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G. Drasch
I. Schupp
H. Höfl
R. Reinke
G. Roider

Mercury burden of human fetal and infant tissues

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G. Drasch (✉) · I. Schupp · H. Höfl
R. Reinke · G. Roider
Institut für Rechtsmedizin,
Frauenlobstrasse 7a,
D-80337 München, Germany

Abstract The total mercury concentrations in the liver (Hg-L), the kidney cortex (Hg-K) and the cerebral cortex (Hg-C) of 108 children aged 1 day–5 years, and the Hg-K and Hg-L of 46 fetuses were determined. As far as possible, the mothers were interviewed and their dental status was recorded. The results were compared to mercury concentrations in the tissues of adults from the same geographical area. The Hg-K (n = 38) and Hg-L (n = 40) of fetuses and Hg-K (n = 35) and Hg-C (n = 35) of older infants (11–50 weeks of life) correlated significantly with the number of dental amalgam fillings of the mother. The toxicological relevance of the unexpected high Hg-K of older infants from mothers with higher numbers of dental amalgam fillings is discussed.

Conclusion Future discussion on the pros and cons of dental amlagam should not be limited to adults or children with their own amalgam fillings, but also include fetal exposure. The unrestricted application of amalgam for dental restorations in women before and during the childbearing age should be reconsidered.

Key words Mercury · Fetuses
Newborns · Infants · Dental amalgam

Abbreviations *Hg-C* total mercury concentration in the cerebral cortex (ng/g wet weight) · *Hg-K* total mercury concentration in the renal cortex (ng/g wet weight) · *Hg-L* total mercury concentration in the liver (ng/g wet weight)

Introduction

Recent investigations [1, 5] have shown in humans that dental amalgam fillings are the principal source of the mercury burden of adults, at least in geographic areas with a moderate consumption of fish and seafood. There is now widespread international focus on the pathophysiological significance of mercury that is continuously released from amalgam tooth fillings [6]. A result of one of these studies [5] was that some of the few infants investigated at that time showed relatively high mercury concentrations in their kidneys. To expand upon this finding, the objective of the present study was to determine the mercury concentration in tissues from a much larger population of infants and also from older children and fetuses. As far as possible the mothers were interviewed and their dental status determined.

Materials and methods

Liver and kidney specimens from 46 fetuses and liver, renal cortex and cerebral cortex from 108 children aged 1 day–5 years were collected during 1990–1992 from autopsies performed at the Pathological Institute and the Institute of Forensic Medicine of the University of Munich.

Abortions had mainly been induced for medical reasons. All infants had died suddenly and most were diagnosed as sudden infant death syndrome.

From 40 mothers of fetuses and 65 mothers of children, information on occupational, domestic or medical mercury burden were

available and the dental status of these mothers was recorded. In no case was an occupational exposure to mercury of the parents or an extreme fish consumption of the mother or the child reported. There was no case of an unusual mercury burden of the child (e.g. by a broken thermometer or the application of mercury containing pharmaceuticals).

Tissue samples of approximately 1 g were digested with 2 ml nitric acid (min. 65%, Supra pure grade, E. Merck, Darmstadt, FRG) for 6 h at 140°C in sealed Teflon lined pressure vessels (Parr Acid Digestion Bomb, H. Kürner, Rosenheim, FRG). After cooling the solutions were diluted with water to 10 ml and the concentrations of total mercury were determined by cold-vapour atomic absorption spectrometry after enrichment on a gold-platinum-net [19]. The accuracy of the method was established by standard reference materials (BCR reference material # 145, bovine liver and IAEA fish homogenate MA-A-2).

Total mercury concentrations were calculated as ng mercury per g tissue wet weight. Because the distribution of the values was nonparametric, medians were calculated. Subgroups were compared by the Mann-Whitney test. Correlations were determined by Spearman rank correlation.

In order to combine the results of fetuses and children into a single figure, the gestational age of the fetuses was converted to "negative weeks of life", i.e. 40 weeks minus gestation.

The group under investigation was classified in 4 subgroups according to the age:

1. Fetuses: from gestation until birth
2. Newborns and young infants: 0–10 weeks
3. Older infants: 11–50 weeks
4. Young children: 1–5 years

Table 1 Spearman rank correlation of the mercury concentrations in human tissues to the number of teeth with amalgam fillings of the mother

		Fetuses	Newborns and younger infants (0–10 weeks)	Older infants (11–50 weeks)	Younger children (1–5 years)
Liver	*n*	40	19	35	11
	r	+0.366	±0.000	+0.254	–0.163
	sig.	b	a	a	a
Renal cortex	*n*	38	19	35	11
	r	+0.537	+0.212	+0.454	+0.273
	sig.	d	a	c	a
Cerebral cortex	*n*	0	18	35	11
	r		+0.213	+0.372	–0.181
	sig.		a	b	a

Significance: a = < 95%; b = > 95%; c = > 99%; d = > 99.9%

All results were compared parallel to those of 34 adults in the same age range as the mothers (16–45 years) having at least two teeth with dental amalgam [5, 19].

Results

Statistical correlations between the mercury concentration in various organs and the number of maternal teeth with dental amalgam fillings are shown in Table 1.

In fetuses the mercury concentration in the liver (Hg-L) was significantly correlated with the number of maternal teeth with amalgam fillings. No such correlation was found for Hg-L in the other age groups.

The mercury concentration in the renal cortex (Hg-K) and maternal teeth with amalgam fillings were significantly correlated in fetuses and older infants but not in the other age groups.

The mercury concentration in the cerebral cortex (Hg-C) was significantly correlated with the number of maternal teeth with amalgam fillings in older infants only.

In fetuses and older infants significantly higher mean mercury concentrations in the liver and the renal cortex were found, if the mothers had ten or more teeth with dental amalgam in comparison to fetuses or older infants from mothers with a maximum of two teeth with amalgam fillings (Table 2). Figures 1–3 illustrate the range of individual mercury concentrations in liver, kidney cortex and cerebral cortex, respectively, of all fetuses and children, compared to the range of adults without dental amalgams. Many older infants have rapidly acquired a tissue burden of mercury in the kidney that is equivalent to or which exceeds the range of mercury in adults who do not have amalgam fillings.

Discussion

The mercury concentration in different tissues of fetuses and infants has been rarely studied and has never been related to maternal amalgam fillings. Suzuki et al. [20] reported the mercury concentrations in five brain and four liver specimens of fetuses and Markesbery et al. [14] in two fetal, one term and three infant brains. Their results lie within the same range of concentrations that we found.

Table 2 Comparison (Mann-Whitney-Test) of the mercury concentrations (ng Hg/g, medians) in tissues of human fetuses and older infants (age: 11–50 weeks) from mothers with either 0–2 or 10 or more teeth with amalgam fillings to age-matched adults (age: 16–45 years) with the same number of amalgam fillings as the mothers [5, 19]

		0–2 Teeth with amalgam	>10 Teeth with amalgam	Significance of difference
Liver	Fetuses	12.68 ($n = 10$)	25.85 ($n = 14$)	b
	Older infants	19.2 ($n = 10$)	34.4 ($n = 8$)	b
	Younger adults	18.7 ($n = 41$)	67.2 ($n = 19$)	d
Renal cortex	Fetuses	5.95 ($n = 10$)	10.3 ($n = 11$)	d
	Older infants	20.75 ($n = 10$)	115.6 ($n = 8$)	c
	Younger adults	47.3 ($n = 41$)	409.25 ($n = 18$)	d
Cerebral cortex	Older infants	2.05 ($n = 10$)	3.95 ($n = 8$)	a
	Younger adults	14.7 ($n = 39$)	25.7 ($n = 19$)	b

Significance: a = < 95%; b = > 95%; c = > 99%; d = > 99.9%

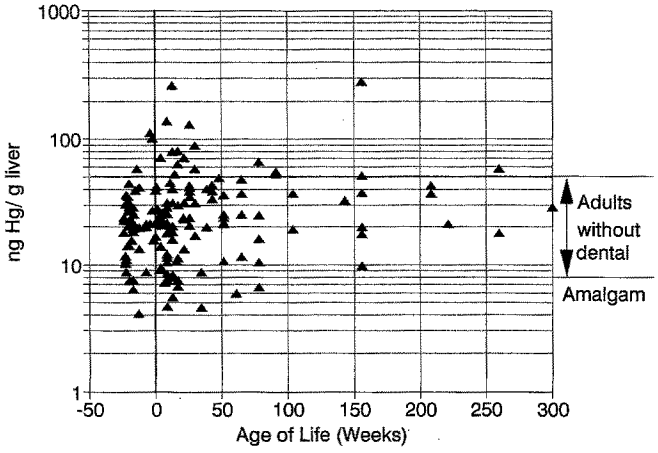

Fig. 1 Total mercury concentration in the liver of human fetuses and infants related to age of life

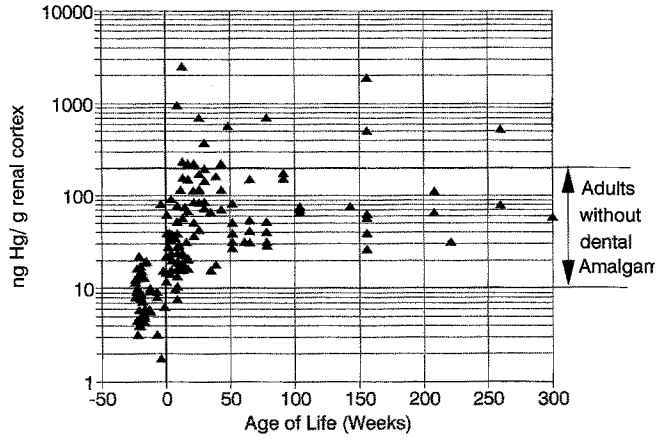

Fig. 2 Total mercury concentration in the renal cortex of human fetuses and infants related to age of life

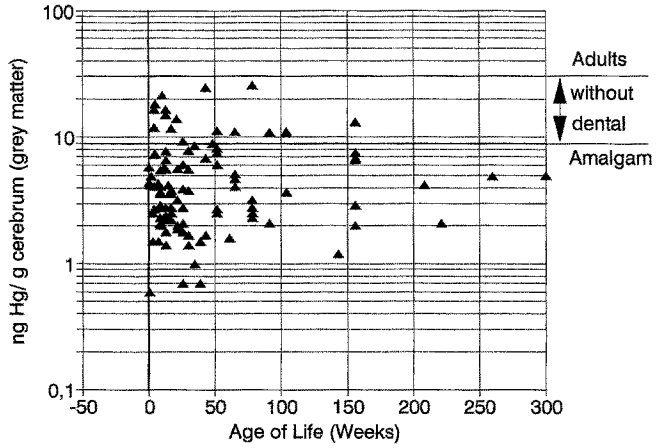

Fig. 3 Total mercury concentration in the cerebral cortex of human infants related to age of life

Data from earlier investigations [15, 16] are less reliable due to the limitations of analytical methods at that time.

Exposure of pregnant guinea pigs to mercury vapour [25, 26] or pregnant ewes to amalgam fillings (containing radioactive ^{203}Hg) [22] resulted in an increase of the mercury concentrations of the fetuses and the newborn. The placental transfer of mercury from the mother to the fetus depends on the maternal mercury burden [7, 10, 12, 21]. Since the number of dental amalgam fillings is significantly related to the mercury concentration in the maternal tissues of animals [22] and humans [5] the number of maternal amalgam fillings should also influence the mercury concentration in human fetal tissues. We were able to confirm this relationship with respect to the fetal liver and kidney. The avidity of maternal kidneys for mercury documented in Table 2 can be explained by the storage function of the maternal kidney for mercury. It can be assumed that the "mobile" mercury, available for a transfer through the placenta, derives predominantly from the maternal liver (and comparable compartments) and not from the maternal kidney. Moreover, the fetal liver seems to trap the transferred mercury to some extent [8, 12, 25, 26] and thus prevents a higher accumulation in the fetal kidney. The present findings in humans compare favourably with similar results reported earlier in sheep [22].

The mercury concentrations in the tissues of newborns and young infants were not well correlated with the number of maternal teeth with amalgam fillings. This may be explained by a superposition of the initial influence of the maternal dental amalgam on the mercury concentration in the infant tissues during pregnancy by a redistribution of mercury from the infant liver to the infant kidney and other tissues in the first months of life and a simultaneous new intake of mercury in this transient period of life [12, 26].

Maternal amalgam fillings appears to influence the Hg-C in older infants approximately as much as they influence Hg-C in adults. The influence on the Hg-K in older infants is approximately half so great as that of own fillings of adults (see Table 2).

Most of the babies under investigation were not nursed or nursed only for a few weeks. Hence it follows that the higher Hg-K and Hg-C of offspring from mothers with amalgam fillings is due at least partly to an exposure derived in utero and not from breastmilk. If and to what extent nursing by mothers with multiple amalgam fillings contributes to the mercury burden of the baby should be further investigated. Dental amalgam mercury does concentrate in sheep milk [22], however, Klemann et al. [9] found no statistically significant correlation between the mercury concentration in human breastmilk and the number of amalgam fillings of the mothers.

At the present time, the toxicity of mercury vapour from dental amalgams is being assessed through a variety of investigations [1]; however, the toxicological consequence of the relatively high mercury concentrations in the renal cortex of infants, as found in the present study, has not been determined. In contrast to the well-known vulnerability of the developing brain to an exposure to mercury vapour (most of the mercury from dental amalgam is released in this form) or methyl-mercury, there are

no reports that the infant kidney is more sensitive to inorganic mercury than the adult kidney [6, 10, 11, 13, 21, 23, 24, 27]. On the other hand, current evidence suggests that the nephrotic syndrome following absorption of mercury compounds results from an immunotoxic response [24]. Amalgam mercury has also been shown to alter several indices of kidney function in sheep [2]. Possible differences in the binding form of the mercury in the kidney of fetuses, infants and adults, e.g. to metallothionein or selenium, are presently not known [4, 17, 18].

The present findings clearly demonstrate that further discussion on the pros and cons of dental amalgam should not be focused exclusively on adults or children with their own amalgam fillings [3, 27], but also on the offspring.

From our results it can be concluded that infants can accumulate mercury, apparently derived from maternal amalgam fillings, in their kidneys to a similar extent as older children or adults do from their own fillings. Therefore the unrestricted application of amalgam for dental restorations in women before and during the child-bearing age should be reconsidered in analogy to the recommendation of the German Health Authorities from 1992 [3], which argued that because of a higher vulnerability of infants to mercury, amalgam cannot be further recommended for dental restorations for children up to 6 years and notably not during the first 3 years of life. At the very least, high numbers of amalgam fillings should be avoided for women before and during child-bearing age. In 1991, the WHO confirmed an earlier statement from 1980: "The exposure of women of child-bearing age to mercury vapour should be as low as possible" [24].

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References

1. Aposhian HV, Bruce DC, Alter W, Dart RC, Hurlbut KM, Aposhian MM (1992) Urinary mercury after administration of 2,3-dimercaptopropane-1-sulfonic acid: correlation with dental amalgam score. FASEB J 6: 2472–2476
2. Boyd ND, Benediktsson H, Vimy MJ, Hooper DE, Lorscheider FL (1991) Mercury from dental "silver" tooth fillings impairs sheep kidney function. Am J Physiol 261: R 1010–R 1014
3. Bundesgesundheitsamt (1992). bga-Informationsschrift "Amalgame in der zahnärztlichen Therapie". Berlin
4. Drasch G, Kretschmer E, Neidlinger P, Summer KH (1989) Cadmium, zinc, copper and methallothionein in human tissues (liver and kidney). Toxicol Environ Chem 23: 207–214
5. Drasch G, Schupp I, Riedl G, Günther G (1992) Einfluß von Amalgamfüllungen auf die Quecksilberkonzentration in menschlichen Organen. Dtsch Zahnärztl Z 47: 490–496
6. Goering PL, Galloway WD, Clarkson TW, Lorscheider FL, Berlin M, Rowland AS (1992) Toxicity assessment of mercury vapor from dental amalgams. Fund Appl Toxicol 19: 319–329
7. Horvat M, Stegnar P, Byrne AR, Dermelj M, Branica Z (1988) A study of trace elements in human placenta, blood and hair from the yugoslav central adriatic. In: Brätter P, Schramel P (eds) Trace elements analytical chemisty in medicine and biology, vol. 5. de Gruyter, Berlin, pp 243–250
8. Klein D, Scholz P, Drasch G, Müller-Höcker J, Summer KH (1991) Metallothionein, copper and zinc in fetal and neonatal human liver: changes during development. Toxicol Lett 56: 61–67
9. Klemann D, Weinhold J, Strubelt O, Pentz R, Jungblut JR, Klink F (1990) Der Einfluß von Amalgamfüllungen auf die Quecksilberkonzentrationen in Fruchtwasser und Muttermilch. Dtsch Zahnärztl Z 45: 142–145
10. Koos BJ, Longo LD (1976) Mercury toxicity in the pregnant woman, fetus and newborn infant. Am J Obstet Gynecol 126: 390 –409
11. Larsson KS (1991) Tereatological aspects of dental amalgam. Adv Dent Res 6: 114–119
12. Larsson KS, Sagulin G-B (1990) Placental transfer of mercury from amalgam. Lancet 336: 1251
13. Lorscheider FL, Vimy MJ (1990) Mercury from dental amalgam. Lancet 336: 1578–1579
14. Markesbery WR, Ehmann WD, Alauddin M, Hossain TIM (1984) Brain trace element concentration in aging. Neurobiol Aging 5: 19–28
15. Mottet NK, Body RL (1974) Mercury burden of human autopsy organs and tissues. Arch Environ Health 29: 18–24
16. Nishimura H, Hirota S, Tannaka O, Ueda M, Uno T (1974) Normal mercury level in human embryos and fetuses. Biol Neonate 24: 197–205
17. Nordberg GF (1989) Modulation of metal toxicity by metallothionein. Biol Trace Elem Res 21: 131–135
18. Nylander M, Weiner J (1991) Mercury and selenium concentrations and their inter-relationship in organs from dental staff and the general population. Br J Ind Med 48: 729–734
19. Schupp I (1994) Untersuchungen an menschlichen Organen zur Frage der Quecksilberbelastung durch Zahnamalgam und weitere Faktoren. Dissertation, München, F.R.G.
20. Suzuki T, Yonemoto J, Satoh H, Naganuma A, Imura N, Kigawa T (1984) Normal organic and inorganic mercury levels in the human feto-placental system. J Appl Toxicol 4: 249–252
21. Thorp JM, Boyette DD, Watson WJ, Cefalo RC (1992) Elemental mercury exposure in early pregnancy. Obstet Gynecol 79: 874–876
22. Vimy MJ, Takahashi, Y, Lorscheider FL (1990) Maternal-fetal distribution of mercury (^{203}Hg) released from dental amalgam fillings. Am J Physiol 258: R939–R945
23. Von Mühlendahl KE (1990) Intoxication from mercury spilled on carpets. Lancet 336: 1578
24. WHO (1991) Environmental Health Criteria 118: Inorganic Mercury. World Health Organization, Geneva
25. Yoshida M, Aoyama H, Satoh H, Yamamura Y (1987) Binding of mercury to metallothionein-like protein in fetal liver of the guinea pig following in-utero exposure to mercury vapor. Toxicol Lett 37: 1–6
26. Yoshida M, Satoh H, Kojima S, Yamamura Y (1989) Distribution of mercury in neonatal guinea-pigs after the exposure to mercury vapours. Bull Environ Contam Toxicol 43: 697–704
27. Zinke T (1992) Amalgame in der zahnärztlichen Therapie. Bundesgesundhbl 35: 613–616