
EFFECTS OF INORGANIC MERCURY ON THE NERVOUS SYSTEM

Mats Hanson, Ph.D.
President, TF-Scandinavian Dental Patient Organization, Sweden

Since ages it is known that exposure to inorganic mercury produces a "mad hatter syndrome" where normal, balanced behavior fails. Also opinions on the possible or real risks of mercury poisoning seem to behave in this way. For several hundred years there was a hot debate on the use of mercury for the treatment of syphilis and opinions ranged from denying mercury poisoning to denying syphilis. Also when mercury comes from amalgam fillings in the teeth, the metal seems to provoke aggressions. There is a great need for serious, unbiased studies to find methods of diagnosis and treatment, to find which diseases can be precipitated or aggravated by mercury, to clarify how the metal acts and the pathological changes caused by this devious metal, once a treasured medical remedy for nearly every disease.

Today anyone knows that mercury is neurotoxic. The severe CNS damage caused by methylmercury in Minamata, Japan and in Iraq caused a major concern about environmental mercury pollution. After these disasters methyl mercury was the focus of mercury research for several years. Now there is renewed interest in the effects of inorganic mercury. Perhaps there are more similarities between the two forms than is immediately apparent.

Presently I will restrict myself to effects of inorganic mercury after a very short comparison:

In Japan people consumed large amounts of methylmercury for a long time. The loss of visual field was used as a diagnostic criterium and other studies indicate that this symptom is present in about a third of cases. Tremor is usually used to diagnose inorganic mercury poisoning but is also shown by about a third of such cases. Zanger in 1930 was the first to notice the formation of organic mercury compounds in the manufacture of acetaldehyde and noticed that exposed workers had more neurological and cardiac problems and less of oral and gastrointestinal symptoms than people exposed to only inorganic mercury. The symptom complexes were, however, overlapping.

In Iraq where peasants consumed bread made from methylmercury-treated grain, the doses could be
estimated. Symptoms started when a cumulative dose of about 40 mg of mercury had been consumed during 1-2 months. Severe disease was produced by 200 mg and 350-400 mg caused deaths. (Bull. WHO, 1976)

Swallowed methylmercury, the most common route of exposure, should be compared to inhaled inorganic mercury, not swallowed mercuric chloride with its low absorption and subsequent mainly kidney localization.

What level of mercury vapor will give an absorbed dose of 40 mg mercury during one month? A crude estimate is 400 ug/m³ when the exposure is 8h/day, 5 days/week or 80-100 ug/m³ for a continuous exposure. Severe effects in Iraq then corresponds to 2 mg/m³ vapor. Such levels produce symptoms and severe symptoms respectively also for inorganic mercury vapor exposures in most persons but some can tolerate these exposure levels for years.

Methylmercury exposure is very likely worse if the exposure is large and continues for a long time since the turnover in the body is slower. However, the effects of both inorganic and methylmercury are largely reversible if further exposure is rigorously prevented. In Iraq blind farmers got their sight back and paralyzed patients could again walk.

Methylmercury has been studied for a few decades. However, the toxicity of inorganic mercury has been describe for centuries and millennia. The metal is harmless but the vapor diffuses easily, only a magnitude less than hydrogen gas, and then ionizes to toxic forms. Swallowed metal will seldom give problems but metallic mercury in other places might give problems. Gabir, an arabian alchemist dead 820 described that: "only if some is poured into the ears or nose will it kill or cause prolonged disease." Rhazes from the same age, wrote "If mercury is poured into the ear there will be severe pain followed by delirium and cramps. If some mercury reaches the narrow passages in the ear severe effects can be expected. Some doctors have told me that they have seen such patients have epilepsy followed by stroke." (Ruska, 1926; Goldwater, 1972)

The most common form of exposure to inorganic mercury is by inhalation of vapor. There is general agreement that this leads to a slowly developing and insidious poisoning which primarily gives psychic effects and is very difficult to recognize until more objective symptoms appear. There are numerous more or less extensive descriptions. This one by Baader in Handbuch der gesamten Arbeitsmedizin is a moderately long one. Others have noted additional symptoms or more rare effects. (Baader, 1933, 1961; Stock 1926, 1936; Moeschlin, 1980; Poulsson 1922, 1949; Oettingen 1958; Burgener & Burgener, 1952; Schulz 1907; Kussmaul, 1861). Baader, E. Quecksilbervergiftung, 1961:

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomatitis</td>
<td>disturbance of sleep</td>
</tr>
<tr>
<td>gingivitis</td>
<td>tremor, jerks, shaky handwriting</td>
</tr>
<tr>
<td>loose teeth</td>
<td>salivation/dry mouth, nose</td>
</tr>
<tr>
<td>difficulty to speak</td>
<td>foul breath</td>
</tr>
<tr>
<td>skin changes, eczema</td>
<td>anxious seclusion</td>
</tr>
<tr>
<td>metal taste</td>
<td>fatigue</td>
</tr>
<tr>
<td>redness of throat</td>
<td>pressure over head, headache</td>
</tr>
<tr>
<td>black line along teeth</td>
<td>irregular menstruation</td>
</tr>
<tr>
<td>diarrhea</td>
<td>dull pain in limbs and joints</td>
</tr>
<tr>
<td>anemia, relative lymphocytosis</td>
<td>disturbance of circulation</td>
</tr>
<tr>
<td>uncertainty</td>
<td>sudden changes of skin color in face</td>
</tr>
<tr>
<td>shyness</td>
<td>increased sweating</td>
</tr>
<tr>
<td>agony</td>
<td>irregular heart</td>
</tr>
<tr>
<td>irascibility</td>
<td>pressure over chest</td>
</tr>
<tr>
<td>labile mood</td>
<td>lowered blood pressure</td>
</tr>
<tr>
<td>forgetful, memory loss</td>
<td>sensory disturbance of skin</td>
</tr>
<tr>
<td>feeling of intellectual inadequacy</td>
<td>thyroid disturbance</td>
</tr>
</tbody>
</table>
major oscillations in intentional movements made by the patient in an effort to get about, similar to those observed in persons stricken with multiple sclerosis. In fact, variety in form and intensity is a characteristic feature of mercury tremor.

Tremor usually disappears during sleep, although sudden generalized cramps or contractions may occur; however, it always increases under emotional stress and this is such a characteristic feature that it provides firm grounds for a diagnosis of mercury poisoning. Tremor usually begins with a subtle trembling of the fingers... In some cases it begins with the eyelids, the area around the mouth and the tongue. A highly characteristic symptom is a desire for sleep and the patient often sleeps for long periods although lightly and is frequently disturbed by cramps and spasms. However, insomnia may occur in some cases.

It is widely agreed that loss of memory is an early and dementia a terminal symptom. Descriptions have been given of vegetative disturbances, mercurial vegetative syndrome, due to basically sympathetic or parasympathetic imbalance. Dermographia and profuse sweating for no obvious reason are frequently encountered." (Perales Y. Herrero 1983)

After this was written there have been many studies on the serological effects of mercury and the immunotoxicology effects of mercury, as it is seen in animals, which seem to closely resemble what is seen in MS. I will return to that subject later.

The best studied cases of human mercury poisonings come from the now almost forgotten disease acrodynia. This disease was first recognized in France in 1828. Mostly children were affected. The disease spread and eventually reached epidemic forms in some parts of the world. In English-speaking countries mostly children up to 2 years age were affected and in Germany and France, children up to about 9 years. In children the skin of edematous fingers and toes was particularly affected and the skin peeled off which gave the disease the name pink disease. Older children and affected adults had thicker skin and often lacked this symptom. The disease was also called erythema arthriticum epidemicum, vegetative neurosis, vegetative encephalitis, erythoderma polyneuritis, thrombocytopenia, etc. There were pains in the limbs, disturbances of circulation, in extreme cases fingers and toes could be lost. Extreme weakness in the muscles and the children gave up standing and walking. Loss of weight, sleep and gastrointestinal disturbances, tremor, chorea, sometimes fever and conjunctivitis. Some of the cases developed salivation, swollen gingiva, periodontitis and necrosis of the jaw bone tissue. Thousands of children died. Everything was suggested as the cause: lack of vitamins, endocrine disturbance, allergy, hysteria, neurosis, mould poisons, virus from contact with animals. Mercury was first suggested in 1846 because of the similarities with symptoms after mercury ointments. Again in 1922 a physician pointed out the similarities with mercury poisoning. In 1945 it was found that in almost every case of acrodynia a mercury exposure could be demonstrated. The most common exposures were from teething powders containing calomel and calomel-containing preparations against gastrointestinal parasites. When these preparations were withdrawn the epidemics disappeared although scattered cases still occur because of other mercury sources.

Warkany and Hubbard in 1953 and Warkany, 1966 have discussed the manifestations of acrodynia and pointed out that although the administration of these mercury preparations were frequent, only a fraction of those exposed developed acrodynia. They calculated the incidence to about one in five-hundred. Therefore, mercury exposure and excretion was often also found in controls although no symptoms were present. Stotte and Groh in 1961 distinguished between calomel-disease, an acute manifestation with poisoning symptoms and acrodynia which developed often months after the exposure. Acrodynia was considered a neuroallergenic reaction to mercury, proceeding in several stages where the primary attack was on the endothelial cells of the blood-brain or blood-nerve barrier. Reviewing the literature they find quite a number of cases of mainly neuropathological manifestations, in some cases only single cranial nerves affected. In small children, exposed to mercury, the whole CNS became edematous, with several nuclei and the spinal cord especially affected. These effects where largely reversible but could in some cases lead to more long-lasting permeability impairments in the blood-brain barrier and a sclerosing development, different from the primary vascular-allergic and not really neuroallergic procress. A good description of an acrodynia case without the skin symptoms but with long-lasting neurological effects, caused by the rectal
administration of metallic mercury in vaseline, can be found in the paper by Stotte and Groh, 1961. This paper also contains a review of the neuroallergic manifestations and further references.

In the late 1940ies when the mercury etiology of acrodynia was clarified, also the possibility of MS as an adult form of acrodynia was considered. No general and widespread source of mercury was then recognized. However, in 1966 Baasch, a Swiss neurologist, recognized the possibility of amalgam fillings being such a source. He concluded that a mercury/amalgam etiology could explain the known facts about MS. Additional protective or aggravating factors in the environment could be fluorine and sugar consumption, both acting indirectly on the dental caries incidence. Lead was also considered as a possible contributing factor because of its widespread occurrence, known demyelinating activity and some reports on MS after lead exposure.

Today we have another significant factor: selenium. Both MS and a high DMF index (diseased, missing and filled teeth) correlate well with low selenium levels as do a number of other diseases. If selenium is considered, anomalies like Japan can be explained (Schalin, 1980).

Baasch noted the presence or absence of amalgam fillings in 500 consecutive MS patients in Zurich. All except 1 or possibly 2 had amalgam fillings. However, amalgam fillings are common and this proved nothing. On the other hand there are also other sources of mercury. For instance, a prolonged stay in a house where a barometer had been broken is known to have caused acrodynia (Gädeke, 1962) and in another case the mercury source was sublimate-impregnated wood which was used to heat the house (Gädeke, 1966). The latter case was only recognized as mercury-related because the author recognized the symptoms from the first, more obvious exposure. Other sources are broken thermometers, broken fluorescent lights, wall paint etc.

Three cases were described by Baasch. Two of these had their amalgam fillings removed and improved. Nothing was done to the third one, a completely paralyzed patient, but is described since the disease had started a few months after she had her first amalgam fillings, 19 years old, and had then had a very rapid progression. She had, 8 years old, been treated with mercury for co-genital syphilis.

Knolle & Günther in Germany described the mercury/amalgam status of 100 MS patients in 1967. Eleven of these had previously been treated with mercury ointments. Seven patients had no teeth and the percentage with amalgam did not differ from the general population. It is not stated whether the edentulous patients were the ones who had been mercury-treated. Loss of teeth is a well-known effect of heavy mercury exposure. There were also other dental metals present in many patients but the paper is unfortunately not detailed enough to evaluate the patients’ metal exposure. The 11% mercury-treated patients seem remarkable.

Additional but rare information has later appeared. Currier (1971, 1974) finds that there are some MS patients who have not had any dental treatments but that the amount of dental work is significantly more than in a control population. Also Ingalls, epidemiologist at Framingham, finds that the geographical distribution of amalgam dental repair could well explain MS (Ingalls, 1983, 1986). The later paper describes his own acute MS attack when a 50 year old amalgam filling was removed (pulverized).

Störtebecker (1961, 1982) suggested that bacterial products from periapical infections migrated to the CNS and caused a variety of neuropathological states, including MS. Several other studies have found a connection between dental health and MS. Schalin in 1980 discussed low selenium areas and its coincidence with high MS prevalence and Dr. Ahlrot-Westerlund (1985) found low selenium levels in platelets and recently (1987) 8 times higher CSF mercury levels compared to controls. Lipid peroxidation was suggested to be a significant factor in the etiology of MS (Ahlrot-Westerlund, 1980). A similar hypothesis was presented by Mickel in 1975. A number of investigators have noted cases of MS precipitated by vaccinations and trauma.

The various theories might not be mutually exclusive.

After the discovery of free radicals as biologically active metabolites there has been a major change in the way we view our existence. A new concept is oxidative stress where transition metals have a central
role. Exposure to metals which take up or release single electrons will cause oxidative stress. So will trauma and infections and the response of our own immune system to such factors. If the increased oxidative stress is of short duration there will be no noticeable lasting effects. If the stress continues severe pathological states might occur (Sies, 1985; Halliwell & Gutteridge, 1984).

Selenium, a number of enzymes and proteins and some vitamins constitute a defence system which is sufficient providing the stress is not excessive or some components in the defense are not deficient.

The general pathology of MS with altered lipid composition in cell membranes, imbalance of the immune system etc. is entirely consistent with MS being a free radical disease. The best animal model, EAE (experimental allergic encephalomyelitis) can be induced by injecting neuronal antigens (Wisniewski, 1977) or endothelial cells from the blood-brain barrier (Tsukada et al., 1987). EAE can be prevented by iron chelators which clearly implicate hydroxyl radicals in the process (Bowern et al., 1984).

In MS the major triggering factor has been missing although trauma and some other external factors in some cases can be triggers. Apparently also microorganisms can cause similar processes, for instance Borrelia from tick-bites (Stiernstedt et al., 1985).

Could mercury be the most common trigger?

Oral or subcutaneous mercuric chloride and met-Hg in moderate amounts (1 mg/kg) were found to cause a long-lasting but not permanent impairment of the blood-brain barrier with extravasation of plasma components (Chang & Hartmann, 1972), demonstrating that acute or subacute exposures could very well be capable of exposing the immune system to neuronal antigens.

The incidence of acrodynia was estimated to be one in five-hundred mercury-treated children. This does not seem to be too far from the incidence of MS which is one in 1000-2000. Mercury allergy is not at all something which can be tested on the skin. Acrodynia children were rarely patch-test positive for mercury, despite the often severe skin reactions from mercury inside. The symptomatology of mercury poisoning suggests that immune reactions are involved. Mercury-induced glomerulonephritis is a suspected autoimmune disease. Baader & Holstein in 1933 and later Stock (1936) reported that both strong mercury poisoning and an insidious chronic poisoning from much lower Hg levels gives a sensitivity towards further mercury exposure. Traces of mercury could produce symptoms, especially if the metal was inhaled through the nose (a few hours delay between exposure and headache).

Today mercury is known to be immunotoxic and is the best studied compound in that respect. Mercury produces an autoimmune disease, characterized by antibodies to a variety of proteins, mainly of endothelial origin but probably also towards environmental antigens. This effects is caused by interaction between mercury and T-cells where the helper/suppressor ratio is increased. A genetically determined polyclonal activation of B cells is the result. Several animal species have been found to react in the same way and there seems to be no reason to expect humans to react in other ways (Bernaudin et al., 1981; Druet et al., 1982; Hirsch et al., 1982; Pelletier et al., 1986).

Mercury has a strong affinity for sulphydryl groups. A simple estimate, however, will lead to the conclusion that not even when there are deadly kidney levels of Hg will there be enough metal to bind to more than 10% of available sulphydryl groups (Clarkson, 1972). Hg levels will at most be in the micromolar range. GSH levels are in the millimolar range and then there are other sulphydryl groups also.

There seems to be two possibilities: 1. That Hg inhibits GSSG-reductase to give a progressive loss of oxidized GSH and 2. a catalytic oxidation of sulphydryl groups where one mercury can oxidize numerous sulphydryl groups. There are data to support both of these interpretations. The two processes could certainly both operate.

Mercury inhibits some enzymes at very low levels. Organic Hg-compounds inhibit at the same concentration as inorganic if there are no stearic factors which protect the sulphydryl group, otherwise at higher concentrations (Webb, 1966).
<table>
<thead>
<tr>
<th>Enzyme/cells</th>
<th>Tissue</th>
<th>Conc.</th>
<th>ng/ml</th>
<th>% inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatine kinase muscle</td>
<td>pMB</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Glutathione reductase</td>
<td>liver</td>
<td>Hg2+</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Glutathione reductase</td>
<td>liver</td>
<td>Hg2+</td>
<td>65</td>
<td>100</td>
</tr>
<tr>
<td>Glutathione reductase</td>
<td>pure enzyme</td>
<td>Hg2+</td>
<td>32</td>
<td>95</td>
</tr>
<tr>
<td>Isocitrate dehydrogenase</td>
<td>heart</td>
<td>pMB</td>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>LDH muscle</td>
<td>Hg2+</td>
<td>0.7</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Myokinase muscle</td>
<td>pMB</td>
<td>6</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Oxaloacetic decarboxylase</td>
<td>heart</td>
<td>pMB</td>
<td>16</td>
<td>50</td>
</tr>
<tr>
<td>Myelin cAMP phosphodiesterase</td>
<td>myelin fraction</td>
<td>Hg2+</td>
<td>100</td>
<td>40</td>
</tr>
<tr>
<td>Fiber outgrowth from dorsal ganglia (inhibition of NGF?)</td>
<td>Hg2</td>
<td>64</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>B-fructofuranosidase yeast</td>
<td>Hg2+</td>
<td>0.02</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

(Data from Webb, 1966; Davis & Williams, 1965; Domanska-Janik & Bourre, 1987; Sharma & Obersteiner, 1981)

In real life Hg will certainly bind also to other sulphydryls than those of enzymes. Glutathione reductase is one of the most sensitive enzymes towards mercury. After mercury exposure all enzymes of GSH metabolism have been found to have reduced activity.

The action of mercury is not the action of the divalent mercuric ion. It is the action of the mercury-chloride complexes; at physiological pH HgCl+, HgCl2 and HgCl2- (Webb, 1966).

HgCl2 is to 99.5% undissociated and adding HgCl2 to biological preparations will lead to a slow exchange where progressively more Hg will form more stable bonds to sulphydryls. The Hg-S bond is, however not at all very stable but there will be a competition with Cl- ions. Excess sodium chloride will dissolve also Hg bound to sulphydryl groups. If HgCl2 is added to red blood cells it will pass the cell membrane as HgCl2 (it is quite lipid soluble) and equilibrate in about 4 minutes. The intracellular mercury will form a complex with one GSH and one hemoglobin. The lifetime of the Hg-S bonds is less than 11 seconds at high Hg concentrations and only a few tenths of a second at lower concentrations. Hg is rapidly migrating between different sulphydryl groups (Rabenstein & Isab, 1982). A likely consequence of the interchange is an oxidation of the sulphydryls and not a return to the reduced state. Mercury in blood or tissues can be chelated or solubilized at every time after administration. With time, more and more will be firmly bound and less easily removed.

It seems important to realize that when HgCl2 is administered it is not the mercuric ion which is given. Most of the HgCl2 after an intravenous injection will end up in the kidneys as unchanged HgCl2. Intramuscular injections will give a slower release and more time for chemical reactions.

What happens when mercury vapor is inhaled? It has been assumed that mercury vapor is oxidized to Hg2+ by catalase in red cells and then released back into the plasma. This seems very unlikely in cells full of sulphydryl groups. From mercury chemistry it is known that in oxygenated distilled water and hydroxide Hg0 is slowly formed. In sodium chloride or Ringer solution it is oxidized to calomel, monovalent mercurous chloride (Stock, 1934). The process is much faster in Ringer than in sodium chloride. Traces of iron might catalyze the oxidation. The saturated value in such solutions corresponds exactly to a saturated calomel solution. Iron in enzymes or as Ferric chloride will catalyze oxidation in both blood and simpler solutions. There is no reason to expect anything else than calomel to be formed in the primary oxidation of mercury by blood. Blood, in contact with mercury-saturated air has been studied a number of times. Examining the figures one will find that the amount of absorbed mercury corresponds to calomel solubility.

Probably the reactions are even more complicated and in chemical experiments it has been found that traces of mercuric mercury will catalyze the oxidation of elemental mercury to calomel. The reaction Hg(gas) + Hg2+ ----> Hg2Cl2 has been suggested. Also the monomeric form HgCl has been identified by spectroscopic methods in pulse radiolysis experiments and found to have a lifetime of a few microseconds.
The general reaction will be Hgo$\rightarrow$ Hg(I) $\leftrightarrow$ Hg(II) which is reversible. Especially the transition Hg(I) $\rightarrow$ Hg(II) requires very little energy and the relative affinities of the surrounding ions will determine the equilibrium (McAuliffe, 1973). Reducing substances will push the reaction to the left, some only to the Hg(I) stage, stronger reductants to Hgo.

A small fraction of the mercury in blood and urine is in the elemental state also days after mercury exposure and after HgCl2 injection (Clarkson & Rothstein, 1964). Adding ethanol will release larger amounts (Dunn et al., 1978). This has been considered an effect of inhibiting catalase and allowing reducing of hydroxyl radicals. These radicals will oxidize mercury. The ethanol radical has a reducing effect on mercury.

It is quite possible that free radicals have a major part in the metabolism and effects of mercury. Adding mercuric chloride to cultured cells produces an immediate burst of superoxide radicals (Cantoni et al., 1984). Higher levels will inhibit the burst which indicates an enzymatic process. Mercury interferes with the measurement of radicals and it has not yet been possible to find out if also other radicals are involved. Concomitant with the radical production there will be single strand brakes in DNA, identical and additive to those produced by X-rays (Cantoni et al., 1982). There is one difference, the X-ray damage is repaired. The Hg-damage is not (Christie et al., 1986). Most studies show that after some time lipid peroxidation is induced. Lipid peroxidation is, however, not sufficient to account for the cell damage caused by mercury. In some systems the cells die without the production of peroxidation products.

These reactions were actually anticipated very early. In 1907 Schulz, professor of pharmacology in Greifswald, suggested cyclic redox reactions as major factors in the toxicity of copper and mercury. He wrote: In contact with organic material mercuric chloride will more or less fast be reduced to calomel, thereby releasing chlorine. On the other hand, calomel can, in the presence of the ubiquitous sodium chloride and in contact with living material regenerate the sublimetate. In this way, when living material and sublimate come into contact, there will be an intense turnover of chlorine atoms which microorganisms and also higher life forms can not tolerate. Just the fact that the calomel formed by the reduction of sublimetate again can be regenerated by living cells is the reason why sublimetate is more effective than for instance potassium permanganate. The latter gives off its oxygen and is then used up since there will be no regeneration of the compound. Also, oxygen behaves in similar ways as chlorine in relation to mercury, something which has been known for a long time from chemistry. Thus, mercury can, in the presence of chlorine or oxygen and living cells or tissues, intensely enhance the normal turnover of these substances. The changes in these basic processes by mercury is the cause of both the substantial medical effects and the toxicity of mercury.

Whether chlorine radicals are formed is not known. However, similar processes produce the strongly oxidizing hypochlorite ion, both in artificial systems and in the myeloperoxidase system.

We should not underestimate the scientists who lived before our time. An enormous amount of information on mercury and at least 95% of all papers on human mercury toxicology can be found in the literature from before the second world war. Also the lessons from acrodynia should not be forgotten. It took more than 100 years to find out that mercury caused this special form of poisoning or neuroallergy. MS appears to be quite identical but to affect another age group. Some of us now treat MS patients by advising them to have a known neurotoxic substance removed from their teeth. Simultaneously and if
possible in advance, we give them substances which improves the defenses against free radicals. This is surprisingly effective. We hope to be able to present statistical material later on.

REFERENCES


Kussmaul, A. Untersuchungen über den constitutionellen Mercurialismus und sein Verhältniss zur constitutionellen Syphilis. Würzburg 1861.


REVIEW/ABSTRACTS

1977.


Clarkson T.W., Friberg L., Hursh J., and Nylander M. have written a chapter titled "The Prediction of Intake of Mercury Vapor from Amalgams." Based on the literature reports the authors have attempted to estimate the rate of release of mercury from amalgams and to assess the contribution of dental amalgam to the human body burden of inorganic mercury. Estimates were made of the daily amount absorbed via inhalation and of the contribution to tissue, blood, and urine mercury levels. These are compared with observed blood or urine concentrations as a function of amalgam fillings and occlusal surfaces. Autopsy data on mercury brain levels are compared with estimated values.

In the 1984 EPA Report Mercury health effects update, Report No. EPA-600/8-84-019F it was estimated that the daily uptake of different forms of mercury from the diet was approximately 2 ug and the amount of vapor inhaled from the ambient atmosphere to be about 0.1 ug. These estimates did not take into consideration any possible contribution of mercury from dental amalgam fillings.

The authors close the body of their chapter with the following statement and conclusions: "It is clear from the uptakes listed in Table 1 - 2.9 to 17.5 ug Hg/day - that release of mercury from dental amalgams makes the predominant contribution to human exposure to inorganic mercury including mercury vapor. This does not take into account the preferred transport of inhaled vapor to the brain which further emphasizes the contribution from amalgams.

CONCLUSIONS
1. The evidence indicates that amalgam surfaces release mercury vapor into the mouth.
2. The rate of release is increased by stressing the amalgam surface by chewing and brushing.
3. The surface layer does not immediately repair after stress and that it may take several hours to completely restore the surface layer.
4. The release of mercury from amalgam results in the deposition of mercury in body tissue and an increase in urinary excretion.
5. The estimated release rates from amalgam appear to be consistent with levels of mercury found in autopsy tissue in the general population and with increases in brain and urinary levels due to amalgam fillings."

6. The release of mercury from dental amalgams makes the predominant contribution to human exposure to inorganic mercury including mercury vapor in the general population.

BIO-PROBE COMMENT: We consider the data presented by these world renowned researchers to be of great significance in validating and adding to the existing benchmark data on the release and deposition of mercury from amalgam. There is however one factor related to the equations that we feel bears additional consideration and that is the gum chewing habits of Americans/Canadians or other gum chewing populations. A recent U.S. consumer survey produced data indicating that 70% of the respondents said they chewed gum. Is it possible that some of the variances in mercury tissue burdens, excretion levels, and health effects relate to how often and how long the individual chewed gum?

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Abstract: Eighty-one women (45 dentists and 36 dental assistants) occupationally exposed to metallic mercury underwent toxicoclinical examination. Total mercury levels (TMLs) were determined in scalp and pubic hair by cold vapour Atomic Absorption Spectrophotometry (AAS). Furthermore, a detailed questionnaire study was made concerning adverse reproductive events. TMLs in the hair of the exposed women examined exceeded significantly those determined in the hair of 34 controls not exposed to mercury. All exposed women had continued working during pregnancy. There was a significant, positive association between TMLs in the hair of exposed women and the occurrence of reproductive failures in their history. The relation between TMLs in the scalp hair and the prevalence of menstrual cycle disorders was statistically significant. These findings indicate that dental work could be another occupational hazard with respect to reproductive processes.


Abstract: Exposure of human erythrocytes in a 50% hematocrit to 0.5-1 mM Hg2+ initiated immediate hemolysis which proceeded at a constant rate without any formation of lipid hydroperoxides. Treatment of 0.03% hematocrits with 0.4 ppm of Hg2+ or 40 ppm of methylmercury caused rapid hemolysis after a short lag period. The kinetics of the process were unaltered by saturation of the cell suspensions with oxygen, by its replacement with He or CO, or by variation in the level of vitamin E in the membranes. The results show that peroxidation of erythrocyte membrane lipids is not the cause of hemolysis induced by either Hg2+ or methylmercury.


Abstract: Mercury accumulation in brain, kidney, liver and heart following insertion of amalgam in the teeth of guinea-pigs has been studied. During the accelerated wear of the amalgam in these gnawing animals, a significant mercury accumulation in the above tissues was demonstrated. Finely diffused and abraded amalgam must not be ignored as source of absorbable mercury.

Wakai E. Potential difference between various kinds of metals applied in oral cavity and their physiologic effects. JADA, vol 23, June 1936.

SUMMARY:
1. When a metal in a tooth acts as a positive pole its presence causes the generation of calcium at that pole.
2. When the metal in the tooth acts as a negative pole, phosphoric acid is liberated.
3. When two contiguous teeth, or two corresponding upper and lower ones, contain different metals, they are liable to destruction.

BIO-PROBE COMMENT: Here again is valid scientific research published more than 50 years ago, in this case in their own Journal of the American Dental Association, that is still normally being ignored by the pro-amalgam hierarchy of the ADA and the practicing pro-amalgam membership. This doesn’t have anything to do with the mercury/amalgam controversy. Simply a scientific fact that two different metals placed in an electrolytic medium will have a potential difference and in the case of doing this in the oral cavity may cause physiological disturbances.


Abstract: When opposing teeth with amalgam and gold restoration are in contact, current flows in the mouth at the instant the dissimilar metals touch. In this study, this condition was simulated by use of resistors and extracted human teeth with amalgam and MOD gold inlay restorations.
When both teeth were in contact in a physiological saline solution, we measured current and electrical potential generated in each pulp chamber. Galvanic current generated in the tooth with amalgam was always larger (as much as 18.2 times at the instant of contact) than that in the tooth with gold. Electrical potential generated in the tooth with amalgam was always larger (as much as 9.7 times at the instant of contact) than that in the tooth with gold. It should be emphasized that the larger current generated in the tooth with amalgam was caused mainly by its larger electrical potential. These results correspond well with the clinical phenomenon of galvanic pain, which occurs in the tooth with amalgam rather than in the tooth with gold.

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Abstract: The toxicity of mercury compounds in dentistry has been an issue of increasing concern. Relatively few data are available concerning the possible in vivo biotransformation of elemental mercury from dental amalgam into more toxic organic mercurials. The present study was designed to evaluate the existence of this in vivo pathway in dentists who work in a confined environment where metallic mercury vapor is constantly present. Two hundred five practicing dentists and twenty-four nondental controls were asked to participate in this study. The total, inorganic, and organic mercury contents of blood were determined by syringe-injection cold-vapor atomic absorption spectrometry. The student t-test indicates that the total and inorganic mercury levels in blood are significantly different between dentists and non dental controls at the significan level of p 0.05. The organomercurial levels are, however, insignificant at the same test level. This implies that high total and inorganic mercury levels are not correlated with high organomercurial levels in the blood of practicing dentists. Therefore, significant enzymatic conversion of inorganic to organic mercury compounds does not occur in vivo.

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Abstract: A previous report [J. Anal. Tox. 11: 149 (1987)] indicated that total and inorganic mercury (Hg) in the blood of practicing dentists are significantly higher than nondentist controls, while organic Hg levels remain remarkably similar between the two groups. Further analyses were conducted to elucidate the major contributing sources of blood mercurials in these two groups. Participating dentists of the Health Assessment Program at the ADA 1986 Annual Session were asked for information regarding their smoking habits, number of amalgam restorations, and weekly seafood consumption. Of 222 samples analyzed, 11 were excluded from the study because of regular smoking habits. The remaining dentists were divided into groups based on their number of amalgam restorations and frequency of seafood consumption. The data indicate no relations between the total, organic and inorganic blood mercurial concentrations with amalgam restorations. However, a linear correlation was demonstrated between seafood consumption and blood mercurials. It can be concluded that amalgam restorations contribute little, if anything to blood mercurial levels, as the major contributor to blood organic mercurials appears to be dietary fish consumption.

BIO-PROBE COMMENTS ON THE ABOVE TWO ABSTRACTS: The researchers evidently didn’t realize the significance of some of the results of the first study, which was designed to prove that there is no conversion of elemental mercury vapor from amalgam fillings into methylmercury. It must have been with some dismay when after publication it was realized just how incriminating the finding was that total and inorganic mercury levels in the blood of dentists were significantly and statistically different than nondentists. This glaring inadmissible fact had to be corrected ASAP. So, what better way to accomplish this than do it again. This was done at the 1986 ADA annual session where in addition to drawing blood, additional data on seafood consumption was collected by non-scientific dietary recall as well as the number of amalgam fillings. The published results of this study are brilliant i.e. "It can be concluded that amalgam restorations contribute little, if anything, to blood mercurial levels, as the major contributor to blood organic mercurials appears to be dietary fish consumption." Now, the first study didn’t have anything to do with
how many amalgam fillings the participating dentists had or whether they smoked or ate seafood. It merely analyzed blood samples for total mercury and organic mercury. Therefore the results of the second study stating amalgam fillings contribute little, if anything to blood mercurial levels is totally meaningless in relation to the first study. Further, it is a well established scientific fact that eating a high seafood diet will contribute to organic mercury blood levels. Therefore we are at a loss to understand what that has to do with the results of the first study showing dentists having a statistically higher level of inorganic mercury blood levels than nondentists. One last point, the second study is also void on any smoking, amalgams or seafood consumption of nondentists. In fact, the authors do not even indicate that any nondental controls were used. Please note the significance of the two following abstracts in relation to this discussion.


Abstract: Mercury exposure among dental assistants has received minimal research attention. To determine if dental assistants were at risk for mercury intoxication, a pilot study was conducted involving 52 dental assistants attending continuing education workshops in Southern California. Urine samples were collected; a demographic and workplace variables survey was administered. The Profile of Mood States, a standard instrument in psychological test batteries for neurotoxicity was also administered. 13.5% of the sample had urine Hg levels above 30 microg/l; a published acceptable level for the occupationally exposed. 34.6% had levels greater than 10 microg/l, the acceptable population level. The mean level was 13 microg/l. Levels as high as 92 microg/l were found. Analysis of variance revealed that years worked in present office space was related to urine Hg level (p=.05). Relationships between type of flooring in office, years of practice, and type of practice employment were not found to be significantly related to urine Hg concentration. The Profile of Mood States was used to correlate affective states to urine Hg levels, no significant results were demonstrated. Preliminary results show dental assistants share the risk of mercury intoxication in a pattern similar to dentists screened by the ADA. Years worked in present office space is related to urine Hg levels.


Abstract: This survey was conducted to correlate the amount of excreted mercury in urine with various clinical, occupational, and domestic variables.

Questionnaires and 20 ml morning urine samples were received from 672 Norwegian dentists. All samples were immediately cooled to 4o C and kept cool until 1 hour prior to analysis, which was performed at room temperature. The amount of mercury in the samples was measured by cold atomic absorption technique. The relationship between the variables and the excreted mercury was estimated by MCA- and Pearson correlation analysis. Inter-group differences were tested by ANOVA. The average value of the samples was 40nmol/l, i.e. 8 ug/l. Only 3.6% contained 100 nmol/l. The highest value was 252 nmol/l. Significant correlation was found between the amount of excreted mercury and many of the variables. A significance of p .001 was found between the excretion of mercury and the number of weekly practice hours, the frequency of clinical procedures involving amalgam, and the respondents’ number of amalgam restorations. The quantities of excreted mercury indicate that the occupational exposure of dentists to mercury is low. However, since the long-term effects of exposure to low levels of mercury vapour are not known in detail, efforts to minimize the occupational exposure to mercury should be administered.

BIO-PROBE COMMENT: It would appear from the two abstracts above that there is much more to the problem of mercury exposure than the ADA would like you to believe.
EDITORIAL
by
Sam Ziff

As a tax-paying citizen I am fascinated and then incensed by the horrendous effort and the hugh sums of tax dollars being expended to defend an empirical position or concept that is being scientifically destroyed by hard research data produced by scientists who have nothing to gain from the results of their studies other than discernment of scientific truth..

It started in 1926 with Professor Stock’s denouncement of amalgam which was immediately attacked by the establishment and has continued unabated ever since. The newest knight riding fiercely to battle in his tarnished amalgam armor is a Ph.D. at the Dental School of the Medical College of Georgia, Augusta. It would appear that grant money is flowing readily to this institution as the "knight" rushes to discredit existing research raising serious questions about the continued use of amalgam.

I find it equally fascinating that there has not been one research study funded by the NIH, NIDR, or the ADA that has a design protocol that would answer the question of amalgam safety once and for all. The current position of these institutions is that there is no scientific data supporting a relationship between mercury from amalgam fillings and any known disease. This is just another attempt to further confuse the public and the poorly informed pro-amalgam membership of the ADA, on the real issue. The real issue is that mercury from any source only causes one disease and that is MERCURY POISONING.

After 100 years of data indicting amalgam fillings as a major source of mercury contamination to the human body, thousands of anecdotal case histories demonstrating amazing curative powers of amalgam filling removal and replacement, scientist researchers throughout the world are finally beginning to accept these indisputable facts: MERCURY IS A POISON - AMALGAM FILLINGS RELEASE MERCURY THROUGHOUT THEIR LIFETIME - MERCURY FROM AMALGAM FILLINGS IS THE MAJOR SOURCE OF MERCURY CONTAMINATION TO THE HUMAN BODY.

When scientific facts are buttressed by a reasonable hypothesis and alternative materials isn’t it time to place the controversy in perspective? It is the patient who receives amalgam fillings that is the pawn in all of this high level conspiracy and controversy. Isn’t it time to admit that a problem may exist and that the potential hazards far outweigh any benefits and can no longer be supported morally, financially, or scientifically? Hasn’t the time come to ban the further use of amalgam and devote the expenditure of scientific research dollars to protocols that might help undue some of the damage?

It is inconveivable to me that in the year 1988, the NIDR is still funding a myriad of research projects investigating the physical or other properties of dental amalgam. Could there be any connection between that astounding fact and the seeming rush to defend amalgam being made by the heads of dental materials departments of certain colleges?
FORUM

We have two dentists who are looking for an associate

1. Tim Kersten, D.D.S., P.O. Box 1460, Burney, CA 96013, 916-335-5491. Dr. Kersten is looking for an associate who believes and is committed to non-mercury and non-toxic dentistry.

2. Wm A. Westendorf, D.D.S. 2818 Blue Rock Rd., Cincinnati, OH 45239, 513-923-3839. Dr. Westendorf operates a general practice and is looking for an amalgam-free dentist to work into an association and future partnership.

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American Academy of Biological Dentistry will present a four day seminar, May 18-21, 1988 on Focal Diagnosis and Therapy featuring Drs. Fritz Kramer and Ralf Türk from West Germany. A special one-day program on The Immune System, Detoxification and Dentistry will be held on May 17, 1988. For more information write the Academy at P.O. Box 856, Carmel Valley CA 93924 or call 408-659-5385

The International Academy of Oral Medicine and Toxicology will be holding its mid-year meeting in Denver, Colorado at the Hyatt Regency on April 16-17, 1988. Meeting chairperson is Don Swartz, D.D.S., 303-778-8262. The annual meeting of the Academy will be held in Chicago, Illinois at the Oak Brook Hills Hotel & Conference Center on September 16-18, 1988. Meeting chairperson is Marcia Basciano, D.D.S., 312-953-2508.

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Transcending Limits of Healing From the Conventional to the Complimentary. Seattle, Washington March 24-27, 1988. SEA-TAC Hilton. This is a combination annual meeting of the AHMA, AHMF, Holistic Dental Association and the AHNA. For more information call the American Holistic Medical Association at 206-322-6842.

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The National Center for Homeopathy sponsors a 3-day seminar every year on Dental Homeopathy. This years seminar will be held July 29-31, 1988 at Endicott College in Beverly, Massachusetts. The seminar has been approved for 24 hours Fellowship & Mastership Accreditation by the Academy of General Dentistry and will designed for both the novice and the advanced student of Homeopathy. For more information contact Richard D. Fischer, D.D.S., 4222 Evergreen Lane, Annandale, VA 22003, 703-256-4441, or The National Center For Homeopathy, 1500 Massachusetts Ave., NW, Suite 41, Washington, DC 20005, 202-223-6182.

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The Foundation For Toxic Free Dentistry needs your support. The contributions and subscriptions to the Foundation Newsletter are coming in more slowly than originally anticipated. The problem isn’t going to go away and the time has arrived to stop giving lip-service only. The Foundation needs every dentist practicing mercury-free to contribute whatever they feel they can. The constitutional rights of you and your patients are being violated and now is just not the time to think that someone else will pick up the slack for you if you don’t participate. Send your donations to FTFD, P.O. Box 580160, Orlando, FL 32858-0160.

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Bio-Probe is soliciting feature articles for the Newsletter as well as full length non-fiction manuscripts for possible publication.

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