

## APPENDIX B RESEARCH STUDIES

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### MERCURY AND CARDIOVASCULAR DISEASE

Brake, J; Thaxton, P; Hester, PY.  
Mercury Induced Cardiovascular Abnormalities in the  
Chicken.  
Arch Environ Contam Toxicol. 6:269-77. 1977.

Juvenile chickens were either chronically exposed to 300 mcg/ml of mercury in the drinking water (chronic dosage-CD) or acutely exposed to either 3 (acute low dosage-ALD) or 12 (Acute high dosage-AHD) mg Hg/kg body weight administered intramuscularly for five consecutive days. Only the CD and AHD treatments retarded normal growth. Relative heart weights were increased by the CD treatment, decreased by the AHD treatment, and remained unchanged from the ALD treatment. Relative aorta weights were increased by the CD treatment but decreased by the AHD treatment. ECG analyses revealed a consistent decrease in the amplitude of the R-S, S, and T waves with the greatest effects present in the acute (ALD and AHD) treatments. These abnormalities indicate that mercury is acting at the cellular level to impair normal propagation of electrical impulses. Histological examination revealed that Hg caused myocardial histopathological changes characterized as a myocarditis with polymorphonuclear and lymphocytic infiltration and fatty degeneration. These changes indicate an acute inflammatory response attributed to a direct influence of mercury on the cardiovascular tissues. The authors concluded that low levels of inorganic mercury

when administered for even a short period of time can cause pathological changes in the cardiovascular system.

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Carmignani, M; Finelli, VN; and Boscolo, P.  
Mechanisms in Cardiovascular Regulation following  
Chronic Exposure of Male Rats to Inorganic Mercury.  
*Toxicology & Applied Pharmacology*. 69:442-450. 1983.

Aortic blood pressure, heart rate, electrocardiogram, and maximum rate of rise of the left ventricular pressure were monitored in ten control rats and ten rats receiving 50 micrograms/ml of mercuric chloride in deionized drinking water for 320 days.

The results indicate that chronic mercury exposure affects cardiovascular function by interfering with the baroreflex mechanisms (controlling blood pressure) and/or the reactivity to catecholamines (dopamine, epinephrine, and norepinephrine).

Mercury exposure also greatly increased the levels of copper and zinc in brain and kidney.

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Carmignani, M; Boscolo, P.  
Cardiovascular Homeostasis in Rats Chronically  
Exposed to Mercuric Chloride.  
*Arch. Toxicol. Suppl.* 7. 383-388. 1984.

Two groups of ten rats each received 50 micrograms/ml of mercuric chloride in deionized drinking water for 320 days and 350 days. Two equal groups of rats (controls) received only deionized water for the same periods. Aortic systolic and diastolic blood pressure, heart rate, electrocardiogram, and the maximum rate of rise of the left ventricular pressure were monitored.

Mercury exposure increased the force of cardiac muscle contraction without affecting the rate of contraction in both test groups, and caused arterial high blood pressure in the test group exposed for 350 days. The mercury exposure

also reduced reaction to blood pressure control mechanisms and drastically increased the levels of copper and zinc in brain and kidney. These actions of mercury may be explained by a reduced influx and intracellular availability of calcium ions for cardiac muscle contraction.

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Carmignani, M; Boscolo, P; Preziosi, P.  
Renal Ultrastructural Alterations and Cardiovascular  
Functional Changes in Rats Exposed to Mercuric  
Chloride.  
*Arch Toxicol. Suppl* 13:353-6. 1989.

It has been previously established that mercury compounds induce renal and cardiovascular damage. Eight male Sprague-Dawley rats received drinking water containing 50 mcg/ml of mercuric chloride for 350 days. Eight control rats received deionized drinking water during the same time.

Blood pressure and cardiac inotropism were increased in the mercury exposed rats without change in the heart rate. Mercury content was significantly higher in the tissues of the exposed rats compared to the controls. The highest levels were in the kidney, followed by the liver, brain, and heart. The levels of copper in the kidney, heart, and brain were also increased.

This study demonstrated that the concomitant effects of mercury on the cardiovascular system and kidney involves interactions among neurogenic, humoral, metabolic and, possibly, immunological mechanisms.

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Cheek, DB; Wu, F.  
Effect of Calomel on Plasma Epinephrine in Rat and  
Relationship to Mechanisms in Pink Disease.  
*Arch Dis Childhood*. 34:502-4. 1959.

In experiment on rats the researchers found that

mercurous chloride (Calomel) potentiated the effects of epinephrine on vasoconstriction. Related this finding to the vasoconstriction and hypertension found in victims of Acrodynia.

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Cheek, DB; Bondy, RK; Johnson, LR.  
Effect of Mercurous Chloride (Calomel) and Epinephrine (Sympathetic Stimulation) on Rats: Importance of Findings to Mechanisms in Infantile Acrodynia (Pink Disease).  
Pediatrics. 23:302-13. 1959.

In experiment on rats the investigators found that mercurous chloride (Calomel) potentiated the effect of epinephrine causing vasoconstriction. They suggested that this was cause of the vasoconstriction and hypertension found in victims of Acrodynia.

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Cutright, DE; Miller, RA; Battistone, GC; Millikan LJ.  
Systemic Mercury Levels Caused by Inhaling Mist During High-speed Amalgam Grinding.  
J Oral Med. 28(4):100-104. October-December 1973.

White rats were anesthetized, placed in containers, and exposed to amalgam mist from the slow grinding of amalgam. Amalgam blocks of 1x3x3 cm were intermittently ground over a period of 15 to 30 minutes with a total grinding time of 10 minutes. The 48 animals were sacrificed at various times, six per group; controls, 0, 8, 16, 24, 32, 48, and 72 hours after cessation of grinding. Tissues were analyzed for mercury with AAS (atomic absorption spectroscopy).

The control heart samples contained an average of 50.72 nanograms of mercury per gram. This rose rapidly to an average of 4113.1 ng Hg/gm at 0 hours (the cessation of grinding) and slowly fell to 293.4 ng Hg/gm at 72 hours, the end of the experiment. The 0 hour level was 81 times higher than the control level and the 72 hour level was

still almost 6 times the control level. At zero hour the mercury levels in heart tissue were 10 times those found in the brain tissue of test animals. The authors calculated that an average sized patient would have an "alarmingly high" body burden of mercury if only 2% of the mercury in one large amalgam filling were inhaled.

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Dahhan, SS; Orfaly, H.  
Electrocardiographic Changes in Mercury Poisoning.  
The Am. J of Cardiology. 14:178-183. August 1964.

Electrocardiographic examination of 42 victims of ethylmercury poisoning in 1960 Iraq episode: 24 female. 18 male; 28 were age 20 or younger.

Classification of ECG changes:

Slight = 5 cases.

Moderate = 10 cases.

Severe = 21 cases.

Very severe = 6 cases.

The predominant finding was S-T segment depression, with or without T wave changes, followed by prolongation of the Q-T interval. Arrhythmias, ectopic ventricular beats and paroxysmal ventricular tachycardia were also found. These were attributed to mercury damage to the sinoauricular node (the heart's pacemaker), the heart's electrical conduction system, and myocardial ischemia (reduced blood flow to the heart muscle).

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Danscher, G; Horsted-Bindslev, P; Rungby, J.  
Traces of Mercury in Organs from Primates with Amalgam Fillings.  
Exper Molec Pathology. 52:291-9. 1990.

In order to trace possible accumulations of mercury, three vervet monkeys received occlusal amalgam fillings, three

others maxillary bone implants of amalgam, and three untreated monkeys served as controls. One year later all animals were sacrificed by transcardial perfusion with glutaraldehyde. Tissue sections from different organs were subjected to silver amplification by autometallography and analyzed at light and electron microscopical levels. It was found that amalgam fillings (total 0.7-1.2 gm) caused deposition of mercury in the following tissues: spinal ganglia, anterior pituitary, adrenal medulla, liver, kidneys, lungs, and intestinal lymph glands.

In monkeys with maxillary silver amalgam implants (total 0.1-0.3 gm), mercury was found in the same organs except for liver, lungs, and intestinal lymph glands. Organs from the three control animals were devoid of precipitate. To evaluate whether silver released from the corroding amalgam fillings added to the staining pattern, tissue sections were exposed to potassium cyanide prior to being autometallographically developed. This treatment removes all traces of silver, leaving mercury sulfide accumulation untouched. By comparing sections that had been exposed to cyanide with untreated parallels no difference was seen in the pattern, confirming that mercury was the only catalyst present in the tissue.

These results strongly support what has been suggested previously that dental fillings in primates cause absorption of mercury released from amalgam fillings through lungs and intestinal tract, and that, depending on the exposure route, mercury is distributed to most organs and will eventually be found in the central nervous system. The present data also show that silver released from the corroding fillings is not absorbed.

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de Bruin, A. (Ed.)  
Biochemical Toxicology of Environmental Agents. Pp. 575-6; 702-3. Elsevier. 1976.

Heavy metals with suspected atherogenic action include mercury and lead. Evidence for such action of mercury is the finding of hypercholesteremia in conjunction with elevation of serum beta-lipoprotein in human mercurialism. After inhalational exposure to mercury, animals also experience elevated levels of plasma cholesterol together with the deposit of cholesterol in the aortic vessels. (pg. 702) Poisoning with mercury vapor elicits a pattern of deviations in enzyme activity in heart muscle, essentially identical with those observed in other organs. In the rabbit there is a fall in the intensity of the reactions for respiratory enzymes and ATPase in the cardiac muscle. Nonspecific esterases commonly showed a raise during experimental mercurialism. Myocardial respiration and oxidative phosphorylation may thus be supposed to be severely affected in chronic mercury poisoning; the corollary of which is reduced energy supply for heart muscle contraction. Mercury intoxicated rabbits show evidence of disorders in the ECG pattern, apparently mediated by the abolition of ATPase in the myocardial membranes, which impairs membranal cation transport from the blood to the sarcoplasm.

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Fellinger, K; Schweitzer, F.  
Gefasserkrankungen nach Quecksilbervergiftungen.  
Arch Gewerbepath Gewerbehyg. 9:269-75. 1938. Reports on vascular damage after mercury exposure are rare, according to the authors. It therefore appeared to be of considerable interest to report serious vascular damage in cases where circumstances and the development of the diseases made it highly probable that mercury damage was the precipitating cause. It is definitely shown that vascular damage should be included with other effects of mercury poisoning.

Fredin, B.

The Distribution of Mercury in Various Tissues of Guinea Pigs After Application of Dental Amalgam Fillings (A Pilot Study).  
Sci. Total Environ. 66:263-268. 1987.

Six guinea pigs received dental amalgam fillings, five animals were used as controls. Two experimental animals were sacrificed after 1 day, two after 3 days, one after 5 days, and one after 10 days. Mercury content in brain, heart, liver, kidney, blood, urine, and feces were analyzed by cold vapour atomic absorption spectroscopy.

All of the mercury contents in the tissues of treated animals differed significantly from those in control animals. The heart absorbed more mercury faster than did brain tissue. At one day, the mercury levels in the heart averaged 10 times that in the brain; at three days heart mercury levels were 3.5-10 times brain levels; at five days the heart mercury level was almost twice that in the brain; and at ten days the amount of mercury in the heart was still 50% higher than in the brain. Throughout the course of the experiment, the mercury concentrations in the heart averaged more than twice that found in brain tissue.

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Gale, TF.

Cardiac and Non-cardiac Malformations Produced by Mercury in Hamsters.  
Bull. Environm. Contam. Toxicol. 25:726-732. 1980.

Timed-pregnant hamsters were injected with a single dose of mercuric acetate (15 mg/kg) on day 7, 8, or 9 of gestation. Control animals received 5 ml/kg of demineralized distilled water. The animals were sacrificed on gestation day 12 or 15 and examined to determine the types and frequency of internal malformations.

The pre-natal mercury exposure produced marked embryotoxicity including embryonic death as well as external and internal abnormalities in living fetuses. The most significant categories of embryotoxicity were resorptions, retardation, edema, pericardial cavity

distention, and abnormal hearts. The mercury exposure produced a high incidence of abnormal hearts characterized by dilation and thinning and weakening of the wall of the right ventricle.

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Griffith, CG; Butt, EM; Walker, JW.  
The Inorganic Element Content of Certain Human Tissues.  
Ann. Internal Med. 41:501-509. 1954.

Concentrations of mercury, as well as a number of other metals, present in the brain, heart, lung, spleen, kidney, and liver were determined by chemical or spectrographic analysis from organs of 910 human autopsy subjects. Material from 410 cases was subjected to chemical analysis; spectrography was utilized in 500 cases.

The organs of only 45 of these subjects were analyzed for mercury content, all of whom had congestive heart failure. One third of these had no record of having been treated with mercury diuretics, 14 had received less than 400 milligrams of mercury, and 16 had received more than 400 milligrams of mercury. The heart mercury levels were measured only in the latter group and found to average 0.27 milligrams of mercury.

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Hahn, LJ; Kloiber, R; Vimy, MJ; Takahashi, Y;  
Lorscheider, FL.  
Dental "Silver" Tooth Fillings: A Source of Mercury Exposure Revealed by Whole-body Image Scan and Tissue Analysis.  
FASEB J. 3:2641-6. Dec 1989.

The sheep was utilized in this study investigating the release and distribution of mercury from dental amalgam fillings because it exhibits molar chewing mechanics similar to that found in humans. Twelve molar teeth were filled with dental amalgam containing a portion of radioactively labelled mercury and left in place for 29 days.

Each filling contained approx. 425 milligrams of mercury, about 50% of the amount in the average adult human filling. Fillings were overcarved in a concave manner to prevent excessive wear. The use of radioactively labelled mercury provided specificity; mercury found in the animal could not be confused with mercury from any other source. Post-chewing intra-oral mercury vapor measurements were periodically taken. These measurements closely approximated measurements derived from human subjects in previously published studies. The fate of dental amalgam mercury was determined by whole-body scanning and measurement of radioactive isotope in specific tissues.

The results of the study clearly demonstrated that "substantial quantities of Hg from amalgam will appear in various body tissues as early as 29 days after placement of amalgam fillings in teeth". Even during this relatively short period of time, Hg accumulation was found in the heart tissue. Follow up study found increasing levels of amalgam-derived mercury in body tissues as time progressed. Levels of mercury found in the blood and urine were much lower than levels found in most tissues.

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Hahn, LJ; Kloiber, R; Leininger, RW; Vimy, MJ; Lorscheider, FL.  
Whole-body Imaging of the Distribution of Mercury Released from Dental Fillings into Monkey Tissues. FASEB J. 4:3256-60. Nov 1990.

The fate of mercury (Hg) released from dental "silver" amalgam tooth fillings into mouth air is uncertain. A previous report about sheep revealed uptake routes and distribution of amalgam Hg among body tissues. The present investigation demonstrates the bodily distribution of amalgam Hg in a monkey whose dentition, diet, feeding regimen, and chewing pattern closely resemble those of humans. When amalgam fillings, which normally contain 50% Hg, are made with a tracer of radioactive <sup>203</sup>Hg and

then placed into monkey teeth, the isotope appears in high concentration in various organs and tissues within four weeks. Whole-body images of the monkey revealed that the highest levels of Hg were located in the kidney, gastrointestinal tract, and jaw. The dental profession's advocacy of silver amalgam as a stable tooth restorative material is not supported by these findings.

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Halbach, S.  
Sulfhydryl-Induced Restoration of Myocardial Contractility after Alteration by Mercury.  
Arch Toxicol. Suppl 13:349-52. 1989.

This study was conducted on muscle tissue excised from the right ventricle of reserpine-pretreated guinea pigs. Organic mercury compounds produce three distinct effects on the function of isolated myocardial tissue; a decrease in contractile response, a release of endogenous catecholamines, and a direct increase in force of contraction by inhibition of the sarcolemmal sodium- and potassium- ATPase. These effects were solely attributable to the mercury atom.

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Jha, LB; Bhatia, B.  
Effect of Mercuric Chloride on Coronary Flow in Perfused Rat Heart.  
Bull Environ Contam Toxicol. 31(2): 132-138. 1983.

Male Wistar rat hearts were perfused with a mercuric chloride solution of 1 microgram/milliliter (1 ppm) concentration. The perfusion cannula was tied into the root of the aorta directed to the aortic valve.

This study found that 1 ppm (1 mcg/ml) mercuric chloride caused a dose-response reduction in the coronary blood flow in rat's heart due to the contraction of the smooth muscle in the coronary arteries of the heart (i.e.- the myogenic response). The vascular smooth muscle contraction reduced the lumen of the arteries, thereby reducing the coronary blood flow within the first minute

of perfusion. The contraction of the vascular smooth muscle was caused by blockage of the sodium ( $\text{Na}^+$ ) gate, and thus inhibition of the potassium pump, by the mercury ions. Contraction of cardiac muscle was also reduced. In 1975, Solomon and associates had demonstrated that mercuric ions caused contraction of vascular smooth muscle.

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Jonek, J.

Histochemische Untersuchungen über das Verhalten einiger Enzyme im Herzmuskel nach experimenteller Vergiftung mit Quecksilberdämpfen.  
Int Arch Gewerbepathol Gewerbehyg. 21:1-10. 1964.

"In our experiments with mercury vapor intoxications we found a decreased activity of respiratory enzymes and sarcoplasmic ATPase. There was a marked reduction of activity of succinic dehydrogenase, DPNH-diaphorase, cytochrome oxidase and ATPase in cryostat sections. These enzymes are connected with oxidative phosphorylation and give energy to muscle contraction. Since the heart muscle response varied between different experimental animals we concluded that sensitivity was individual. The respiratory enzymes are most sensitive to mercury. This is possibly connected with an oxidation of SH-groups to S-S groups caused by heavy metals and especially mercury. We consider that similar mechanisms are responsible for lead action on the heart muscle. Also a direct action of mercury on cell membranes can not be excluded."

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Kahler, HJ.

Zur Frage der Kardiotoxischen Wirkung des Quecksilbers, insbesondere des Saatfruchtbeizmittel "Ceresan".

Zbl Arbeitsmed Arbeitsschutz. 10:25-31. 1960.

The author points out the well known cardiotoxic effects of mercurial diuretics and all of the attempts to find mercury compounds which had diuretic effects without

killing the patient from heart damage. The usual side effect was cardiac arrest preceded by EKG disturbances (besides the many other earlier side effects caused by the mercury). There was no evident heart muscle damage, although there is no doubt that mercury can eventually cause irreversible damage to the myocardium. Severe disturbance of heart rhythm was very common (about 20% according to one report). The damage to the heart could come after the first injection or suddenly and unpredictably after many injections.

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Khayat, A; Dencker, L.

Whole Body and Liver Distribution of Inhaled Mercury Vapor in the Mouse: Influence of Ethanol and Aminotriazole Pretreatment.  
J Applied Toxic. 3(2):66-73. 1983.

Mice were exposed to radioactive mercury 203 by inhalation of vapor form and by intravenous injection of mercuric chloride. Organ and tissue distribution was determined by autoradiography and gamma counting.

The distribution of mercury was much different after inhalation of mercury vapor. After injection of inorganic mercury, most of the mercury was found in the liver and kidneys. After inhalation of mercury vapor, much larger amounts of mercury were found in the heart, lungs, and brain, with smaller accumulations in the thyroid, adrenals, spinal ganglia and nerves, testes and ovaries. The concentrations of mercury in the blood were considerably lower after inhalation of vapor than in the injected group.

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Khayat, A; Dencker, L.

Organ and Cellular Distribution of Inhaled Metallic Mercury in the Rat and Marmoset Monkey (Callithrix Jacchus): Influence of Ethyl Alcohol Pretreatment.  
Acta Pharmacol et Toxicol. 55:145-152. 1984.

Rats and monkeys were exposed to inhalation of

radioactive mercury vapor 203. Organ and tissue distribution was determined by whole-body autoradiography, microautoradiography, and scintillation counting.

The distribution of mercury vapor largely conformed to earlier results found in the mouse. High accumulations of mercury were found in the lungs, heart, and brain. Further high accumulations and activity in the endocrine glands such as the adrenal cortex, thyroid, retina, corpora lutea of the ovary, and specific areas of the liver. After only one hour of exposure to mercury vapor, the mercury levels in the heart were 3-4 times those found in the brain.

The authors concluded that after exposure to mercury vapor the lung, heart, and brain are target organs in most species, including humans. They also stated that they had studied a considerable number of elements and organic compounds and that to their knowledge "mercury vapor is the first to exhibit this distribution pattern, characterized by a rapid diffusion from blood vessels into cells where it is immediately trapped by oxidation".

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Kleinfeld, M; Stein, E.  
Action of Divalent Cations on Membrane Potentials and Contractility in Rat Atrium.  
*Amer J Physiol.* 215(3):593-9. Sept 1968.

The effects of the chlorides of barium, cadmium, cobalt, zinc, magnesium, manganese, strontium, nickel, copper, and mercury on the transmembrane action potential and isometric tension developed in the rat atrium were observed. The concentrations in the perfusate bathing the atrium were from  $10^{-3}$  to  $10^{-6}$  m. Mercury, barium, and strontium produced an increase in isometric tension ranging from 60 to 175%. Mercury in concentrations of  $0.2 \times 10^{-5}$  m. produced an increase in contractile tension of approximately 60%. At concentrations of  $0.4 \times 10^{-4}$  m. mercury decreased the contractile tension by 42%. With

regard to the dual action of mercury on contractility the authors attribute the positive inotropism observed at lower concentrations to mercury displacing calcium from its sulfhydryl binding storage site, allowing the released calcium to activate the contractile mechanism. At the higher concentrations, mercury inhibits the contractile mechanism by chelating the sulfhydryl groups essential for the inotropic response. Manganese, magnesium, copper, cadmium, zinc, cobalt, and nickel produced a decrease in contractile tension ranging from 50-90%. There was only partial return to control value in the cases of cadmium, copper, zinc, and mercury. When calcium was added to the perfusate, depressed contractile tension returned to control or near control state within 5 minutes, except with mercury. No consistent correlation was found between the various parameters of the action potential and contractility. This lack of consistent correlation can be explained on the basis that the divalent cations not only alter the transmembrane action potential but, more probably, act on the excitation-contraction coupling.

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Kostka, B; Michalska, M; Krajewski, U; Wierzbicki, R.  
*Pol J Pharmacol Pharm.* 41(2):183-9. Mar-Apr 1989.

The effects of methylmercuric chloride on the coagulability of blood were studied in rats. The administration of a single dose (17.9 mg Hg/kg) and a repeated dose (5X8 mg Hg/kg/day) of this compound resulted in hypercoagulation. The reduction of the clotting time, the increase of fibrinogen level in plasma and changes characteristic of hypercoagulation in the thromboelastographic parameters were observed. Simultaneously, signs of impaired activity of blood platelets: decreased aggregation velocity and clot retraction as well as prolongation of the bleeding time were noticed.

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Kussmaul, A.  
 Untersuchungen ueber den constitutionellen  
 Mercurialismus und sein Verhaeltniss zur  
 constitutionellen Syphilis.  
 Wuerzburg. 1861.

In mercury poisoning the activity of the involuntary muscles will be affected. Together with a weakness of the voluntary muscles there will generally be an impairment of the heart. Many observers have noticed that the pulse will be slower. The most common change is great lability. Resting rate is 60-70 beats/minute, but at the slightest agitation the rate will rapidly rise to 80-100. Sometimes pronounced tachycardia occurs. Often the pulse is weak but the muscular tremor and spasms impairs and sometimes makes a determination impossible. The loss of consciousness that sometimes occurs may be a consequence of the profoundly impaired heart activity.

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lu, KP; Zhao, SH; Wang, DS.  
 The Stimulatory Effect of Heavy Metal Cations on  
 Proliferation of Aortic Smooth Muscle Cells.  
 Sci China [B]. 33(3):303-10. Mar 1990.

Heavy metal cations  $Cd^{2+}$ ,  $Pb^{2+}$ , and  $Hg^{2+}$  were added to substitute for  $Ca^{2+}$  in culture media to study their effect on the relationship between CaM and the proliferation of cultured rabbit aortic smooth muscle cells (ASMC). It was found that all the heavy metal cations studied stimulated the proliferation of ASMC in varying degrees, increased the CaM content in cells at late G1 stage and decreased the activity of cAMP PDE. These results suggest that the adverse effect of heavy metals may be related to the pathogenesis of atherosclerosis and hypertensive disease.

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Matsuo, N; Suzuki, T; Akagi, H.  
 Mercury Concentration in Organs of Contemporary  
 Japanese.  
 Arch Environ Health. 44(5):298-303. Sept-Oct 1989.

Concentrations of inorganic mercury (IHg), methylmercury (MeHg), and total mercury (THg) were determined for autopsy samples from 46 Japanese subjects. The averages were several hundreds of ng/g in kidney cortex, kidney medulla, and liver, and were several tens of ng/g in cerebrum, cerebellum, heart, and spleen. Inorganic mercury accumulated more in kidney and liver, while methylmercury levels in tissues were uniform through all organs except the liver. Age was a significant factor in increased IHg concentrations and increased values of % IHg in the cerebrum and heart, and decreased values of % MeHg in the cerebrum, cerebellum and heart. The authors noted that people are exposed to elemental mercury vapor from smoking and from dental amalgam fillings. The authors also pointed out literature reports demonstrating that tissue analysis by Neutron Activation Analysis (NAA) consistently showed tissue mercury levels more than 10 times those found from the utilization of Atomic Absorption Spectrometry (AAS). Further considerations in analysis noted by the authors were (1) a slower elimination of IHg than MeHg from the brain, (2) demethylation of MeHg in the brain, and (3) the influence of formalin fixation of tissues inducing various changes, such as loss of mercury or breakage of the C-Hg bond of organic mercury.

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Oettingen, WF von.  
 Poisoning: A Guide to Clinical Diagnosis and  
 Treatment. 2nd Ed. Saunders Co. London. 1958.

In mercury poisoning, cardiac and vascular disturbances characterized by endarteritis in the smaller and smallest vessels may be observed.

Orlowski, JP; Mercer, RD.  
Urine Mercury Levels in Kawasaki Disease.  
Pediatrics. 66(4):633-636. October 1980.

Six patients diagnosed with Kawasaki disease (MLNS) had mercury levels determined by 24-hour collections and compared to six controls matched by age, sex, and geographic location. The appearance of Mucocutaneous Lymph Node Syndrome (Kawasaki disease) has been related temporally and geographically to environmental pollution with mercury. The clinical signs and symptoms of Kawasaki disease are markedly similar to those of Acrodynia, an acknowledged mercury syndrome.

The six patients had abnormally high urinary excretions of mercury compared to the controls. One patient was administered penicillamine to chelate mercury from the body; urine mercury levels increased and the patient recovered.

Pathologic findings in the subjects included: Myocardial infarction (heart attack), abnormal electrocardiograms, A-V block, premature ventricular contraction, myocarditis (inflammation of the heart muscle), and aneurysms of the coronary (heart) arteries.

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Perry, HM, Jr.; Yunice, A.  
Acute Pressor Effects of Intra-arterial Cadmium and Mercuric Ions in Anesthetized Rats.  
Proc Soc Exp Biol Med. 120:805-8. 1965.

Inorganic and organic mercury and cadmium compounds were injected into the femoral arteries of adult Sprague-Dawley rats. Mercuric ion produced greater increases in diastolic blood pressure than did cadmium ion and, unlike the latter, did not depress the diastolic pressure in large concentrations. Quantities ranging from 280 mcg (one fourth of the average acutely lethal dose) to 70 mcg of mercuric ion, as either the chloride or sulfate, per 100 gm of body weight elevated the diastolic blood pressure

more than 40 mm Hg. Organic mercury compounds had no effect on the diastolic blood pressure. Vanadyl, barium, copper, and silver ions were markedly pressor, while lead was inert even in very large quantities.

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Perry, HM, Jr.; Schoepfle, E; Bourgoignie, J.  
In Vitro Production and Inhibition of Aortic Vasoconstriction by Mercuric, Cadmium, and Other Metal Ions.  
Proc Soc Exp Biol Med. 124:485-90. 1967.

Aortic strips from New Zealand white rabbits were tested by exposure to epinephrine and then exposed to various metals. A 10(-6) molar concentration of mercuric chloride produced a 10% shortening of the aortic strip, compared to the 20% shortening caused by the 10(-7) molar epinephrine. The degree of shortening of the strip was a function of the concentration of mercuric ion, ranging from 2.5% with 10(-7) to 21% with 10(-4) molar mercuric ion. Organic mercury compounds had no effect on the aortic strip. Contractions induced by epinephrine and angiotensin II were inhibited by mercuric ion for more than 2 hours. A search for other vasoactive metals revealed none that was effective in concentrations as low as 10(-6) molar concentrations. Silver, copper, barium, vanadyl, and mercurous ions produced significant aortic contractions at 3x10(-4)-10(-6) molar. All other tested metals, including lead, had no effect.

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Perry, HM, Jr.; Erlanger, M; Yunice, A; Schoepfle, E;  
Perry, EF.  
Hypertension and Tissue Metal Levels Following Intravenous Cadmium, Mercury, and Zinc.  
Amer J Physiol. 219:755-61. Sept 1970.

Small amounts of intra-arterial injected cadmium or mercuric ions produce prompt and marked transient increases in both diastolic and systolic blood pressure in

rats. Both ions have been shown to increase peripheral resistance. In this study 3.6, 0.36, or  $0.036 \times 10^{-6}$  moles of cadmium or mercuric ions, when injected intra-arterially or intravenously, induced significant hypertension in rats within 1-4 minutes. Cadmium, but not mercury, produced initial transient hypotension. From 4-8 minutes after injection, the diastolic pressure averaged 13-18 mm Hg above baseline following injection of either metal by either route. The changes in systolic pressure paralleled those in diastolic pressure, and there were no significant changes in pulse rate. Unlike cadmium, the mercury-induced hypertension did not produce a change in cardiac output. Similar amounts of zinc were inert. Concentration of metal circulating in the blood was unrelated to induced changes in blood pressure. Both metals were found to rapidly leave the blood, beginning as early as 30 seconds following injection. In an experiment to determine the affinities of these metals to bind to vascular tissue, 4-8 times as much mercury bound to isolated aortic strips. Mercury, but not cadmium, was able to produce contraction in the isolated aortic strips.

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Perry, HM, Jr.; Erlanger, M.  
Hypertension and Tissue Metal Levels After  
Intraperitoneal Cadmium, Mercury, and Zinc.  
*Amer J Physiol.* 220:808-11. March 1971.

Cadmium, mercury, and zinc were induced into female Wistar rats by intraperitoneal injection. Effects on blood pressure and amounts of metals in various tissues were determined. Mercury caused only transient elevations in blood pressure and only with a dose of 0.88 micromoles. This was in marked contrast to the pressor effects when mercury had been induced intravenously or intra-arterially. Concentrations of injected metal in blood and five solid tissues of 200-gm rats were measured 1, 8, 60, and 120 minutes after the intraperitoneal injections (0.44

micromoles of mercury). At the 1 and 8 minute intervals, the largest concentrations of mercury were found in the aortic tissue. Subsequently, only levels of mercury in the kidney exceeded those in the aortic tissue. Significant amounts of mercury were found in the heart tissue throughout the time intervals. Two hours following comparable doses, mercury and cadmium concentrations were similar in aorta and heart.

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Piikivi, L.  
Cardiovascular Reflexes and Low Long-term Exposure  
to Mercury Vapour.  
*Int Arch Occup Environ Health.* 61:391-5. 1989.

Subjective symptoms related to autonomic dysfunction and quantitative non-invasive tests measuring both sympathetic and parasympathetic functions of the autonomic nervous system were studied among a group of 41 chlorine-alkali workers with low long-term exposure to mercury vapour and their matched referents. The test battery included measurements of pulse rate variation in normal and deep breathing, in the Valsalva maneuver, and in vertical tilt as well as blood pressure responses during standing and isometric work. The exposure time had been 16 years on average, and the mean exposure to Hg vapour was estimated to have been about 30 mcg/cubic meter of air. Of the 41 subjects in the test group of chlorine-alkali workers, 5 were excluded from the study because of positive findings to medical criteria and three were excluded because of hypertension medicated by beta-blocking agents. Since 1972, the workers had been offered a salary bonus to use protective masks and had been rotated out of the higher mercury exposure tasks on a monthly basis. Only a tendency for a subtle reduction of cardiovascular reflex responses and a slight increase of subjective symptoms were seen in the remainder of the exposed group, but no significant autonomic dysfunction

was associated with the low level of exposure. In the isometric work test the rise of the diastolic blood pressure in the exposed group was higher than in the referents. There was an unexpected positive correlation of the beat-to-beat variation in pulse rate to the actual Hg concentration in urine of the exposed workers. The exposed workers also exhibited more complaints of somatic symptoms related to early dysfunction of the autonomic regulation mechanism. [ED. NOTE: Previously published research has clearly demonstrated that significantly less mercury vapor is absorbed when it is mixed with chlorine vapors. Chlorine combines with mercury to form mercurous chloride, which is very poorly absorbed. The research also demonstrated that pathological effects of exposure to mercury vapor alone are much more severe than when it is mixed with vapors of chlorine. (Viola, PL; Cassano, GB. The Effect of Chlorine on Mercury Vapor Intoxication: Autoradiographic Study. *Med Lavoro*. 59(6-7):437-44. 1968.) Years ago, mirror factories were sprayed with chlorine gas to relieve the toxic effects of mercury vapor exposure. One must also wonder what the results of this study would have been if exposed workers with frank cardiovascular pathology had not been eliminated from consideration.]

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Placidi, GF; Dell'Osso, L; Viola, PL; Bertelli, A.  
Distribution of Inhaled Mercury (203Hg) in Various  
Organs.  
*Int J Tiss React*. 5:193-200. 1983.

Whole-body autoradiograms showed significant uptake of labelled mercury by the kidney, brain, myocardium, intestine and liver in descending order.

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Prabhu, SD; Salama, G.  
The Heavy Metal Ions  $\text{Ag}^+$  and  $\text{Hg}^{2+}$  Trigger Calcium  
Release from Cardiac Sarcoplasmic Reticulum.  
*Arch Biochem Biophys*. 15;277(1):47-55. Feb 1990.

Heavy metal ions have been shown to induce  $\text{Ca}^{2+}$  release from skeletal sarcoplasmic reticulum (SR) by binding to free sulfhydryl groups on a  $\text{Ca}^{2+}$  channel protein and are now examined in cardiac SR.  $\text{Ag}^+$  and  $\text{Hg}^{2+}$  (10-25 microM) induced  $\text{Ca}^{2+}$  release from isolated canine cardiac SR vesicles whereas  $\text{Ni}^{2+}$ ,  $\text{Cd}^{2+}$ , and  $\text{Cu}^{2+}$  had no effect at up to 200 microM.

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Rhee, HM; Choi, BH.  
Hemodynamic and Electrophysiological Effects of  
Mercury in Intact Anesthetized Rabbits and in Isolated  
Perfused Hearts.  
*Exp Molec Pathol*. 50:281-90. 1989.

Using intact anesthetized rabbits and isolated perfused hearts, the hemodynamic and electrophysiological effects of mercury (Hg) were examined in order to assess the role of cardiovascular dysfunction in Hg intoxication. In intact animals, different doses of mercuric chloride (50, 100, 200, 500, 1000, and 2000 mcg/kg) in 0.25 ml saline solution were injected into the femoral vein over a period estimated to be 2 seconds. These were considered to be acute exposures. Controls received injections of the same volume of saline via the femoral vein. The most consistent and prominent cardiovascular effect was a significant reduction in blood pressure, both systolic and diastolic. Heart rate was also dramatically reduced. Lower Hg concentrations reduced the force of contraction to less than 30% of the control value, while the higher concentration (10 mg%) of mercury exposure to perfused heart stopped contractions within 20 seconds. This cardiodepressive action was probably brought about by the primary action of Hg on the heart (direct cardiotoxicity) rather than by altered

sympathetic activity, as evidenced by normal renal nerve activity at times when the hemodynamic actions of Hg were clearly manifest. The profound hemodynamic effects of mercury observed emphasize the potential importance of Hg cardiotoxicity and indicate the need to differentiate between the primary and secondary effects of Hg intoxication on CNS tissues for evaluation of the toxic effects of Hg compounds.

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Rieselmann, SD.  
Einfluss der Quecksilberintoxikation auf die inneren Organe.  
Arch Gewerbepathol. 1:496. 1930.

"One of the most important and most feared consequences of acute mercury poisoning is, as is well known, a paralyzing influence on heart and circulation, followed by reduced blood pressure and death. The rather common occurrence of similar changes in acutely poisoned workers was confirmed by numerous anamnestic data and our examinations of the vascular system".

"...a reduced pulse pressure, indicating that the heart works with impaired effectiveness and that the emptying into the arterial system is incomplete during the systolic phase. This, in turn, indicates a low permeability of precapillary arteries..."

"We found in 50% of the workers a normal function and in 48% values which showed increased irritability or insufficiency of the coronary vessels (2% could not be examined because of tremor). The condition of the heart muscle was clinically examined and we could divide the workers into two groups; the first one with damage to the muscle (cardiomyopathy) and changes in nerve regulation (cardioneuropathy) constitutes the second group. Electrocardiographic analysis of some of the workers confirmed the diagnosis of heart muscle insufficiency."

Shiraki, H; Nagashima, K.  
Essential Neuropathology of Alkylmercury Intoxications In Humans from the Acute to the Chronic Stage With Special Reference to Experimental Whole Body Autoradiographic Study Using Labeled Mercury Compounds.  
Neurotoxicology. Ed: Roizin, L; Shiraki, H; Grcevic, N. 247-260. 1977.

The authors discuss research on the pathology found in victims of Minimata disease and the experimental results of time-dependent whole body autoradiography in different animals using labeled alkylmercury and/or inorganic mercury compounds.

The authors clearly found that, in alkylmercury poisoning, circulatory disturbances of a hemodynamic origin were responsible for the development of pathology. In studies in humans, scleroses of the cerebral blood vessels were found, as well as thrombus formation and fibrohyalinous thickening of arteries. Victims demonstrated hypertension, vascular scleroses, damage to heart muscle, and cardiac arrest, as well as damage to the Islets of Langerhans in the pancreas. Nerve damage resulted from reduced blood flow. Experiments on rabbits determined conspicuous elevations of cholesterol and blood sugar.

Radiographic studies in monkeys administered radioactive ethylmercury chloride detected high levels of mercury in the heart (4.62 ppm) after one hour. The walls of the aorta and large arteries adjacent to the heart had high levels of mercury 20 hours and 8 days after administration, suggesting migration of mercury into the muscle layers of these arteries. This was not found after administration of radioactive inorganic mercuric chloride. The mercuric chloride was found mostly in blood plasma rather than corpuscles, whereas the ethylmercury was found almost entirely within the cells, combined with thiol (SH) groups of cysteine portions of hemoglobin molecules. [Note: Mercury vapor easily penetrates cell membranes like

alkylmercury compounds; inorganic mercury compounds do not!]

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Siblerud, RL.

The Relationship Between Mercury from Dental Amalgam and the Cardiovascular System.  
Sci Tot Environ. 99:23-35. 1990.

The findings presented here suggest that mercury poisoning from dental amalgam may play a role in the etiology of cardiovascular disorders. Comparisons between subjects with and without amalgam showed amalgam-bearing subjects 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. The data suggest that inorganic mercury poisoning from dental amalgam does affect the cardiovascular system.

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Simmons, MS; Rhodus, NL; Little, JW; Verrusio, AC; Kunik, RL.

EKG Screening of Dentists for Cardiac Arrhythmias.  
J Dent Res. 68(Spec Issue):958. Abst. 731. June 1989.

This study was undertaken to ascertain the presence of undetected arrhythmias in a population of dental professionals. The results also served as a follow-up study to correlate with data from an earlier study performed on a larger population in multiple health care settings.

A portable EKG 3-lead unit (Vitel-III-EKG system) was used to obtain a one-minute record. This was transmitted via telephone to a cardiac technician or nurse trained in EKG interpretation. A cardiologist overread each report. The results were compiled from 1165 (1002 male and 163

female) dentists who participated in the ADA Annual Health Evaluation Program in Washington, D.C. at the 1988 ADA/FDI World Dental Meeting.

The data was consistent with earlier study in that it revealed that 14% of those dentists screened had an abnormal EKG showing one or more arrhythmias, while 4% screened were identified as having an arrhythmia that needed further medical follow-up. Two dentists were hospitalized with potentially life-threatening disorders that had not previously been diagnosed. The results underlined the positive application of EKG screening of populations for updated arrhythmias suggestive of underlying potential heart disease.

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Solomon, HS; Hollenberg, NK.

Catecholamine Release: Mechanism of Mercury-induced Vascular Smooth Muscle Contraction.  
Amer J Physiol. 229(1):8-12. July 1975.

The mechanism by which mercuric ion ( $\text{HgCl}_2$ ) induces contraction of vascular smooth muscle was defined in the kidney of anesthetized dogs and in rabbit aortic strips. In vivo,  $\text{HgCl}_2$  injected into the renal artery induced a dose-related reduction in renal blood flow (electromagnetic flowmeter) and glomerular filtration rate (creatinine clearance). The threshold dose for both blood flow and creatinine clearance was 0.01 mg/kg into the renal artery, with an ED-50, the dose that induced a 50% reduction, between 0.03 and 0.10 mg/kg. A dose of 1.0 mg/kg produced an 80% reduction in both renal blood flow and glomerular filtration rate. The threshold for response on rabbit aorta strips was approx. 0.3 mcg/ml, with a maximum at about 10 mcg/ml. Alpha-adrenergic blockade with phentolamine and phenoxymethamine prevented the response to mercuric ion. The authors cited seven previously published studies demonstrating vascular smooth muscle contraction caused by mercuric ion. It is

apparent from this series of experiments that mercuric ion does not act directly on the alpha-adrenergic receptor, but rather does so indirectly by causing the release of endogenous catecholamines.

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Summers, AO; Wireman, J; Vimy, MJ; Lorscheider FL. Increased Mercury Resistance in Monkey Gingival and Intestinal Bacterial Flora After Placement of Dental "Silver" Fillings. *The Physiologist*. 33(4), A-116. August 1990.

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

in the proportion of Hg resistant bacteria in both the oral cavity and the intestine. Since Hg resistant bacteria convert Hg(II) or methyl-Hg(I) to volatile, lipid soluble Hg(0) (Summers, AO. *Ann Rev Microbiol*. 40:607-34. 1986.), the increased incidence of such bacteria in flora may influence the pharmacodynamics and toxicity of ingested Hg from dental amalgam.

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Tayarani, I; Lefauconnier, J-M; Bourre, J-M. The Effect of Mercurials on Amino Acid Transport and Rubidium Uptake by Isolated Rat Brain Microvessels. *Neurotoxicol*. 8(4):543-52. 1987.

Previous studies have indicated that mercury damages the blood-brain barrier. This study was undertaken to investigate the in vitro effects of mercuric chloride (HgCl<sub>2</sub>) and methylmercury chloride (CH<sub>3</sub>HgCl) on the uptake in rat brain microvessels of various amino acids (alanine, phenylalanine, glutamic acid, alpha-methylaminoisobutyric acid) as well as rubidium. Marked inhibition (about 70%) of uptake was seen at concentrations of 10<sup>-5</sup> and 10<sup>-4</sup> M of both mercury compounds, but the uptake was not inhibited at concentrations less than 10<sup>-5</sup> M. A substantial decrease in rubidium uptake was also caused by the mercury compounds. The effect of mercuric chloride on the amino acid uptake was different in that it was not dependent on mercuric chloride concentrations. The results indicate that the main toxic effect of mercury compounds is inhibition of amino acid transport through the small blood vessels, thereby depriving cells of their vital amino acid nutrients. The concentration at which mercury exerts its inhibitory effect in this study is similar to that estimated to have been present in the brains of victims during the Minamata epidemic.

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Togna, G; Dolci, N; Caprino, L.  
Inhibition of Aortic Vessel Adenosine Diphosphate  
Degradation by Cadmium and Mercury.  
Arch Toxicol. Suppl. 7:378-81. 1984.

The effects of cadmium and mercury on ADP breakdown by vessel walls were investigated. These metals reduce the ADP clearance promoted by arterial tissue. This effect could be attributed to the inhibition of vessel wall ADP-ase enzyme which plays an important role in the genesis of thrombotic phenomena.

Thrombosis of glomerular capillaries, selective damage to vascular endothelium, induction and progression of atherosclerosis and hypertension have been ascribed by many authors to several heavy metals. The non-thrombogenic properties of vascular endothelium are partially due to the production of prostacyclin by vessel wall and to the degradation of circulating adenosine nucleotides by adenosine diphosphatase (ADPase), a membrane-bound enzyme. In previous studies it has been shown that cadmium chloride in vitro and in vivo and mercuric chloride in vitro affect the vessel wall prostacyclin production and platelet responsiveness to the aggregating agents. In the present paper the in vitro activity of cadmium and mercury on the ADP breakdown induced by vascular tissue has been studied.

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Tomera, JF; Harakal, C.  
Mercury- and Lead-Induced Contraction of Aortic  
Smooth Muscle In Vitro.  
Arch Int Pharmacodyn. 283(2):295-302. Oct 1986.

Thoracic aorta segments from normotensive New Zealand White female rabbits were prepared and exposed to mercuric chloride, cadmium chloride, lead acetate, cadmium acetate, ethylmercury, and methylmercury. Mercuric chloride and lead acetate, in concentrations of  $2.0-2.5 \times 10^{-9}$  M., caused a concentration-dependent

contraction of the rabbit aorta segments. Mercury caused a 4 times higher maximal response than did lead. This metal-induced contraction was greatly suppressed or nearly abolished when calcium-free physiological solution was utilized, indicating that the tensile effect relied on extracellular calcium. Ethylmercury, methylmercury, and cadmium did not evoke aortic contraction.

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Trakhtenberg, IM.  
Chronic Effects of Mercury on Organisms.  
The Micromercurialism Phenomenon in Mercury  
Handlers. Chap. VI:109-134.  
DHEW Publ. No. (NIH) 74-473. 1974.

A number of investigations of humans exposed chronically to small concentrations of mercury vapor (hundredths of a milligram/cubic meter) revealed a number of cardiovascular effects: tachycardia (abnormally rapid heart rate), unstable pulse, cardiovascular fluctuations, diminished tone of the blood vessels, increased and decreased blood pressure, cardiovascular insufficiency, and pain in the vicinity of the heart.

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Trakhtenberg, IM.  
Chronic Effects of Mercury on Organisms.  
Cardiotoxic Effects of Mercury. Chap. XI:199-210.  
DHEW Publ. No. (NIH) 74-473. 1974.

1. Rabbits exposed chronically to low doses of mercury exhibited ECG changes and tachycardia followed by bradycardia. Pathologic changes in animals exposed to low mercury concentrations included granular dystrophy of the heart muscle, dystrophic changes in the endothelial lining of the capillaries of the heart (swelling and shedding of cells), and disorders in coronary blood formation. Functional disturbance in the heart muscle was caused by disruption of heart regulation activity as a result of the continuous toxic effect of mercury on the heart muscle

and heart valves, primarily by blockage of the critical sulfhydryl groups.

2. Animals subjected to prolonged exposure to low concentrations of mercury vapor (0.01 mg/cubic meter) developed coronary ECG changes and coronary insufficiency. Experiments demonstrated that this was due to mercury interaction with vasopressin, a cardiac regulatory hormone from the posterior pituitary gland.

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Vimy, MJ; Takahashi, Y; Lorscheider, FL.  
Maternal-fetal Distribution of Mercury (203 Hg)  
Released From Dental Amalgam Fillings.  
*Amer J Physiol.* 258:R939-45. April 1990.

Five pregnant adult ewes were utilized in this study. The sheep exhibits molar chewing mechanics similar to that found in humans, has a body weight similar to humans, and is the animal of choice for obstetrical investigation. Each ewe received 12 molar dental amalgam fillings containing a portion of radioactively labelled mercury. The use of radioactively labelled mercury provided specificity; mercury found in the animals could not be mistaken for mercury from any other source. Each filling contained approx. 425 milligrams of mercury (approx. 50% of the amount in an average adult human amalgam), and was overcarved in a concave form to prevent excessive wear. Cannulation was performed to permit serial sample collection during the course of gestation. Intra-oral mercury vapor measurements were periodically taken. These measurements closely matched measurements derived from human subjects in previously published studies. All tissue and fluid specimens were analyzed for radioactivity and total Hg concentrations were calculated.

Dental amalgam-derived mercury was found in the maternal blood, fetal blood, and amniotic fluid within 2 days after the mothers received amalgam fillings. Mercury levels in fetal blood were 4 times higher than those found

in maternal blood. By 29 days after amalgam placement, maternal heart tissue contained approx. 10 nanograms/gram of mercury. After 16-41 days of in utero exposure, fetal heart tissue contained a mean of slightly less than 10 nanograms/gram of mercury. Mothers' milk obtained 2 days after birth contained levels of mercury 6-8 times than levels found in mothers' blood. The study demonstrated that dental amalgam fillings are a source of continuous mercury exposure to both mother and fetus and that mercury from this source does accumulate in heart tissue.

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Vimy, MJ; Body, ND; Hooper, DE; Lorscheider, FL.  
Glomerular Filtration Impairment by Mercury Released  
from Dental "Silver" Fillings in Sheep.  
*The Physiologist.* 33(4), A-94. 1990.

In humans mercury (Hg) vapor is released from silver amalgam fillings which contain 50% Hg by wt. When such fillings are placed in sheep teeth, the kidneys will concentrate amalgam Hg at levels ranging from 5-10 ug Hg/g renal tissue 4-20 weeks after placement (*FASEB J.* 3:2641-2646, 1989; *Am. J. Physiol.* 258:R939-945, 1990). In another report (publ. elsewhere) we demonstrate that the monkey kidney will likewise concentrate large amounts of amalgam Hg. For the present study occlusal fillings (12, total Hg 5100 mg) were placed in each of six adult female sheep under general anesthesia, using standard dental procedures. Glass ionomer occlusal fillings (12) were inserted in two control sheep. At several days prior to dental surgery, and at 30 and 60 days after placement of fillings, renal function was evaluated by glomerular filtration rate (GFR, inulin clearance) and by blood and urine electrolytes, urea and proteins. Average GFR of  $69.5 \pm 7.2$  ml/min before amalgam placement was reduced to  $32.3 \pm 8.1$  ml/min by 30 days and remained low at  $27.9 \pm 8.7$  ml/min after 60 days. GFR did not change in controls. After amalgam placement urine  $[Na^+]$  increased steadily from

24.8 ± 7.7 to 82.2 ± 20.3 mmoles/L at 60 days. Urine [K<sup>+</sup>] also increased. Levels of urea and total protein increased from 0-60 days in urine while albumin levels declined. Blood levels of Na<sup>+</sup>, K<sup>+</sup>, and urea showed moderate declines from 0-60 days after amalgam. Thus, amalgam Hg levels in kidney are sufficient to significantly reduce GFR, either by reducing renal blood flow or by alteration of the glomerular membrane. Electrolyte, urea and protein patterns in urine are also consistent with impaired renal tubular reabsorption.

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Vulliamy, GD.  
Vasomotor Disturbance in Pink Disease.  
Lancet. 2:1248-51. 1952.

The author evaluated 11 victims of Acrodynia. Ten of the 11 victims exhibited excessive vasoconstriction. In addition, the reflex vasodilatation of the hands, which normally follows heating of the trunk and legs, was absent.

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Wierzbicki, R; Michalska, M; Cierniewski, S.  
Interaction of Fibrinogen With Mercury.  
Thrombo Res. 30 (6): 579-585. 1983.

The interaction of bovine fibrinogen with mercuric chloride was studied. Fibrinogen complexed with mercury, or in the presence of mercuric ions at concentrations above 10(-6) molar concentrations, was clotted more effectively than in the control system which was devoid of mercury. The authors also cited a number of other studies on various animals that demonstrated the increased coagulability of blood in the presence of various mercury compounds.

Both enzymatic and polymerization steps appeared to be influenced by mercury. The binding experiments showed that fibrinogen binds substantial amounts of mercury, presumably at disulfide sites that are reduced to sulfhydryl

groups at physiological pH.

The authors stated that mercury compounds at low concentrations accelerate the blood coagulation process and that it has been found that hypercoagulability accompanies mercury intoxication. They stated "Due to an industrial and environmental pollution with mercury and a common appearance of blood circulation diseases, pathological changes in blood coagulation accompanying mercury intoxication seem to be an unquestionably important problem to investigate".

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Wronski, R; Hartmann, F.  
Uber eine besondere Verlaufsform der Panarteritis  
Nodosa bei chronisch-sleichender  
Quecksilbervergiftung.  
Dtsch Med Wschr. 102:323. 1977.

A 50-year old woman who for more than 10 years had worked as an assistant in a dental clinic had developed a chronic mercury poisoning. The most pronounced symptoms were psychic and neurologic changes, erethism, tremor and psellismus mercurialis. The further development showed arterial circulatory disturbances, abdominal pains and polyneuropathy. These clinical manifestations indicated a panarteritis nodosa. A biopsy confirmed the diagnosis. This panarteritis nodosa can be considered a special development of chronic mercury poisoning.

\*\*\*\*\*

Yoshida, M; Satoh, H; Aoyama, H; Kojima, S;  
Yamamura, Y.  
Distribution of Mercury in Neonatal Guinea Pigs after  
Exposure to Mercury Vapor.  
Bull Environ Contam Toxicol. 43(5):697-704. Nov 1989.

Hartley strain guinea pigs in the late gestation period were utilized. Dams and newborn infants were exposed to

mercury vapor (8-10 mg Hg/cubic meter) for 120 minutes within 12 hours after birth. Directly after exposure, mercury concentrations in blood, brain, heart, lung, liver and kidneys were measured by AAS. The mercury levels in neonatal whole blood was approx. 64% higher than that in mothers. Mercury levels in blood plasma were 2-3 times higher than in maternal plasma, but erythrocyte levels were similar. Neonatal mercury concentrations were 28% higher in the brain, 58% higher in the lung, and 64% higher in the heart than those in mothers. Mercury levels in neonate kidney and liver tissue were lower or similar to those in mothers. In mothers and neonates, mercury levels were 2.5-5 times higher in heart tissue than in brain tissue, ranging from 258-1263 ng Hg/gm in the heart tissue.

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