Mercury and selenium concentrations and their interrelations in organs from dental staff and the general population

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Abstract

Mercury (Hg) and selenium (Se) concentrations were determined by radiochemical neutron activation analysis in samples from the pituitary glands, occipital cortices, renal cortices, abdominal muscles, and thyroid glands of cadavers. Samples were retrieved from dental staff occupationally exposed to Hg and from the general population. Increased concentrations of both Hg and Se in samples from dental staff showed that Se accumulated together with Hg. Regression analysis of data from the pituitary glands and occipital cortices of dental staff indicated the accumulation of Se at a rough stoichiometric ratio of 1:1 with Hg. The same stoichiometric ratio between the elements was seen in the renal cortices from the general population. The regression analysis showed that a substantial fraction of Se was not associated with Hg; it is assumed that this corresponds to biologically available Se. Concentrations of biologically available Se decreased with advancing age in the pituitary gland, but not in other organs, and varied appreciably between organs.

Mercury (Hg) is a non-essential heavy metal the compounds of which differ in metabolism and toxicity. Due to its volatility elemental mercury (Hg^0) is the most important form from the point of view of occupational hygiene. After uptake in the lungs Hg^0 is oxidised to mercuric mercury (Hg^{2+}) in the blood and other tissues.¹

As a result of preparing and working with amalgam dental staff are exposed to mercury vapour and particulates.^{2,3} This exposure implies a potential risk

for deleterious effects.⁴⁻⁶ Recently interest has focused on the possibility of health effects in the general population due to exposure to inorganic mercury from amalgam restorations.⁷⁻⁹ Amalgam fillings continuously emit Hg^0 vapour, which is absorbed in the lungs and distributed to various organs.^{8,10-12} Mercury released from amalgam is a predominant source of exposure to inorganic mercury in the general population.¹³ The other major source is organic Hg (methylmercury (MeHg)) in food. In mammals MeHg is converted into inorganic Hg, assumed to be Hg^{2+} . In several tissues from humans with high oral intake of MeHg a significant fraction of Hg is in the form of Hg^{2+} . Usually the kidney contains the highest fraction in this form.¹

Selenium (Se) is an essential trace element in several species including humans. In experimental studies on rodents, combined administration of inorganic Hg and Se (mostly selenite (SeO_3^{2-})) altered their protein binding and sub-cellular and organ distribution, and a significant part became attached to certain high molecular weight protein fractions in a 1:1 stoichiometric ratio.¹⁴⁻¹⁷ Combined administration also resulted in an increased long term retention of the elements.¹⁸⁻²¹

When Se and Hg were administered to mice at highly variable ratios after an initial elimination phase their stoichiometric ratio in the whole body approached 1:1.²² Studies on organs from seals, dolphins, and porpoises have also shown a roughly 1:1 relation between Hg and Se in liver and brain tissues over a wide range of concentrations.^{23,24} In 1975 Kosta *et al* reported a roughly 1:1 stoichiometric ratio of Hg and Se at high concentrations in several organs of former Hg miners.²⁵ We also found a high correlation between high total Hg and Se concentrations in four pituitary glands from dental staff.²⁶ The main purpose of our present work was to further elucidate the relation between Hg and Se concentrations in several tissues from subjects with varying exposure to mercury vapour.

Materials and methods

Pituitary glands, occipital cortices, renal cortices, abdominal muscle and a few samples of thyroid

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Table 1 Mercury and Se concentrations ($\mu\text{mol/kg}$ wet weight) in tissue samples from dental personnel*

Case No	Sex	Age (y)	Pituitary gland		Occipital cortex		Renal cortex		Thyroid gland	
			Hg	Se	Hg	Se	Hg	Se	Hg	Se
1	M	80	20	23	1.43	3.4	—	—	—	—
2	M	82	18	22	0.42	2.5	10.5	14.4	140	135
3	M	60	28	36	0.08	—	7.7	—	1.4	—
4	M	50	1.7	9	0.19	2.1	4.7	9.4	—	—
5	W	30	1.5	—	0.07	1.8	—	—	—	—
6	M	61	0.7	—	0.07	1.8	—	—	—	—
7	M	60	2.2	4.7	0.25	3.1	11.3	11.1	0.32	10
8	W	67	6.4	12	0.09	2.5	—	—	—	—
No		8	8	6	8	7	4			
Min		30	0.7	4.7	0.07	1.8	4.7			
Max		82	28	36	1.43	3.4	11.3			
Median		60.5	1.1	17	0.14	2.5	9.1			
Average		61	9.8	17.8	0.33	2.5	8.6			
SD		17	10.6	11.5	0.46	0.62	3.0			

*Cases 1 to 7, dentists; case 8, dental assistant; case 1, Parkinson's disease and diabetes mellitus, professionally inactive for about 10 years according to detailed medical records; case 2, professionally inactive for 15 years according to information from relatives; case 4, glomerulonephritis; case 6, diabetes mellitus. M = man, W = woman.

glands were collected at necropsy from seven dentists and one dental assistant (table 1). The samples were collected at different pathology departments and at the National Institute of Forensic Medicine in Stockholm. Pituitary glands, occipital cortices, renal cortices, and abdominal muscle samples, from subjects without known occupational exposure to Hg were also collected (table 2). All deaths had been

sudden and unexpected. The sampling was carried out at the National Institute of Forensic Medicine.

According to detailed medical records and information from relatives, two of the dentists had not been professionally active for several years due to retirement and incapacitating chronic illness (cases 1 and 2, table 1). Medical records and necropsy reports indicated that the others had been professionally

Table 2 Mercury and Se concentrations ($\mu\text{mol/kg}$ wet weight) in tissue samples from subjects in the general population*

Case No	Sex	Age (y)	Pituitary gland		Occipital cortex		Renal cortex		Abdominal muscle	
			Hg	Se	Hg	Se	Hg	Se	Hg	Se
1	M	24	0.14	10.77	0.050	1.90	1.63	11.1	—	—
2	M	48	0.08	7.92	0.012	1.43	0.16	8.4	0.005	1.0
3	M	29	0.09	6.84	0.032	1.82	1.27	11.4	0.011	2.3
4	M	63	0.17	5.19	0.051	1.68	0.24	7.5	0.024	1.2
5	M	79	0.06	5.32	0.027	1.76	0.15	8.2	0.009	1.0
6	M	73	0.08	7.09	0.020	2.00	0.11	9.6	0.010	1.0
7	M	80	—	—	0.060	2.35	—	—	0.024	1.1
8	M	71	3.88	13.93	0.114	1.96	3.79	12.8	0.047	2.0
9	M	74	0.08	5.70	0.046	2.00	0.29	8.2	0.022	1.0
10	M	40	0.15	7.09	0.053	2.00	1.57	9.2	0.017	1.3
11	M	67	0.20	5.70	0.061	1.81	0.52	9.7	0.024	1.5
12	M	16	0.19	8.23	0.037	1.77	4.04	12.4	0.004	1.0
13	W	30	0.38	8.36	0.079	1.78	2.59	11.9	0.027	1.1
14	M	30	—	—	0.036	1.84	—	—	—	—
15	M	52	—	—	0.098	2.08	—	—	—	—
16	M	76	0.08	4.46	0.049	1.92	—	—	—	—
17	W	56	0.14	4.97	—	—	—	—	—	—
18	M	61	0.03	4.79	—	—	—	—	—	—
19	M	88	0.11	4.36	—	—	—	—	—	—
20	M	70	5.83	10.51	—	—	—	—	—	—
21	M	71	0.05	6.14	—	—	—	—	—	—
22	M	47	0.05	4.52	—	—	—	—	—	—
23	W	75	0.19	2.75	—	—	—	—	—	—
24	M	63	0.04	4.28	0.081	2.57	—	—	—	—
No		24	21	21	17	17	12	12	12	12
Min		16	0.03	2.75	0.012	1.43	0.11	7.5	0.004	1.0
Max		88	5.83	13.93	0.114	2.57	4.04	12.8	0.047	2.3
Median		63	0.11	5.70	0.050	1.90	0.89	9.7	0.020	1.5
Average		58	0.12	6.6	0.053	1.9	1.4	10.0	0.019	1.5
SD		20	0.08	2.6	0.027	0.26	1.4	1.7	0.012	0.4

*Cases 8 and 20 excluded from the calculation of average and SD for pituitary Hg concentration.

inactive for months before death. Medical records did not mention signs or symptoms of Hg intoxication, though one of the dentists (case 2) was investigated before his death for peripheral nerve disorder.

After subsampling and dissection, analysis of total Hg and Se was carried out in collaboration with the Swedish Environmental Research Institute (IVL) using a radiochemical neutron activation (RNAA) method.²⁷⁻²⁹ Detailed description and quality control for the Hg analyses have been published.⁸ The detection limit is 2 µg/kg for Se. The accuracy of the RNAA method (IVL) to determine Se was established by analyses of standard reference material (SRM) 1577a from the National Bureau of Standards (NBS), with a certified value of 0.71 (SD 0.07) mg Se/kg dry weight. The results of three analyses were 0.79, 0.75, and 0.78 mg Se/kg dry weight. A few samples (cases 3 and 7, table 1) were analysed by RNAA at Isotopcentralen, Denmark, with a detection limit of 0.2 µg/kg for Hg and 3 µg/kg for Se.³⁰ The accuracy was tested through simultaneous analysis of NBS SRM 1577 certified for 16 (SD 2) µHg/kg and 1.1 (SD 0.07) mg Se/kg, which gave 16.0 and 15.8 µg Hg/kg and 1.1 and 1.1 mg Se/kg.

For the organs with six or more samples the relation between Se concentrations, Hg concentrations, and age was investigated by linear regression analysis³¹ with Se concentration as dependent variable. Examination of residuals indicated that the linear models were adequate. All regression analyses were performed using the SAS statistical package for VAX/VMS.³²

Results

MERCURY AND Se IN ORGANS FROM DENTAL STAFF

The highest concentrations of Hg were seen in thyroid gland and pituitary gland samples. Even though two of the dentists (cases 1 and 2, table 1) had been professionally inactive for a decade or longer, they still had extremely high concentrations in these organs. Tables 1 and 2 show that organs of dental staff had considerably higher Hg concentrations than those from the general population. They also had higher concentrations of Se. In pituitary gland and occipital cortex tissue differences were significant according to the Mann-Whitney test.³³

Regression analysis of data from the pituitary glands with Se concentration as dependent variable showed a strong effect of Hg concentration. The slope coefficient for Hg was 1.1. Addition of age to the regression equation resulted in a negative regression (slope) coefficient. At zero Hg concentration and 58 years of age (average age for all the material) the Se concentration predicted by the regression equation was 4.8 µmol Se/kg (fig 1 and table 3). A positive correlation exists ($r = 0.34$) between pituitary Se

concentration and age if the effect of Hg is not considered.

Similar regression analysis of data from the occipital cortices also showed an effect of Hg concentration. The slope coefficient for Hg was 1.0 but the confidence interval was wide. The statistical significance of the slope coefficient was dependent on case 1 with the highest concentrations of Hg and Se in the occipital cortex. No effect of age was seen. The intercept of 2.1 µmol Se/kg showed a significant fraction of Se not associated with Hg (table 3).

Too few renal and thyroid samples were taken to make regression analysis meaningful. At the very high concentrations of the elements in one thyroid sample, however (case 2), the stoichiometric ratio of the elements of about 1:1 is worth noting.

MERCURY AND Se IN ORGANS FROM SUBJECTS WITHOUT OCCUPATIONAL EXPOSURE TO Hg

The renal cortex had the highest Hg concentration (table 2). Regression analysis showed a strong influence of Hg on Se concentration. The slope coefficient for Hg was 1.1. No effect of age was seen. The intercept of 8.5 µmol Se/kg showed that a significant fraction of Se was not associated with Hg (table 3, fig 2).

Regression analysis of data on Se in the occipital cortices showed a slope coefficient for Hg of 4.6, but with a wide confidence interval. No effect of age was seen. The intercept of 1.7 µmol Se/kg indicated that a significant fraction of Se was not associated with Hg (table 3).

Abdominal muscle had the lowest Hg concentrations among the tissues studied. Regression analysis showed an effect of Hg concentration and also a small and borderline significant ($p < 0.10$) effect of age on Se concentration in this tissue. The slope coefficient for Hg was surprisingly high, but the confidence interval was wide (table 3).

Regression analysis of data from pituitary gland samples with Se concentration as dependent variable showed a clear effect of both Hg concentration and

Figure 1 Mercury and Se concentrations (µmol/kg wet weight) in pituitary gland samples from dental personnel. Least squares regression line and 95% CI for the predicted means are shown.

Table 3 Results of linear regression analysis with Se concentration ($\mu\text{mol/kg}$ wet weight) in different tissues as dependent variable†

Tissue	No of samples	Independent variable	Estimate of parameter (β s)	(95% CI of parameter)	Cumulative R^2
Dental staff					
Pituitary gland	6	Intercept‡	4.8*	(1.0 to 8.5)	
		Hg	1.1***	(0.9 to 1.4)	0.96
		Age	-0.16	(-0.4 to 0.1)	0.99
Occipital cortex	7	Intercept	2.1***	(1.6 to 2.7)	
		Hg	1.0*	(0.01 to 1.9)	0.57
		Non-occupationally exposed			
Renal cortex	12	Intercept	8.5***	(7.7 to 9.3)	
		Hg	1.1***	(0.7 to 1.6)	0.77
Pituitary gland	21	Intercept	5.8***	(5.0 to 6.7)	
		Hg	1.3***	(0.8 to 1.9)	0.43
		Age	-0.06**	(-0.1 to -0.02)	0.65
Occipital cortex	17	Intercept	1.7***	(1.4 to 2.1)	
		Hg	4.6*	(-1.8 to 10.6)	0.24
Abdominal muscle	12	Intercept	1.2***	(0.8 to 1.7)	
		Hg	17.5*	(-4 to 39)	0.10
		Age	-0.01	(-0.02 to 0.001)	0.39

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

†Model: $[\text{Se}]_i = \beta_0 + \beta_1 \times [\text{Hg}]_i + \beta_2 \times \text{age}_i + \varepsilon_i$, $\varepsilon_i \sim N(0, \sigma)$.

In all analyses the concentration of Hg ($\mu\text{mol/kg}$ wet weight) was entered as an independent variable. If significant improvement (partial F test $p < 0.15$) of the model was achieved age was also included in the model. For the analyses where age was included this variable was "centred"—that is, transformed to actual age (y) minus average age of all cases (dental staff plus non-occupationally exposed; that is, 58 years). Significance tests regarding the parameter estimate for the effect of Hg were performed as one sided t tests and regarding intercept and the effect of age as two sided t tests.

‡The parameter β_0 in the model equation—that is, the predicted Se concentration ($\mu\text{mol/kg}$ wet weight) at zero Hg and 58 years of age.

age. The regression coefficient for Hg was 1.3. The regression coefficient for age was negative—that is, concentrations of Se decreased with age. At Hg concentration of zero and average age of 58 years the Se concentration predicted by the regression equation was $5.8 \mu\text{mol Se/kg}$, showing a significant fraction of Se not associated with Hg (table 3).

Two cases (8 and 20) showed extremely high Hg concentration in the pituitary (more than 40 standard deviations (SD) above the mean of the rest of the cases; (table 2)) and the source was most likely other than food and amalgams (for instance, occupational). They had retired owing to old age and no data on former occupations were available at the time of sample collection. Later retrieval from the National population and housing census of 1980 showed that one of them had worked as an electrician and thus may have been exposed to mercury through broken electrical equipment. For the other subject no occupational history was obtained.

When the two cases with high pituitary Hg concentrations were excluded from the analysis the slope coefficient for Hg remained essentially unchanged, but was no longer statistically significant ($R^2 = 0.11$). The effect of age remained unchanged ($p < 0.01$, cumulative $R^2 = 0.53$).

It was notable that Hg concentrations in the other tissues of case 8, although comparatively high, were of the same order as in other non-occupationally exposed persons. Exclusion of this case did not change the outcome of the regression analyses for the renal cortices or occipital cortices, but for abdominal

muscle the effect of Hg became statistically non-significant.

Discussion

Concentrations of Hg in tissues from dental staff were higher than in the corresponding tissues of the general population. Differences were most prominent in pituitary glands (tables 1 and 2). The concomitantly increased Se concentrations in the pituitary glands and in occipital cortices of dental staff show that Se accumulates together with Hg. Regression analysis showed slope coefficients for Hg of around unity (table 3 and fig 1). The regression equations thus imply that each increment in Hg concentration

Figure 2 Mercury and Se concentrations ($\mu\text{mol/kg}$ wet weight) in renal cortex samples from non-occupationally exposed subjects. Least squares regression line and 95% CI for the predicted means are shown.

results in a roughly equal increment in Se concentration. These results are in close agreement with those of Kosta *et al* who found accumulation of Se with Hg at a 1:1 stoichiometric ratio in several organs from five mercury miners who had retired 5–16 years earlier.²⁵

In the additive reaction product of Se and inorganic Hg, irrespective of whether it is Hg/Se or Hg/Se-protein complex, the stoichiometric ratio of the elements is 1:1. Even a slope of unity, however, does not rule out non-associated forms of Hg—for example methylmercury or Hg²⁺ bound to protein binding sites—although at the extremely high coefficient of determination in the pituitary glands of dental staff such forms are unlikely to be other than a minor fraction.

Because Se is essential a certain concentration must be present free of Hg. This concentration is represented by the intercept term in the regression equations. Crude Hg/Se ratios from single samples will be confounded by this Se and are therefore generally not suitable for assessing the association between the elements. With increasing concentration of the elements the effect of free Se can be expected to be reduced and as can be seen from tables 1 and 2 the Hg/Se ratio in the samples increases and approaches unity.

Regression analysis of data from non-occupationally exposed persons indicated the accumulation of Se with Hg at a rough 1:1 stoichiometric ratio in the renal cortex (table 3 and fig 2). An association between the elements, although statistically weaker, was also seen in the occipital cortex, pituitary gland, and abdominal muscle. It is expected that at lower Hg concentrations only a small amount of Se is associated with Hg and natural variations in the much higher concentration of free Se will result in lower statistical correlations. Methylmercury in varying concentrations may also obscure a relation between inorganic Hg and Se. This source of error could be cancelled by the speciation of Hg. The results are in agreement with a study of Japanese forensic cases from the general population, which also showed a high correlation between Se and Hg in the kidney but not in the cerebrum.³⁴

Selenium in human organs may also bind to metals other than Hg—for example cadmium.³⁴ If such binding were of importance here it would most likely have induced variation in Se concentrations that could not be explained by the linear model. The very high coefficients of determination in part of the regression analyses therefore suggest that such binding to other elements was not important. The Se that is free of Hg thus probably corresponds to biologically available Se. The regression analyses did not indicate a difference in this amount between dental personnel and the general population but an appreciable variation was found between tissues.

Whereas cases without occupational exposure

clearly had the highest concentrations of Hg in the kidneys, occupationally exposed dental staff and retired Hg miners²⁵ showed the highest concentrations of Hg in the pituitary and thyroid glands. Based on concentration of Hg in the air³ and urinary excretion of Hg,^{35–37} which is a good indicator of ongoing exposure to Hg vapour,^{1,38} the present exposure to mercury in Swedish dentistry has been shown to be moderate. The average contribution of occupational exposure to urinary excretion of Hg in dental staff was about the same as the average contribution from dental amalgam fillings.^{35–37} The very large difference between pituitary Hg concentrations in dental staff and non-occupationally exposed subjects is therefore surprising. Three dentists had about 200 times higher mercury concentrations in their pituitary glands than the median for non-occupationally exposed subjects (tables 1 and 2). One explanation may be higher exposure earlier in Swedish dentistry. Although limited, reports from 1957³⁹ and 1970⁴⁰ do not indicate that exposures to Hg were previously orders of magnitude higher. (See also Nylander.⁴¹) Another possibility is that the accumulation of Hg in the pituitary depends not so much on the average exposure but on high exposure peaks when preparing amalgam or when drilling old amalgam fillings.^{2,39,42,43} Such a hypothesis is in line with animal studies by Khayat *et al* showing that the increased retention of Hg after pretreatment with Se was not seen when the doses of inhaled Hg vapour and injected Se were small. One hypothesis was that at low concentrations Hg is bound to sites with low capacity but higher affinity than that of the proposed Se metabolite.⁴⁴

In the pituitary glands of non-occupationally exposed persons and dental staff the concentrations of biologically available Se decreased with age. Over the age span for the non-occupationally exposed subjects (72 years) the regression equation predicts an age related difference of 72×0.06 —that is $4.3 \mu\text{mol Se/kg}$. The effect of advancing age on Se concentrations in different organs of adults is not well known. In the brain Se concentration has been reported to increase,⁴⁵ but also to decrease⁴⁶ with age. In the renal cortex it has been reported to increase with age.⁴⁶ We did not find an effect of age on biologically available Se in organs other than the pituitary gland. None of the previous studies considered Hg concentrations, however, and therefore age effects in these studies may be secondary to variations in Hg concentration that correlated to age.

In conclusion, we have shown accumulation of Se together with Hg at a relation consistent with a 1:1 stoichiometric ratio in several organs from dental staff and the general population. The results also show the importance of simultaneous analyses of both Hg and Se when organ concentrations of these elements are evaluated.

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