while 22.52% of the subjects with amalgam fillings for more than five years had positive reactions.

White and Brandt (1976) patch tested 396 dental students and found a weak correlation of increasing incidence of mercury allergy to length of time subjects had amalgam fillings. Of subjects having amalgam fillings for five years or less, 3.8% had positive mercury patch tests while 6.0% of those with amalgam fillings for more than five years were positive.

Miller and associates (1987) tested 171 dental students and found a greater correlation to the number of amalgam fillings subjects had than to the length of time the fillings were in place. The percentage of subjects testing positive to mercury ranged from 26.9%-38.7% by class.

**CLINICAL REPORTS OF DENTAL AMALGAM AND SYSTEMIC PATHOLOGY**

The medical scientific community is now aware of the chronic exposure to mercury patients receive from dental amalgam fillings. Controlled investigations are now underway and some preliminary results have appeared in medical and dental journals. Attempts to correlate the pathophysiologic effects of mercury from dental amalgam to measurements of mercury in blood or urine will not be addressed as the National Institute of Dental Research formally acknowledged these parameters to be invalid in 1984. (NIDR. Workshop: Biocompatibility of Metals in Dentistry. JADA. 109:469-71. 1984.)

Ahquist and associates (1988) reported no difference in 30 specific questionnaire symptoms in 1024 women with amalgam fillings. The subjects were divided into two groups, one with less than five surfaces of amalgam and the other with 20 or more surfaces of amalgam. The number of amalgam surfaces was determined by panoramic x-rays and there was no control group of amalgam-free references.

Lavstedt and Sundberg (1989) surveyed 1204 subjects with 14 questions and 4 clinical tests. Subjects were divided into five groups with mean number of amalgam surfaces being 6.4, 21.1, 32.6, 39.2, and 37.9. No positive correlations were found.

Siblerud (1989) compared psychological parameters of 50 subjects with amalgam fillings (average 10.1 amalgams in males and 9.8 in females) to 51 subjects with no amalgam fillings. Two mental health questionnaires and two laboratory tests to evaluate tissue mercury burden were utilized. An additional 86 subjects were surveyed by health questionnaire after amalgam removal. The findings suggested that inorganic mercury exposure from dental amalgam fillings does adversely effect the mind and emotions.

In a second study, Siblerud (1990) investigated cardiovascular parameters in 50 subjects with and 51 subjects without amalgam fillings. Subjects with amalgams had significantly higher blood pressure, lower heart rate, lower hemoglobin, and lower hematocrit. Hemoglobin, hematocrit, and red blood cells were significantly lower when correlated to increased levels of urine mercury. The amalgam subjects had a greater incidence of chest pains, tachycardia, anemia, fatigue, tiring easily, and being tired in the morning.

In a preliminary study on 2 subjects, Eggleston (1984) reported alterations of T-lymphocyte percentages after removal of amalgam fillings and upon re-insertion of amalgams.

Mackert (1991) investigated total number of leukocytes, percentage of lymphocytes, absolute number of lymphocytes, and lymphocyte subset populations in 21 subjects with an average of 7.8 (+/- 3.7) occlusal surfaces of amalgam and 16 subjects with no amalgam fillings. He found no immune system differences in subjects with and without amalgam fillings.

Molin (1990) investigated a number of health parameters with blood tests and found no correlations to the presence of amalgam fillings. The investigation was conducted in four parts.
Part I compared twelve subjects with a mean number of 34.6 amalgam surfaces to twelve controls with a mean number of 30.5 amalgam surfaces. All of the controls had amalgam fillings. The twelve subjects had symptoms thought to be attributed to oral galvanism.

Part II studied two groups of dental personnel with no indication that any subject in either group had no amalgam fillings. Eighteen subjects in the high urine mercury group (HUM) had a mean urinary value of 6.5 mcg/g creatinine and a mean number of 39.9 amalgam surfaces. Thirteen subjects in the low mercury urine group (LUM) had a mean urinary value of 2.0 mcg/g creatinine and a mean number of 31.5 amalgam surfaces.

Part III consisted of eight recent immigrants to Sweden, none of whom had ever had mercury amalgam dental fillings and were in need of dental care. Amalgam fillings (16.1 mean surfaces) were placed in one sitting in each subject and the subjects were followed for three months. After amalgam placement, the erythrocyte glutathione peroxidase level in the study's lone female elevated to twice the level of the other seven subjects, so she was dropped from the study. The remaining subjects exhibited a significant increase in plasma selenium and urine beta2-microglobulin, but both indicators remained within the reference interval. During the short duration of this study, the plasma and urine mercury levels of the subjects failed to reach levels found in the subjects in the other three studies.

In Part IV, all amalgam fillings were removed from ten healthy subjects with a mean number of 19.9 amalgam surfaces. Parameters were compared before amalgam removal to twelve months after amalgam removal and to a control group of ten subjects with a mean number of 24.7 amalgam surfaces.

Dr. Molin concluded that dental amalgam contributes to the mercury concentration in plasma and urine, but that the mercury exposure does not influence selenium status or organ functions.

CASE REPORTS OF ADVERSE SYSTEMIC EFFECTS TO DENTAL AMALGAM

Current documentation of case reports of adverse systemic effects of dental amalgam has also appeared. The time limitations of this presentation does not permit discussion of earlier reports.

Katsumura and associates (1990) reported a case of exercise-induced anaphylaxis (EIA) that corrected only after removal of the patient's amalgam fillings.

Zamm (1990) documented twenty two patients with multiple severe immune dysfunctions that were resistant to standard therapies. After removal of dental amalgam fillings, an improvement of 63% of the specific symptoms was noted.

Since April of 1991, 320 Adverse Reaction Reports to dental amalgam have been filed with the United States Food and Drug Administration, with more continuing to be filed each day. After replacement of dental amalgam fillings, 303 patients reported improvement of illnesses or symptoms, 7 reported worsening (one of these were 0% worse), and 10 reported no changes. Relief from numerous symptoms are being reported, with the preponderance related to neurologic or immune dysfunction.

CONCLUSIONS AND RECOMMENDATIONS

BENEFIT/RISK RATIOS: The total absence of data on the incidence and severity of adverse reactions, oral or systemic, to dental amalgam prevents identification of benefit/risk ratios.

DENTAL: Sufficient documented evidence exists to warrant thorough investigation of possible adverse effects of dental amalgam on the periodontal structures and to possible allergic responses, such as oral lichen planus. Potential influences of vagrant electric currents generated by dental amalgam, particularly in combination with other dental alloys, on oro-facial neuromuscular function should be investigated.

MEDICAL: A significant contribution of mercury from dental amalgam fillings to the body burden of subjects has now been confirmed (WHO, 1991). Investigations of possible adverse health effects should be conducted by multi-disciplinary teams with emphasis placed on review and publication in qualified medical journals. Attention should be directed to organs and systems known to be targets of mercury accumulation, particularly the nervous system, the kidneys, the endocrine glands, and the cardiovascular system.

REFERENCES


