Accumulation and Biotransformation of Mercury and its Relationship to Selenium after Exposure to Inorganic Mercury and Methyl Mercury - A Study on Individuals with Amalgam Fillings, Dental Personnel, and Monkeys.

by

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Stockholm 1990

Mercury and Selenium Concentrations and Their Inter-Relationships in Organs from Dental Staff and the General Population

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ABSTRACT

Mercury and selenium concentrations in organs samples from cadavers were determinded by radiochemical neutron activation analysis. The relationship between the elements was analysed by linear regression. In pituitary gland samples and one thyroid gland sample from dental staff, occupationally exposed to mercury vapour, accumulation of Se together with Hg at an approximate 1:1 stoechiometric ratio was found. Biological half-times of several years of the accumulated elements were indicated. Accumulation of Se together with Hg at an approximate 1:1 stoechiometric ratio was seen also in renal cortex samples from the general population, i.e. individuals exposed to inorganic mercury from amalgam fillings and organic mercury from food including fish. The possibility of a protective effect of Se against the toxicity of Hg is discussed. The amount of Se that was not associated to Hg, which probably represents the biologically available Se, varied markedly between organs. Decreasing concentrations of biologically available Se with advancing age was seen in pituitary gland samples, but not in other organ samples. Renal cortex samples from three dentists showed low Se relative to Hg. It was suggested that a comparatively large fraction of Hg was bound to other ligands than Se or that the biologically available amount of Se had decreased. The results show the importance of simultaneous analysis of Hg and Se when evaluating organ concentrations of these elements.

... selenium, organ concentrations, trace element interactions,

INTRODUCTION

Mercury (Hg) is a non-essential heavy metal the compounds of which differ in metabolism and toxicity. The adverse effects of exposure to elemental mercury vapour (Hg^0) have been known for centuries. After uptake in the lungs Hg^0 is oxidised to mercuric mercury (Hg^{2+}) in the blood and other tissues. In the non-oxidised form it readily passes through biological membranes, e.g. the blood brain barrier and the placenta. The central nervous system and the kidney are considered the critical organs at long time exposure to elemental mercury. The classical intoxication picture, mercurialism, includes tremor, psychic symptoms, notably erethism, and gingivitis.[1] Animal studies suggest that the immune system also might be a critical organ at exposure to inorganic mercury, especially in genetically susceptible individuals.[2,3]

In the 1960's organic mercury compounds, mainly methyl mercury (MeHg), were demonstrated as widely spread environmental dangers. MeHg is highly lipid soluble and passes readily into all tissues. The central nervous system is considered the critical organ for methyl mercury in man.[1,4]

As a result of preparing and working with amalgam dental staff is exposed to mercury in the form of vapour and particlulates.[5-8] This exposure implies a potential risk for deleterious effects.[9-13]
Recently interest has focused also on the possibility of health effects in the general population due to exposure to inorganic mercury from amalgam restorations.[14-16] Amalgam fillings continuously emit elemental mercury vapour which is absorbed in the lungs, and distributed to various organs.[8,15,17-19] This mercury makes the predominant contribution to exposure to inorganic mercury in the general population.[20]

Selenium (Se) is an essential trace element in several species including man. It is an integral part of the enzyme glutathione peroxidase in man and other mammals. It may also have other important functions. At high doses Se becomes toxic, e.g. through intake with food in some geographical areas with high Se content in the soils.[21] Organ concentrations of minerals and trace elements depend on age. For different organs there have been reports of increasing Se concentrations,[22,23] but also decreasing Se concentrations[22] with advancing age in adults. Plasma Se has been reported to decline markedly after 65 years of age.[24]

Experimental animal studies show that selenium compounds, both organic and inorganic, protect against the acute renal and intestinal necrosis induced by subcutaneously administered mercuric (Hg^{2+}) chloride.[25-28] With oral administration the protective effect of selenite against the renal toxicity of $HgCl_2$ has been demonstrated with exposures up to 20 months.[29-31] Conversely mercury has been demonstrated to protect against the growth retarding effect of toxic doses of selenium in rats and chicks.[30-32]

After combined administration to rodents, both elements become attached to certain high molecular weight protein fractions in a 1:1 stoechiometric ratio.[33-36] The in vitro binding of Hg to a single plasma protein in a 1:1 stoechiometric ratio with Se was preceeded by the conversion of selenite to Se^{2-}, which may readily react with Hg^{2+} to form HgSe.[37] Simultaneous administration also causes changes in the organ distribution of mercury. In most studies a decreased concentration in the kidney and increased concentrations in other organs are reported.[26,38,39] These changes in distribution are accompanied by increased retention of mercury. The effect on distribution and retention is maximal when the elements are administered in equimolar doses.[26,35,38-41] Conversely $HgCl_2$ alters the distribution and retention of selenium.[35,40]

There are no animal data on the effect of Se treatment on the toxicity of inhaled elemental mercury vapour. A study in mice has shown that except for increased uptake in the lungs Se pretreatment did not markedly change the initial distribution of Hg. However, the retention of mercury in the whole body and several organs was markedly increased. The authors concluded that while injected selenite and mercuric mercury interact strongly in serum and are retained especially in the reticuloendothelial system, elemental mercury interacts with selenium mainly after oxidation intracellularly.[42]
In 1975 Kosta et al. reported an approximate 1:1 stoechiometric ratio of Hg and Se at high concentrations in several organs from former mercury miners.[43] We also found a very high correlation between high total Hg and Se concentrations in four pituitary glands from dental staff.[44] The main purpose of the present work was to further elucidate the relationship between mercury and selenium concentrations in several tissues from individuals with varying exposure to mercury vapour.

MATERIAL AND METHODS

Pituitary gland, occipital cortex, renal cortex, abdominal muscle as well as a few samples from thyroid gland were collected at autopsy of 7 dentists and one dental assistant (Table 1). The samples were collected at different pathology departments and at the coroner's office in Stockholm. Pituitary gland, occipital cortex, renal cortex, and abdominal muscle samples, from individuals 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 coroner's office in Stockholm.

Two of the individuals with no known occupational exposure to Hg (Nos. 8 and 20, Table 2) had much (>10-fold) higher Hg concentrations than the rest in the pituitary gland. This suggests that occupational exposure may have occurred. They had retired due to old age and with no data on former occupations at the time of sample collection. Later retrieval of data from the National population and housing census of 1980, showed that one of these cases had worked as an electrician. A major

industrial usage of mercury is in electrical equipment,[1] therefore an occupational exposure is not unlikely. For the other individual, no data on former occupations could be obtained.

According to detailed medical records, one dentist (case No.1, Table 1) had not worked for several years due to retirement and incapacitating chronic illness. Another dentist (case No.2) had not worked since retirement, a total of 15 years, according to information from relatives. Detailed data on the remaining cases were not obtained. However, based on the medical records and autopsy reports we concluded that they had not been professionally active during the last months before death. There were no reported signs or symptoms of mercury intoxication in available medical records. However, one of the dentists (Case No. 2) suffered from disturbances of peripheral nerves and was at the time of death investigated for these problems at a neurological clinic.

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.[45-47] Detailed description and quality control for the mercury analyses have been published earlier.[15] The detection limit is 2 ug/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 • 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 Nos. 3 and 7, Table 1) were analysed by RNAA at Isotopcentralen, Denmark. The detection limit is 0.2 ug/kg for Hg and 3 ug/kg for Se.[48] The accuracy was tested through simultaneous analysis of NBS SRM 1577, certified for 16 • 2 uHg/kg and 1.1 • 0.07 mg Se/kg, which gave 16.0 and 15.8 ug Hg/kg and 1.1 and 1.1 mg Se/kg.

For the organs with 6 or more samples the relationship between Se, Hg and age was investigated by linear regression analysis[49], with Se as dependent variable. In all analyses Hg was entered as an independent variable then age was added to the model if this resulted in a significant improvement (Partial F-test $p<0.10$). Examination of residuals indicated the linear models to be adequate. Based on previous studies it was decided that the alternative to the null hypothetis of no association between Hg and Se is a positive association, therefore significance tests regarding the effect of Hg were performed as one-sided tests. Significance tests regarding the effect of age were performed as two-sided tests. All regression analyses were performed using the SAS statistical package for VAX/VMS.[50]

Mercury and selenium in organs from dental staff

The organ samples from dental staff had considerably higher Hg concentrations than those from the non-occupationally exposed cases. The pituitary glands of the dental staff also had considerably higher Se concentrations than pituitary glands from non-occupationally exposed cases. Significantly higher concentration of Se for dental staff was also seen in occipital cortex (Mann-Whitney test[51]), although the magnitude of the difference was less than for pituitary gland (Tables 1 and 2).

Regression analysis of data from pituitary gland with Se concentration as dependent variable demonstrated a strong effect of Hg concentration. The regression coefficient for Hg was 1.0. The intercept (the predicted Se concentration at zero Hg) was 4.6 umol Se/kg, however, this parameter estimate was not statistically different from zero (Figure 1 and Table 3). Addition of age resulted in a borderline significant (Partial F-test $p<0.11$) improvement, which effect if included in the model would show a negative parameter estimate. The coefficient of determination of the model including also age was, $R^2=0.99$.

Regression analysis of data from occipital cortex samples with Se concentration as dependent variable demonstrated an effect of Hg concentration. The regression coefficient for Hg was 1.0, but the confidence interval was wide. No effect of age was seen. The intercept of 2.1 umol Se/kg showed a significant fraction of Se not associated to Hg (Table 3).

There were too few renal samples (Table 1) to make regression analysis meaningful. The association of Se to Hg generally can not be assessed in single samples, but at the extremely high concentrations of the elements in one thyroid sample (case No. 2) the stoechiometric relationship of approximately 1:1 should be noticed.

Mercury and selenium in organs from individuals without occupational exposure to Hg

In average renal cortex showed the highest Hg concentration. Regression analysis showed a strong relationship between Hg and Se. The regression coefficient for Hg was 1.1. No effect of age was seen. The intercept of 8.5 umol Se/kg showed a significant fraction of Se not associated to Hg (Table 3, Figure 2).

Regression analysis of data from pituitary gland samples with Se concentration as dependent variable demonstrated a clear effect of both Hg concentration and of age. The regression coefficient for Hg was 1.3. The regression coefficient for age was negative, i.e. decreasing concentrations with advancing age. At a Hg concentration of zero and 58 years of age (average age of cases with pituitary data) the mean Se concentration predicted by this linear model was 5.8 umol Se/kg, thus showing a sig-

Hg concentrations were excluded (see also material and methods) the point estimate of the effect of Hg remained essentially unchanged, but the effect was no longer statistically significant. The negative effect of age did not change and was still statistically significant. These two cases have a good fit to the linear model based on the pituitary glands of the dental staff cases. Only one of these two cases had data on Hg concentrations in other tissues, but it was notable that the mercury concentrations in these tissues were of about the same level as for the other non-occupationally exposed cases.

Regression analysis demonstrated a relationship between Hg and Se in occipital cortex. The regression coefficient for Hg was 4.6, with a wide confidence interval. No effect of age was seen. The intercept of 1.7 umol Se/kg showed a significant fraction of Se not associated to Hg (Table 3).

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

Discussion

Dental staff is occupationally exposed to elemental Hg vapour. Concentrations of Hg in tissues from dental staff cases were higher than in corresponding tissues from non-occupationally exposed cases, most prominently so in the pituitary gland (Table 1 and 2). Even though two of the dentists (cases Nos. 1 and 2) had not been occupationally active for several years, they still had extremely high levels of Hg in some organs. This implies biological half-times for the mercury in the order of years. Very long biological half-times of mercury in the human brain have also been indicated in some previous reports.[52] In a study on human volunteers with single adminstration of a small dose of radioactively labelled mercury Hursh et al. reported the biological half-time of mercury accumulated; in the kidney region to be approximately 60 days; in the head to be approximately 20 days and in the other gross regions of the body (except lungs) to be in between these figures.[53] Thus different fractions of mercury with very large variations in biological half-times appear to exist.

In the non-occupationally exposed individuals the highest concentration of mercury was seen in the kidney. Short term animal studies with exposure to mercury vapour have shown the highest concentrations to accumulate in the kidney.[42,54-56] In human volunteers the kidney region accumulated the highest levels of radioactive mercury.[53] However, in dental staff (Table 1) and mercury retired miners[43] the highest Hg concentrations were not seen in the kidney.

Also the levels of Se were increased in pituitary gland of dental staff. Regression analysis indicated that Se accumulated together with Hg at a relationship consistent with a 1:1 stoechiometric ratio in the pituitary gland (Figure 1 and Table 3). Accumulation of Se together with Hg was seen also in occipital cortex, but here the quantitative estimate of the relationship was subject to a larger random variation (Table 3). The data from one thyroid gland, with extremely high concentrations of the elements, indicated accumulation at a 1:1 stoechiometric ratio.

The results are in close agreement with those of Kosta et al.[43] who reported accumulation of Se together with Hg at a 1:1 stoechiometric ratio in several organs from five mercury miners, retired since 5-16 years. The relationship between concentrations of mercury in different organs was similar to those in samples from dental staff in the present study, but the levels of Hg and Se were higher. There were no statements regarding health status in the deceased subjects. However, the authors conclusion that the interaction between the elements protected against the toxic properties of these seems to indicate that at least there were no evident signs or symptoms that they related to Hg or Se toxicity.

Ashe et al.[57] exposed rabbits intermittently (5 days/week, 7 h/day) to high levels (0.9 mg/m^3) of mercury vapour for 1-12 weeks. Pathologic changes in brain tissue were seen at organ levels from 1-2 umol Hg/kg wet weight. Kidney tissue showed pathologic changes at levels slightly below 100 umol Hg/kg. In the heart pathologic changes were seen at slightly lower organ concentrations than in the brain, and in the liver and lungs at slightly higher levels than in the brain. Fukuda et al.[58] exposed rabbits (4 days/week, 6 h/day) to high levels of mercury vapour (4 mg/m^3) for 13 weeks. Tremor and clonus were seen at concentrations of 2-15 umol Hg/kg wet weight in different parts of the brain. Selenium status was not considered in these studies.

Thus, in several organ samples from dental staff Hg concentrations were in same order of magnitude as those where toxic effects have been seen in animal studies. The relationship between organ levels of mercury and toxic effects in humans is not known.[1]

The findigs of an association between Hg and Se, with long biological half-time, in several human organs after long term exposure to elemental mercury vapours is in agreement with findings in experimental animal studies with administration of inorganic mercury.[29,36,40,42] The very high tissue concentrations of Hg that were demonstrated in samples from human organs in the present study and that of Kosta et al. may suggest that this Hg has a comparatively low biological activity. The association of Se to Hg may provide a mechanism of inactivation of Hg and Se. This would be in agreement with data from animal studies where it appears that the formation of protein-Hg-Se complexes or HgSe, which diverts Hg from binding-sites where its toxic effect is normally exerted, is of importance for the protection by Se against the toxicity of Hg and vice versa.[26,28,30-32,34,59] However, neither in the

cases of the present study nor in those of Kosta et al. can toxic effects of Hg exposure be excluced. Furthermore the high organ concentrations off Hg appear to be at least partly due to an increased retention resulting from the association with Se.

A protective effect might, as proposed by Frost,[60] imply that the toxic effect of mercury becomes manifest when the amount of Se^{2-} is inadequate to inactivate Hg. A recent paper reported on two Swedish goldsmiths who developed symptoms of mercury intoxication after being unknowingly exposed to mercury vapour during recovery of gold from metal scraps of dental restorations. After cessation of exposure both slowly recovered. Interestingly, during the recovery period, both reported alleviation of symptoms in connection with supplementation of 50 ug organically bound Se daily.[61] This is a moderate amount of Se, but still it is nearly twice the supply in an average Swedish diet,[62] which is considered suboptimal in Se.[63] The possibility of a protective effect of Se aginst Hg toxicity in long term exposure in humans needs further clarification.

A linear relationship indicating that Se accumulated together with Hg was seen also in the renal cortex of non-occupationally exposed individuals (Figure 2). This relationship was consistent with an accumulation at a 1:1 stoechiometric ratio. In occipital cortex and pituitary gland of non-occupationally exposed individuals a relationship between the elements was also seen, but it was less clear than in the renal cortex with higher mercury concentrations. A significant part or the mercury in human organs, i.e. brain, kidney and pituitary gland has been shown to emanate from amalgam fillings.[8,15,17-19] The other major source of mercury exposure in the general population is through intake of MeHg with food including fish.[1] In contrast to the occupational exposure in dental staff this exposure continued until death.

A recent study of Japanese forensic cases from the general population also showed a high correlation between inorganic Hg and selenium in renal cortex, but no correlation in cerebrum. Concentrations of mercury in different organs of these cases were markedly higher than for the non-occupationally exposed individuals in the present study, probably resulting from a higher intake of methyl mercury with food including fish in the Japanese population.[64,65]

A correlation between Hg and Se was seen also in abdominal muscle, but the point estimate of the regression coefficient for Hg suggested the possibility of a relationship different from that seen in the other tissues. There were two cases with high Se concentration in relation to Hg concentration. If these two cases are excluded, a very good fit to a linear model including only Hg is obtained, R^2=0.81 (Figure 3). The regression coefficient for Hg becomes 24 (95%-confidence interval [14, 33]). As two cases were excluded this comparatively high slope coefficient may be an artifact.

For occipital cortex and pituitary gland the linear models explaining Se concentra-

occupationally exposed individuals can be compared. The parameter estimates of the intercept for occipital cortex and of the slope coefficient for Hg for pituitary gland are approximately the same in both groups. For the remaining two parameter estimates the random variations are large, but there is no indication of a difference between the groups.

Both in the occupationally exposed and in the non-occupationally exposed individuals, accumulation of selenium together with mercury was clearly seen only in the organs with the highest concentrations of Hg. There are several possible explanations e.g.; at lower concentrations of Hg an interaction may be obscured by natural variations in the Se concentration; an interaction between Hg and Se takes place only above a certain threshold; as only total Hg was analysed the influence of methyl mercury may obscure a relationship between inorganic Hg and Se.

In animal studies the increased retention of Hg after pretreatment with Se was not seen when the doses of inhaled mercury vapour and injected Se were small. One hypothetis forwarded was that at low concentrations Hg is bound to sites with low capacity but higher affinity than that of the proposed Se metabolite (Se^{2-}).[66]

Based on concentration of Hg in the air[7] and urinary excretion of Hg,[67-69] which is a good indicator of ongoing exposure to Hg vapour,[1,70] the present exposure to mercury in Swedish dentistry has been shown to be moderate. The contribution of occupational exposure to urinary excretion of Hg in dental staff was approximately the same as the contribution from dental amalgam fillings, i.e. in average about 1-3 ug Hg/l or g creatinine from both sources. Urinary excretion of mercury ranged up to approximately 35 ug Hg/l or g creatinine in dental staff and about 15 ug/l or g creatinine in non-occupationally exposed subjects.[67-69,71] Air concentrations of mercury and urinary mercury excretion in dental staff was lower in public health dentistry than in private dental care.[7,67,68] Considering the moderate urinary mercury levels in dental staff the very large difference between pituitary Hg concentrations in dental staff and non-occupationally exposed individuals is somewhat surprising. Three dentists had about 200 times higher mercury concentration in the pituitary gland than the median for non-occupationally exposed (Tables 1 and 2).

The highly elevated mercury concentrations in pituitary gland samples from dental staff might be the result of higher exposure earlier in dentistry. Two reports on urinary Hg concentrations in dental staff from 1957[72] and 1970[73] did not, however, indicate a markedly higher exposure previously in Swedish dentistry. These studies were limited and did not present an adequate analytical control, therefore they do not allow a precise assessement of previous exposure.

The female dentist that was only 30 years old at death had worked in public health dentistry and had given birth to two children after graduation as a dentist. Therefore she had only had limited duration of exposure to contemporary levels in dentistry. Still the concentration of Hg in her pituitary gland was more than 10 times higher than the median value of non-occupationally exposed.

Thus there seems to exist factors other than the relation between average levels of exposure that is of importance for the difference in mercury levels in pituitary gland between the two groups. This large difference might partly be the result of an interaction between Hg and Se, that takes place only above a certain threshold, and results in long term accumulation of the elements. Possibly the exposure pattern in dentistry with comparatively low exposure most of the time, but with high exposure peaks, e.g. when preparing amalgam or when drilling in old amalgam fillings[3,72,74,75] may be of importance for the organ distribution and sub-cellular binding of Hg. The difference between the groups was not as large in occipital cortex where also the interaction between the elements appeared to be less pronounced.

In mammals MeHg is converted to inorganic mercury mainly in the liver, which then is redistributed also to other organs, especially the kidney.[1,76-79] In several tissues of humans with high oral intake of MeHg a significant fraction of the mercury has been found to be in inorganic form. The kidney usually contained the highest fraction of inorganic Hg.[1] Part of the mercury associated with selenium in the kidney probably emanates from intake of methyl mercury.[64,65]

Mercuric mercury does not readily pass the blood brain barrier. Significant accumulation of inorganic Hg emanating from intake of methyl mercury therefore requires demethylation in the brain. Recent data from long term exposure of monkeys to MeHg indicated such demethylation.[80] Further analysis of brain tissue samples from the same animals showed a high correlation between inorganic Hg and Se. However, total Hg (including MeHg) did not show a relationship with Se (unpublished observation). It is not clear if a significant demethylation occurs in the human brain.[65] In the present study only total Hg was analysed, therefore organic mercury from food may obscure a relationship between inorganic Hg and Se, especially in the brain.

A chemical association or complex formation involving Hg and Se might also inactivate biologically available Se.[81] However, in organs studied by regression analysis the intercept indicated a substantial amount of Se that was not associated to Hg, i.e. probably representing biologically available Se. There was a significant variation in this amount between tissues. If binding to other metals, e.g cadmium,[64] were of importance it would most likely have induced variation in the data that could not be explained by the linear models. The very high correlation between Hg and Se in pituitary gland of dental staff and to some extent also in renal cortex of non-occupationally exposed individuals therefore suggests that in the present material such binding of Se to other elements is less important.

For the pituitary glands non-occupationally exposed cases demonstrated decreasing concentrations of biologically available Se with advancing age. This was also suggested by the dental staff cases. The effect of advancing age on Se concentration in different organs of adults is not well known. In the brain Se has been reported to increase,[23] but also to decrease[22] with age. In renal cortex it has been reported to increase with age.[22] We did not find an effect of age on biologically available Se in

these organs. However, none of the previous studies considered Hg concentrations, therefore age effects in these studies may be secondary to variations in Hg concentration that correlated to age.

Compared to the linear models bases on data from the non-occupationally exposed individuals three samples from renal cortex of dental staff all lay below the regression line and outside a 95%-confidence interval for predicted values, i.e. showing lower than expected Se concentrations. This may imply that a comparatively large part of the Hg in the kidney of the dental staff cases was not associated to Se. Such Hg may be inactivated by binding to other protective cell-components, e.g. metallothionein, or it may be associated to binding-sites where it is potentially harmful. In animal studies with administration of mercuric chloride in combination with selenite large amounts of both Hg and Se accumulated in the renal tubule cells.[29-31] The renal tubule is a sensitive indicator of effects of occupational exposure to Hg vapour and effects have been demonstrated after moderate exposure.[32-34]

Alternatively, the amount of Se that was not associated to Hg was lower than in kidney samples of non-occupationally exposed individuals, implying that the mercury might have lowered the amount of biologically available Se.[31] However, due to the long exposure free period in at least one of the dental staff cases this alternative would seem less likely.

As noticed above the concentration of Hg in the kidney of dental staff was surprisingly low, displaying only moderately increased levels compared to those of non-occupationally exposed subjects. In dental staff case No. 2 (Table 1), who had not been occupationally exposed for several years, the amount of Se accumulated in the kidney was also low compared to that accumulated in pituitary gland and thyroid gland. As an association between the elements is shown to occur in the kidney of non-occupationally exposed individuals such an association seems likely to occur also in the kidney of occupationally exposed. A possible explanation for the relatively low concentration of the elements in the kidney after occupational exposure is that the biological half-time of Hg and Se that are accumulated together might be shorter in the kidney than in pituitary gland, thyriod gland and brain where extremely long biological half-times have been indicated.

In conclusion, this study demonstrated accumulation of Se together with Hg at a relationship consistent with a 1:1 stoechiometric ratio in organs with comparatively high concentrations of mercury from dental staff and the general population. Long biological half-times of the accumulated elements were indicated. The results show the importance of simultaneous analyses of both Hg and Se when organ concentrations of these elements are evaluated.

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Table 1. Mercury and selenium concentr

from dental personnel*

Case No.	Sex	Age years	Pituitary gland Hg µmol/kg	Se	Occipita. cortex Hg µmol/kg
1	M	80	20	23	1.43
2	M	82	18	22	C.42
3	M	60	28	36	C.08
4	M	50	1.7	9	0.19
5	F	30	1.5	-	0.07
6	M	61	0.7	-	0.07
7	M	60	2.2	4.7	0.25
8	F	67	6.4	12	0.09

*) Cases Nos. 1 to 7 dentists and case N

Medical diagnoses of possible significan
concentrations:
case 1: Parkinson's disease and diabete:
case 4: Glomerulonephritis.
case 6: Diabetes mellitus.

Table 2. Mercury and selenium concentration in tissue samples from individuals without occupational exposure to mercury

Case No.	Sex	Age years	Pituitary gland Hg µmol/kg	Se	Occipital cortex Hg µmol/kg	Se	Renal cortex Hg µmol/kg	Se	Abdominal muscle Hg µmol/kg	Se
1	M	24	0.14	11	0.050	1.90	1.63	11.1	-	-
2	M	48	0.08	08	0.012	1.43	0.16	8.4	0.005	1.05
3	M	29	0.09	07	0.032	1.82	1.27	11.4	0.011	2.38
4	M	63	0.17	05	0.051	1.68	0.24	7.5	0.024	1.28
5	M	79	0.06	05	0.027	1.76	0.15	8.2	0.009	1.05
6	M	73	0.08	07	0.020	2.00	0.11	9.6	0.010	1.27
7	M	80	-	-	0.060	2.35	-	-	0.024	1.77
8	M	71	3.88	14	0.114	1.96	3.79	12.8	0.047	2.01
9	M	74	0.08	06	0.046	2.00	0.29	8.2	0.022	1.52
10	M	40	0.15	07	0.053	2.00	1.57	9.2	0.017	1.39
11	M	67	0.20	06	0.061	1.81	0.52	9.7	0.024	1.53
12	M	16	0.19	08	0.037	1.77	4.04	12.4	0.004	1.84
13	F	30	0.38	08	0.079	1.78	2.59	11.9	0.027	1.66
14	M	30	-	-	0.036	1.84	-	-	-	-
15	M	52	-	-	0.098	2.08	-	-	-	-
16	M	76	0.08	04	0.049	1.92	-	-	-	-
17	F	56	0.14	05	-	-	-	-	-	-
18	M	61	0.03	05	-	-	-	-	-	-
19	M	88	0.11	04	-	-	-	-	-	-
20	M	70	5.83	11	-	-	-	-	-	-
21	M	71	0.05	06	-	-	-	-	-	-
22	M	47	0.05	05	-	-	-	-	-	-
23	F	75	0.19	03	-	-	-	-	-	-
24	M	63	0.04	04	0.081	2.57	-	-	-	-
n		24	21	21	17	17	12	12	12	12
Min		16	0.03	03	0.012	1.43	0.11	7.5	0.004	1.05
Max		88	5.83	14	0.114	2.57	4.04	12.8	0.047	2.38
Median		63	0.11	5.7	0.050	1.90	0.89	9.7	0.020	1.52
Average		58	01	07	0.053	1.92	1.36	10.0	0.019	1.56
SD		20	01	03	0.027	0.26	1.42	1.7	0.012	0.40

Table 3. Results of linear regression analysis with selenium concentration (umol/kg wet weight) in different tissues as dependent variable.*

tissue	n	independent variable of parameter	point estimate	95%-confidence interval	cumulative R^2
Dental staff					
pituitary gland	6	intercept+	4.6	[-0.1, 9.2]	
		Hg	1.0[a]	[0.8, 1.3]	0.96
occipital cortex	7	intercept	2.1[a]	[1.6, 2.7]	
		Hg	1.0[c]	[0.01, 1.9]	0.57
Non-occupationally exposed					
renal cortex	12	intercept	8.5[a]	[7.7, 9.3]	
		Hg	1.1[a]	[0.7, 1.6]	0.77
pituitary gland	21	intercept	5.8[a]	[5.0, 6.7]	
		Hg	1.3[a]	[0.8, 1.9]	0.43
		age	-0.06[b]	[-0.1, -0.02]	0.65
occipital cortex	17	intercept	1.7[a]	[1.4, 2.1]	
		Hg	4.6[c]	[-1.8, 10.6]	0.24
abdominal muscle	12	intercept	1.2[a]	[0.8, 1.7]	
		Hg	17.5[c]	[-4, 39]	0.10
		age	-0.01	[-0.02, 0.001]	0.39

*) Model: $[Se]_i = + \beta^*[Hg]_i + \beta^*age_i + _i \quad _i \; N(0,)$

In all analyses the concentration of Hg (umol/kg wet weight) was entered as a dependent variable, if significant improvement (Partial F-test $p<0.10$) of the model was achieved, age was also included in the model. For the analyses where age (yr) was included it was scaled to actual age minus average age of cases with available samples, i.e. 52 years for non-occupationally exposed subjects with pituitary gland data and 56 years for non-occupationally exposed subjects with abdominal muscle data. Significance test regarding the parameter estimate for the effect of Hg were performed as one-sided T-tests and regarding the effect of age as two-sided T-tests (footnotes a,b and c).

a) $p<0.001$ b) $p<0.01$ c) $p<0.05$

+) The parameter in the model eqation, i.e. the predicted Se concentration when all independent variables are zero.

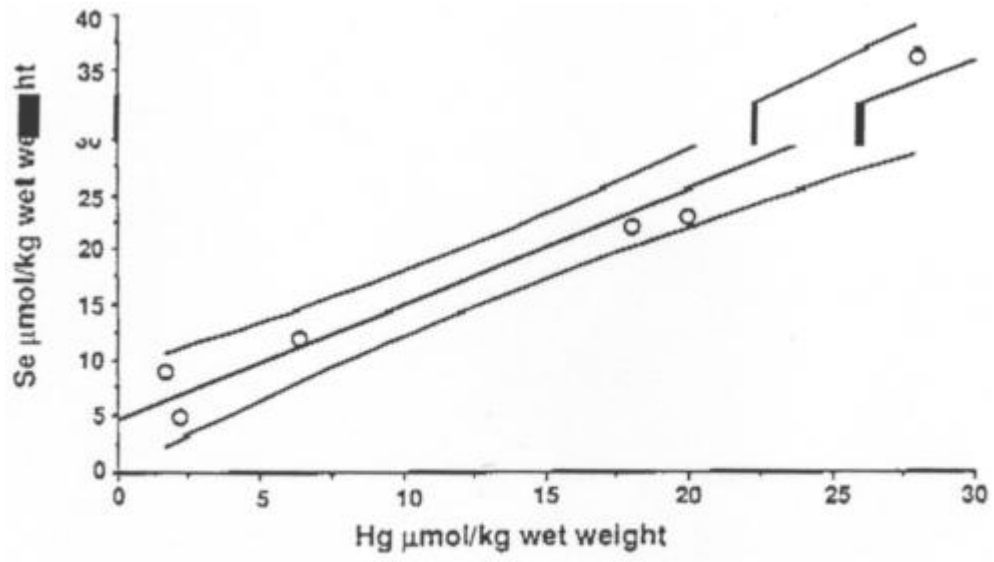

Figure 1. Mercury (Hg) and selenium (Se) concentrations (umol/kg wet weight) in pituitary gland samples from dental personnel. Least squares regression line and 95%-confidence limits for the predicted means.

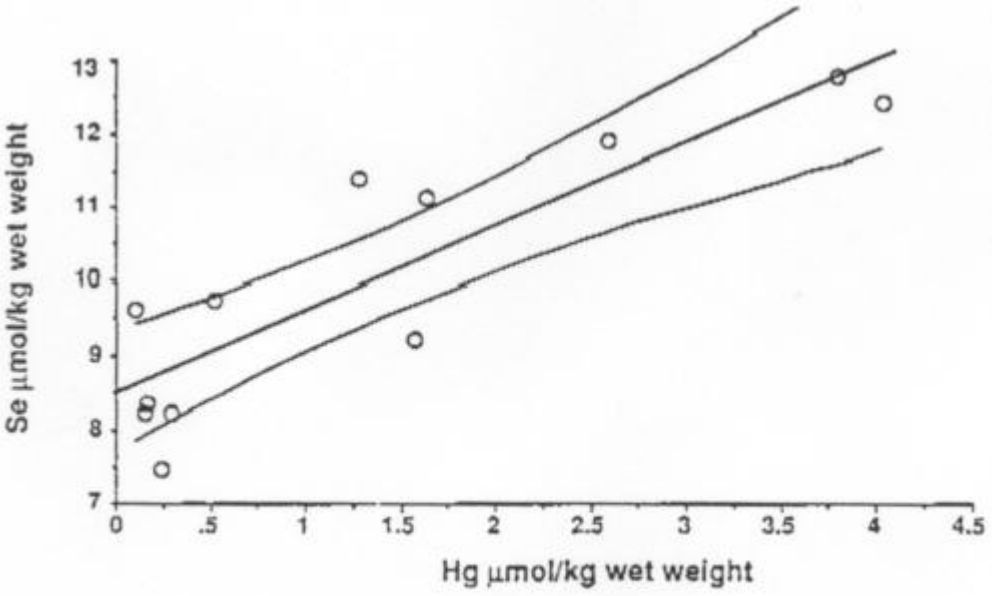

Figure 2. Mercury (Hg) and selenium (Se) concentrations (umol/kg wet weight) in renal cortex samples from non-occupationally exposed individuals. Least squares regression line. 95%-confidence limits for the predicted means.

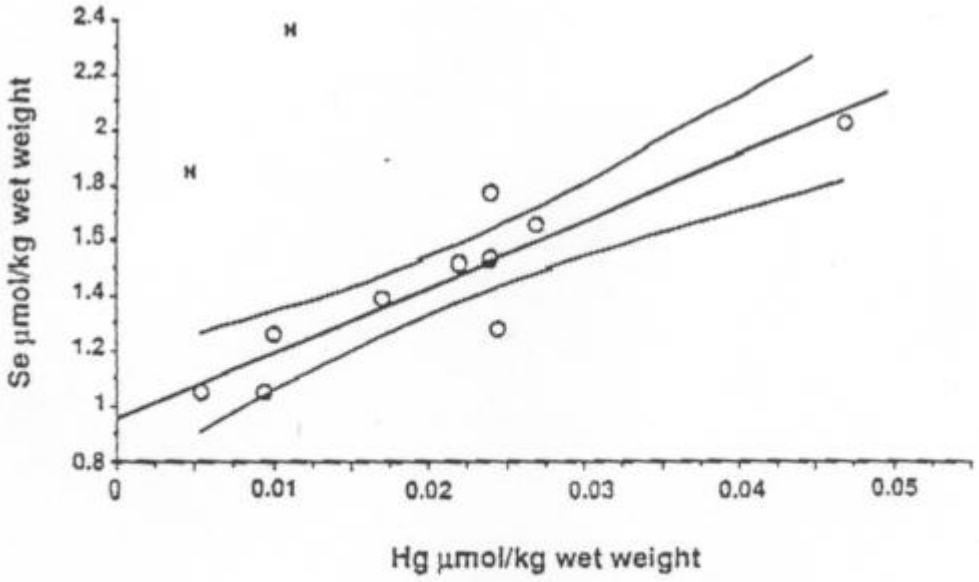

Figure 3. Mercury (Hg) and selenium (Se) concentrations (umol/kg wet weight) in abdominal muscle samples from non-occupationally exposed individuals. Least squares regression line and 95%-confidence limits for the predicted means. Data from two cases are included in the figure (x), but not in the calculation of the regression line