

ANNUAL MEETING, SFOPOM
SORIA MORIA CONGRESS CENTER
Voksenkollveien 60, 0394 Oslo 3.
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Oslo, August 11th - 12th 1989

FINAL PROGRAMME

Friday August 11th

9:00 - 11:00 a.m.	Registration. Coffee.
11:00 a.m. - 15:15 p.m.	<u>Seminar on Toxicology:</u>
11:00 - 11:45 a.m.	Basic principles in toxicology Researcher Jon E. Dahl, Scandinavian Institute of Dental Materials, Oslo
11:45 a.m. - 12:30 p.m.	DNA damage and chemical carcinogenesis. Researcher Jørn A. Holme, The National Institute of Public Health, Oslo
12:30 - 12:45 p.m.	Break.
12:45 - 13:30 p.m.	Man's mercury loading from dental amalgams. Research assoc. Asbjørn Jokstad Dep. of Anatomy, Dental Faculty, University of Oslo.
13:30 - 14:30 p.m.	Lunch, Soria Moria
14:30 - 15:15 p.m.	Metal toxicology. Chief physician Jan Alexander The National Institute of Public Health, Oslo
15:15 - 16:00 p.m.	Pindborg lecture.
16:00 - 16:45 p.m.	Slide seminar on Oral Viral Infections. Conducted by Stina Syrjänen, Dental Faculty, University of Kuopio.
16:45 - 17:05 p.m.	Coffee break
17:05 - 18:15 p.m.	Slide seminar cont.

Lecture at the Annual meeting of the Scandinavian Society of Oral pathology and oral medicine.
Soria Moria Congress Center, Oslo august 11. 1989.

Bioavailability of mercury from dental amalgam

What is amalgam?

An amalgam is a solid solution composed of mercury and one, or multiple metals. Two types of amalgams have been used in dentistry in this century. Dental copper amalgam and dental silver amalgam. Copper amalgam contained mercury and copper, and was used when a dry field of operation in the patient could not be attained. The amalgam was used mostly on children. The use of copper amalgam was abandoned in Scandinavia approximately 10 years ago. The dental silver amalgam in use today invariably include silver, tin and copper. Other metals that sporadically have been added are zinc, gold, paladium, fluoride or indium. The metals are powdered and blended before they are mixed with the mercury. This powdered blend is what is described as a dental alloy. The powdered particles may be irregular, spherical or both. Amalgams are also discerned by the copper content. When the alloy containing less than 6% Cu is mixed with mercury the amalgam is recognized as a conventional type amalgam. Until approximately 15 years ago this was the only silver amalgam in use. Amalgams made from alloys containing more than 6% Cu are sometimes called non-gamma-2 amalgams, ternary amalgams or single composition amalgams.

Reaction of alloy and mercury

When the powdered alloy is mixed with the mercury different solid crystal phases develop. These phases are composed of mercury-silver - the gamma-1 phase which is extremely resistant in the oral environment. Phases that are more corrosion prone are also formed to a smaller degree: mercury-tin (called gamma-2), and copper-tin (called eta). Some of the original alloy and some of the mercury will remain unbound for prolonged periods. The exact distribution of these 5 components in the amalgam matrix depend on the proportions of the elements of alloys, the size and the form of the alloy particles, the producers treatment of the alloys and the ratio of alloy: mercury. A study of amalgam specimens will also reveal voids and porosities which more or less vary with the material handling of the dentist. Incorrect techniques for blending the alloy and the mercury, or inadequate handling of the material, result in restorations with inferior corrosive properties in the oral environment.

Degradation and corrosion

As soon as the amalgam is placed in an oral environment the material will be subjected to chemical and physical attacks which over time will degrade the amalgam. This can also be seen macroscopically as substance loss. The degradation is primarily a combination of corrosion and mechanical stress. The corrosion behaviour in the oral cavity is complex and involves several parameters besides the composition of the amalgam, pH and oxygen variations in the oral cavity, the presence of proteins in the saliva and pellicle, masticatory function (abrasion), presence and morphology of crevices, combinations of different restorative materials in the oral cavity etc.

Toxicologic characteristics

On the basis of toxicologic characteristics there are three biochemical forms of mercury: Elemental Inorganic Organic compounds (alkyl-hg). The biologic effects of the different biochemical forms is highly diverse. The toxicity is however related to the cationic mercury per se whereas solubility, biotransformation and tissue distribution are influenced by valence state and anionic component. Only the elemental and inorganic form of mercury is relevant in the context of possible mercury exposition from amalgam restorations. It has been shown that oral bacteria can produce methyl-mercury from pulverized amalgam in vitro. It is however unprobable that methylation occur intra-orally. These types of studies are on the other hand relevant due to the extremely high toxicity of the end product.

Mercury exposure from amalgam therapy

May theoretically be possible due to

Exposure during insertion or removal of restorations

Release from amalgam restorations in situ.

Amalgam inadvertently implanted in the soft tissues.

The mercury exposure can be in the form off:

I: Ionic species i.e. Hg^{2+} , Hg^{2+} .

Gastrointestinal absorption of inorganic salts of mercury is less than 10%, presumably 2%.

Ionic species that are protein-bound will increase the absorption to 10-15%. It is unknown to what degree autooxidation of Hg^{2+} forms elemental mercury according to the reaction $Hg^{2+} \rightarrow Hg^0 + Hg^{2+}$.

P: Particles comprising different phases of the amalgam

Animal experiments indicate that .03% is absorbed.

The major part of small amalgam particles with dimensions of .3-.5 mm pass through the gastrointestinal tract without absorption. It is theoretically possible that small particles may be dissolved in the gastric acid but it is not known if elemental mercury vapor is produced from

small particles and absorbed in the gut.

E: Elemental mercury In the vapor form

The uptake of mercury vapor in the respiratory system is approx 80%.

Acute mercury exposure during insertion or removal of restorations

Patients is exposed to elemental mercury in the liquid or vapor phase, or to amalgam particulates. Although there is a potential for acute toxicity this has never been reported in the literature.

Reported values have been:

Cooley 78- Up to 1000 $\mu\text{g}/\text{m}^3$ may be produced by dry cutting of amalgam with a turbine

Brune80- If both vapor and particles is included, the Short time TLV (STEL) exceed 10 x. (500) if the water spray is not used. With water, level was below TLV.

Reinhardt83- High speed cutting with no water and placement of restorations in 5 pas. increased the level of intra-oral mercury vapor only slightly, 2 min after placement. Breath into silver wool-Heat-AAS 1 - 4 1.2 <1- 11 1.1 $\mu\text{g}/\text{m}^3$

Gastrointestinal absorption of elemental mercury in the liquid form is negligible. The use of appropriate procedures can keep the mercury levels well below the value for short-term exposures of 500 $\mu\text{g}/\text{m}^3$. Exposures during dental treatment, which are of short duration and infrequent occurrence, are of no clinical significance to the patient. The biocompatibility concern is therefore related to the possible chronic mercury exposure.

Assessment of the mercury release

Our knowledge of the mercury release from amalgam is based on:

1. Extrapolation from in vitro experiments
2. Measurements of exhaled mercury vapor
3. Measurements of the mercury concentrations in various body fluids or in nails.

I will present some of these studies and summarize the results and conclusions.

Study of Biopsies

Frykholm55- With the help of radioactive Hg an increase up to .1 $\mu\text{g}/\text{g}$ was seen after 7 days in the pulp of individual teeth. Sjøremark68, identified higher mercury content in the teeth of patients with amalgam restorations

Freden 74- The gingiva in contact with cl.V rest contained 147 $\mu\text{g}/\text{g}$.

Schiele87- The hg in the pulp was x35 higher in the filled teeth than unfilled teeth. i.e. 25.7/.75 $\mu\text{g}/\text{g}$, 7 weeks after placement

Basinger89- The Hg concentration in the pulp increased up to 7 days before returning to

control levels.

These studies definitely show that mercury is liberated from amalgam restorations. Extrapolation to daily doses is however impossible due to parameters as e.g. cavity depth, use of cavity liner and pulp vitality

Study of restorations in extracted teeth

Radics⁷⁰- Measured the hg concentration on the surfaces of old restorations. In an area of 100 mm² the author estimated the cumulative loss to 30-70 mg Hg. The author calculated the loss to be 8-19 µg/day/100 mm². This would indicate that the daily release with 20 restorations (6 cm) was of 140 µg/day.

The amalgam phases show different corrosion behavior. The gamma-2 phase (Hg-Tin) is the most active electrochemical element (or eta, if it is a non-gamma²-type amalgam). Studies have shown that liberated tin will form heavy tin-chloride-oxide complexes in crevices and on the surface while the mercury will diffuse into the bulk of the restoration and react with unreacted alloy. Although Radics measurements of the hg concentration on the surface are correct it is impossible to estimate if the mercury have diffused into or out of the restoration. The relevance of these studies for the daily estimation of mercury loss is therefore questionable.

General discussion

The rate of release of mercury from an amalgam specimen immersed in either natural or artificial saliva without application of force, i.e. under static conditions show a time dependent decrease. Various corrosion products composed of tin-oxide-chloride complexes are deposited on the amalgam surfaces and act as a semi-protective layer reducing the corrosion rate. The products are loosely bound and may be removed by brushing. If the specimens were subjected to cyclic loading the total mercury release (comprising elemental, ionic and particulate matter form) were higher than under solely static conditions. The increase was mainly caused by particles fracturing off the surface. It is difficult to extrapolate these findings since various proteins in saliva can affect the corrosion in different ways. One possibility is that the protein film protects the surface corrosion. It has on the other hand also been shown that proteins may promote corrosion of other biomaterials by having the ability to increase the release rate of specific ions. A general problem with these studies is that the values refer to total mercury release, i.e. the release of the different forms of mercury are not measured. It is necessary to know the fractions of the different forms in order to estimate the daily intake. Given a person with 20 restorations the in vitro studies indicate a release of mercury in the range of .3-30 µg/day. 90% of this mercury is in the form of ionized mercury, while 10% will be in the vapor

form. The additional intake from particulates can be ignored. These figures thus indicate a daily intake between less than .1 to 5 µg. For many years it was believed that the degradation products from amalgam restorations mainly consisted of particles and possibly ionized mercury. Advances in analytical chemistry in the early seventies enabled scientists to prove that also mercury vapor escaped from amalgam restorations. Keywords are here the thin film gold analyser and the silver wool absorption techniques. The first study appeared in Lancet in 1979 and the discovery initiated the latest worldwide concern about the toxic potential of amalgam. The importance of the discovery may be reflected by the Swedish 'LEK' low-dose-effect report from 1988. This report focus only on mercury vapor while the bioavailability and bioactivity of the other forms of mercury from amalgams are completely ignored.

There have been several investigations since the first of this type:

Discussion, vapor measurements

There are numerous methodological problems associated with these measurements. Parameters that must be assessed are:

The frequency of chewing and the length of the chewing period.

Mouth emptied before trial: Y/N

Breathing through nose during chewing: Y/N

Inhalation through nose or mouth before expiring: Y/N

Measure inside mouth, open or closed, or outside : O/C/E

The extrapolation of the values to daily exposure is connected with many problems, as reflected by the conflicting conclusions of the many review articles. The mercury-vapor analyzer is a device customarily used in factories, where it measures the mercury levels in workplace air. Only the elemental vapor is measured, not particulates. The device makes it easy to content that mercury doses exceed occupational standards. Vigorous chewing for 10 minutes generates heat and friction that maximize the release of mercury vapor. The analyzer senses the mercury contained in .125 liter air- about one-half cup of- air. Instead of displaying the concentrations as ng/.125liter the values are multiplied by 8000 and given as readout corresponding to hg in cubic meter of air. (About the amount inhaled in 1 hour).

In the early publications the authors proposed that release of mercury from amalgams could be more important than previously thought. This was however not substantiated by other authors and by later measurements performed over 24 h.

Despite the problems certain consistent features characterize the data. Tooth brushing and probably other oral activities like smoking, chronic gum chewing, bruxism and mouth breathing elicit release vapor, and the amount vary with the number of these restorations. The increased levels do not return to normal levels after cessation of the stimulation. The

concentrations are highest over newly placed restorations, after active chewing and can be greater for persons with many versus few restorations.

Implantation studies on animals

Amalgam implants can be found in 8% off the Swedish population. The potential of local toxic action from implanted amalgam particles have been assessed by several investigators.

Tissue reactions differ as to whether the material is finely ground ($< 55 \mu\text{m}$) or as particles. Small particles are engulfed by macrophages and giant cells and Hg disappear leaving diffusely distributed small particles of silver and sulphur. Larger masses becomes surrounded by a fibrous capsule which restrict breakdown with little tendency to a tattoo. Gamma2 degrade mainly extracellularly and leave no tattoo. The Hg and Sn are in these cases lost. Gamma1 degrade less rapidly and produce only small tattoo with loss of Hg. The original alloy -Gamma- degrade solely intracellularly and produced large tattoos. The persistence of Ag and S is associated with the basal lamina and connective tissue. Eley 81 Implanted finely grounded particulates in guinea pigs. this resulted in a release calculated to be $10 \mu\text{/day}$. The authors did however state that the quantities were much higher than likely to be introduced clinically. The exposure from these implants can accordingly be ignored clinically.

Steady State

It is believed that a person exposed to a constant average concentration of mercury achieves a state of balance, or steady state after 1 year of exposure, and it can be expected that there is a consistent relationship between this exposure and the mercury content of various body organs and in blood and urine.

Nail and Saliva

Viala78- no difference in Saliva for 25 part. 46 & 47 ng/g

Ott84- Increase in saliva from 5 to 13 $\mu\text{g/l}$ after chewing gum, $r = .30$ fillingnr, Higher than for non-bearers .3 $\mu\text{g/l}$

Takaku85- -> 198 patients measured hg in saliva. 2 $\mu\text{g/day}$

Ott86- Increase in saliva after chewing gum from 6 to 8 $\mu\text{g/l}$

Pallotti79- Higher values for amalgam bearers.No statistics, Cold Digest+AAS , nr 80, $1.53 \pm 1.76 \mu\text{g/l}$ with amalgam . $86 \pm .55 \mu\text{g/l}$ without.

Discussion blood and urine values

A problem with correlating these concentrations to the amalgam status is that the daily exposition to other mercury sources remains unknown. Daily x ug/70 kg --> .8x+1 = urine

excretion daily (WHO 76)

ThiomersalNa used as a conservative in pharmacotherapeutic products. Furthermore, the toxicokinetics and effects of mercury on humans is still relative obscure. 50% of the mercury vapor is excreted into the urine, but the urine concentrations may also be influenced by the daily organic mercury. Ionized mercury may also give high values. Additionally, due to demethylation and chemical transformation of the mercury in the organ it is difficult to assess the exact proportion of mercury in blood and in the urine which derive from the amalgam. Finally, the detection of the very low concentrations require sophisticated analytical techniques with a number of inherent methodological problems as a result. The procedure for calibration and the precision of the analytical procedures are only described in some of the reports. In view of the great range of the mercury levels in blood and urine comparisons of the results must be evaluated with caution. A marked individual variability may also reflected by the unusually high standard deviations which quite often are larger than the mean values. Besides the analytical problems but this may be a reflection of the fact that the ingestion, body retention, metabolism and toxicity of any toxic chemical are markedly influenced by various diseases, social habits, ill-defined conditions of stress and possible interactions with other synergistic or antagonistic environmental chemicals. A number of patients claim that their amalgam restorations elicit neurological disorders. It is therefore important to relate the mercury concentration in the target organ i.e the brain with the amalgam status. Some investigators have attempted to measure the mercury concentrations in various parts of the brain. Due to the extremely low amounts in this organ a correct methodology is even more critical than for measurements of body fluids.

Brain

Friberg⁸⁶- Found a correlation between the Hg in the occipital cortex and nr surfaces. n=15
The correlation was also to age so organic mercury in food could not be excluded.

Schiele⁸⁷- Hg in brain correlated to number of restorations

Eggleston⁸⁷- Claim correlation , but not supported by data

Nylander⁸⁷- Additional 23 cases to Friberg.

The concentrations in all the studies fell within what is considered normal values. The studies do therefore not give any indications of the daily amounts.

I had not prepared to discuss the possible bioactivity of daily low mercury intake in this lecture since this should have been covered by Dr Alexander. Because of the circumstances I will try to relate some of these findings to the daily intake and body burden.

Body burden

Average intake

For persons in the general population it is estimated that the daily absorption of all forms of mercury is less than 1 µg/day from air, less than 2 µg/day from water and less than 20 µg/day from food. The amount may be up to several hundred µg/day depending on the amount of fish in the diet. Various studies estimate the daily dose to be 10 µg in Sweden, 6 µg in USA, between 13 and 27 in W-Germany, while it is as high as 35 µg in Japan. Extreme values have been estimated for esquimoes who eat much seal and whale meat. These estimates are seriously influenced by such confounding factors as degree of environment pollution peculiar to each geographic zone, ambient temperature, humidity, social habits of people, age, sex, race, prevalence of diseases and other conditions of stress, dietary habits and possible interactions of mercury with other environmental chemicals.

There is general agreement that amalgam restorations contribute to the total body burden of mercury. The exact amount and form of mercury released from amalgam restorations is however controversial. It is generally believed that the amount of mercury deriving from restorations is low. It is probable that the release vary with different types of amalgams. With the basis of the available investigations the daily absorbed mercury is probable 3-5 micrograms for an average patient with 20 restorations.

This view has been however been challenged by a minor, although very vocal, group of scientists. Other controversial questions are what is the possible bioactivity of low daily intakes, are there are persons that may be more sensitive to mercury than the general population, are there are typical symptoms that can be recognized, and how can these potentially sensitive persons be identified.

So far the only adverse reactions that have been reported are affections of the mucosa in areas local to amalgam restorations. The histological diagnosis is most frequent lichen planus and leukoplakia and the term electrogalvanic white lesions have been suggested for these lesions. It is unclear if these are connected to patient intolerance (humoral biochemistry) or hypersensitivity (tissue biochemistry) to metals. The mechanism may also be a non-specific primary irritation or a local dose-dependent toxic contact mucositis. I will refrain from discussing the etiology of white lesions in the oral mucosa as I am sure You know more about this than I do.

However, these findings focused on the electrochemical corrosion of the material. Restorations made of different metals form a galvanic cell with the saliva as the electrolyte. A galvanic effect may sometimes be experienced from newly placed restorations. However, the galvanic process allegedly also caused subclinical and diffuse symptoms, and the unprecise diagnosis

oral galvanism appeared. The biological effects of intraoral currents could, from a theoretical point of view be due to either electrical stimulation of excitable cells, such as nerve, muscle or gland cells, or be secondary to a concentration of ions in the tissue with associated chemical irritation. Subsequent electrochemical studies did however show that the current magnitude and flow of the currents are so small that the probability that this phenomena should appear in the oral cavity was minimal. The risk of influencing regions outside the oral cavity could be considered to be still smaller.