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Time trends in burdens of cadmium, lead, and mercury in the population of northern Sweden

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Abstract

The time trends of exposure to heavy metals are not adequately known. This is a worldwide problem with regard to the basis for preventive actions and evaluation of their effects. This study addresses time trends for the three toxic elements cadmium (Cd), mercury (Hg), and lead (Pb). Concentrations in erythrocytes (Ery) were determined in a subsample of the population-based MONICA surveys from 1990, 1994, and 1999 in a total of 600 men and women aged 25–74 years. The study took place in the two northernmost counties in Sweden. To assess the effect of changes in the environment, adjustments were made for life-style factors that are determinants of exposure. Annual decreases of 5–6% were seen for Ery-Pb levels (adjusted for age and changes in alcohol intake) and Ery-Hg levels (adjusted for age and changes in fish intake). Ery-Cd levels (adjusted for age) showed a similar significant decrease in smoking men. It is concluded that for Pb and maybe also Hg the actions against pollution during recent decades have caused a rapid decrease of exposure; for Hg the decreased use of dental amalgam may also have had an influence. For Cd, the decline in Ery-Cd was seen only in smokers, indicating that Cd exposure from tobacco has decreased, while other environmental sources of Cd have not changed significantly. To further improve the health status in Sweden, it is important to decrease the pollution of Cd, and actions against smoking in the community are important.

Keywords: Heavy metals; Erythrocytes; Smoking; Fish intake; Amalgam fillings

1. Introduction

Environmental exposure to heavy metals has varied considerably over time. Knowledge of the time trends of these exposures is important for the guidance of preventive measures. However, for almost all countries there is remarkably limited information available.

The exposure to lead (Pb) has been extensively studied in different areas. However, in Sweden time trends have been investigated only in the south and only in children (Strömberg et al., 2003). Hence, there is little information on other regions and almost none on other elements (Skerfving et al., 1999). In particular, health effects of exposure to cadmium (Cd) (Friis et al., 1998; Vahter et al., 1998) and mercury (Hg) (Skerfving et al., 1999) have been debated, although there is only little information available on time trends of these exposures.

In addition to the levels of these metals in food and the general environment, some life-style factors have influences on the exposure, and these factors may vary over time. Thus, smoking can enhance levels of Cd and Pb because of the content of these heavy metals in tobacco, and alcohol intake causes Pb exposure (Skerfving et al., 1999). Since fish is the main source of methyl mercury (MeHg), fish intake affects the exposure of Hg (Hallgren et al., 2001). In addition, low iron depots are associated with increased Cd retention (Bárány et al., 2005; Olsson et al., 2002; Skerfving et al., 1999).

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For the heavy metals Cd, Pb, and Hg, biological monitoring through determination of the metal concentrations in blood is often used (Skerfving et al., 1999). Thus the concentrations in erythrocytes (Ery) are informative, since all three elements are present in blood and predominantly in the red cells.

In this study, we retrospectively monitored concentrations of Cd, Hg, and Pb in erythrocytes during 1990–1999 in adults living in northern Sweden. Time trends of some life-style factors and other determinants were taken into account.

2. Materials and methods

2.1. Population

Samples were collected within the framework of the WHO MONICA Project (Monitoring Trends and Determinants in Cardiovascular Disease), which is a population-based survey of the general population. Women and men aged 25–74 years in the counties of Västerbotten and Norrbotten in the north of Sweden were invited to participate in a health survey. They were asked to fill out a detailed questionnaire regarding, e.g., socio-economic conditions, medical history, education, and life-style factors (Stegmayr et al., 2003).

2.2. Life-style factors

The intake of lean fish (perch, cod, etc.) and fat fish (herring, salmon, etc.) was asked about in a food-frequency questionnaire and summarized into an estimate of the total number of fish meals per week.

The intake of spirits, wine, and strong beer according to the food-frequency questionnaire was summarized to times per week of alcohol intake. Smoking habits were recorded as never-smokers, ex-smokers with number of smoke-free years, and current smokers with number of cigarettes per day.

2.3. Blood sampling

In the MONICA screening, samples from 5327 individuals were collected during the years 1990–1999 (Stegmayr et al., 2003). Blood was obtained by venipuncture into Venoject tubes (Terumo, Leuven, Belgium) with heparin after at least 4 h fasting. After centrifugation at 1500*g* for 15 min, erythrocytes and plasma were separated into aliquots and kept at −80 °C in a biobank.

In this study we analyzed 600 erythrocyte samples. One sample from 1990 was excluded from statistical analyses because contamination was evident. The samples were randomly chosen from the MONICA biobank, stratified for sex, year of sampling (1990, 1994, and 1999), and age at sampling (25–34, 35–44, 45–54, and 55–74 years). Subjects aged 65–74 years were included only in 1994 and 1999, since only subjects up to 64 years of age were invited to the 1990 study.

2.4. Chemical analyses

All samples were analyzed in one campaign. All concentrations are given as μg/L (1 μg Cd/L = 8.9 nmol/L; 1 μg Pb/L = 0.1 μg/dL = 4.8 nmol/L; 1 μg Hg/L = 5.0 nmol/L).

Cd and Pb in erythrocytes (Ery-Cd and Ery-Pb, respectively) were determined by inductively coupled plasma-mass spectrometry (ICP-MS; Barany et al., 1997). The detection limits, calculated as three times the standard deviations (SD) of the blank, were 0.09 and 0.26 μg/L, respectively.

The analytical accuracy in blood (Seronorm; batches 404107 and MR9067; Nycomed, Oslo, Norway) was for Cd 0.71 ± 0.06 (mean ± SD; $n = 25$) and 6.3 ± 0.22 ($n = 25$) μg/L (recommended 0.67–0.76 and 5.4–7.2 μg/L), respectively, and for Pb 31 ± 1.6 ($n = 25$) and 410 ± 13 ($n = 25$) μg/L (recommended 31–39 and 353–443 μg/L), respectively. The data for certified blood samples from United Kingdom National External Quality Assessment Service deviated on average for Cd by ±3.7% for target values 3.7–15 μg/L ($n = 55$) and for Pb by ±4.0% for target values 51–95 μg/L ($n = 26$).

Hg in erythrocytes (Ery-Hg) was determined in acid-digested samples by cold vapor atomic fluorescence spectrophotometry (Sandborgh-Englund et al., 1998). The detection limit was 0.20 μg/L.

The analytical accuracy for Hg in blood (Seronorm; batches 404107 and 404109x, Nycomed) was 2.3 ± 0.18 ($n = 63$) and 13 ± 0.49 ($n = 61$) μg/L (recommended 2.2–3.3 and 13–16 μg/L), respectively. The data for certified blood samples from Centre De Toxicologie du Quebec Interlaboratory Comparison Program (batches M-01-07 and M-01-09) were 3.3 ± 0.21 ($n = 16$) and 5.1 ± 0.27 ($n = 18$) μg/L (certified values 3.4 and 5.4 μg/L, respectively).

All determinations were made in duplicate preparations and the method imprecisions, calculated as the coefficient of variation for the duplicate measurements, were 6.0, 2.3, and 5.0%, for Cd, Pb, and Hg, respectively.

Special care was paid to the possibility that the samples had dried during storage. That was because the storage time varied between the samples from different years, which potentially could have resulted in incorrectly too high values after long storage times. To assess this, we obtained 21–29 samples from each year, and the essential elements copper, selenium, and zinc were determined by ICP-MS. The analysis showed no significant effect of storage time on the concentration of these elements. We thereby concluded that drying of the samples during storage had not occurred.

Ferritin in serum (S-ferritin) was determined in the samples from 1990 and 1999 by an immunochemical method using monoclonal antibodies (Department of Clinical Chemistry, Lund University Hospital).

2.5. Statistics

In the statistical analyses, we used results below the formal detection limit to avoid distorting distributions. Distributions of values were compared using the independent samples test of Mann–Whitney, and P for trends was analyzed using the Kruskal–Wallis nonparametric test. Univariate associations were tested by Spearman's rank correlation (r_S) or Kendall's tau (τ). To examine time trends in exposure to the metals, modeling was made by multiple linear regression. Logarithmic transformations of the metal concentrations were done to take care of skewed distributions, as indicated by residual and goodness-of-fit analyses. We adjusted for age calculated from year of birth in the multivariate analysis. We also included potential background factors, smoking habits, intake of alcohol, and intake of fish, when they were statistically significantly associated with the elements in the univariate tests. We did not adjust for background factors that had no or only weak previous scientific evidence, even when statistically significant in the univariate analyses. S-ferritin was associated with calendar year, age, and sex but, to avoid overadjustment, S-ferritin was not included in the models. A P value <0.05 was considered statistically significant.

We calculated the temporal changes both in absolute (linearly, as μg/L per year) and relative (% per year) terms. The results were similar. We chose to here report the relative values, because we regard them to be easier to visualize. Also, it is reasonable to believe that the pattern is curvilinear in the way that we have previously seen for blood Pb in children (Strömberg et al., 2003).

3. Results

3.1. Life-style factors

There were clear differences between men and women in smoking, alcohol intake, and S-ferritin but not in fish

intake (Tables 1 and 2). The proportion of smokers decreased with time in men but not in women. For daily smokers there was a statistically significant decrease over time in the number of cigarettes smoked per day ($P = 0.006$). The decrease corresponded to 3.9% per year in men and 2.0% per year in women. In neither men nor women were the results statistically significant (Table 1). Alcohol intake and S-ferritin increased. In men fish intake decreased, while women showed no clear trend.

3.2. Cadmium

Median Ery-Cd decreased in men over the time period studied, while the change among women was only marginal (Table 1).

Smoking was associated with an increase of Ery-Cd (Table 3), and there was a positive correlation between number of cigarettes per day and Ery-Cd in daily smokers (Table 3). Information on previous number of cigarettes per day was not available for ex-smokers, but in ex-smokers there was a negative association between Ery-Cd and number of smoke-free years. Those who gave up smoking less than 2 years prior to the sampling had an Ery-Cd median of 1.1 μg/L ($n = 15$); quitting 2–5 years ago had 0.68 μg/L ($n = 22$) quitting and 6–10 years ago had 0.41 μg/L ($n = 43$). In the group with more than 10 smoke-free years, the median Ery-Cd was also 0.41 μg/L ($n = 103$). Use of moist snuff had no influence on Ery-Cd among never-smoking men: median Ery-Cd among never-smoking snuff-using men ($n = 28$) was 0.24 vs. 0.26 μg/L in never-smoking men not using snuff ($n = 110$). There was only one never-smoking snuff-using woman.

Women had higher Ery-Cd than men and Ery-Cd was associated with age, with a peak at about 50 or 60 years of age (Tables 1–3). An individual's Ery-Cd appeared to peak at higher ages, but this was masked by a low proportion of smokers in the oldest group, where only 3% were smokers, compared to 14–28% in the other age groups. Analyses with never-smokers only showed that for men the highest median Ery-Cd was in the oldest age group (0.38 vs. 0.18–0.33 μg/L in the other age groups) and for women the highest median level was in the age group 55–64 years (0.59 vs. 0.27–0.52 μg/L).

Table 1
Median (range) cadmium (Cd), lead (Pb), and mercury (Hg) concentrations in erythrocytes 1990–1999, along with factors that may influence these concentrations

	Men			Women		
	1990	1994	1999	1990	1994	1999
Ery-Cd (μg/L)	0.46 (<0.09–15) $n = 99$	0.39 (<0.09–8.7) $n = 99$	0.31 (<0.09–3.7) $n = 100$	0.58 (0.15–8.7) $n = 99$	0.58 (<0.09–7.2) $n = 100$	0.54 (<0.09–5.3) $n = 100$
Ery-Pb (μg/L)	86 (22–270) $n = 99$	62 (14–380) $n = 100$	49 (21–450) $n = 100$	54 (13–190) $n = 99$	46 (19–120) $n = 100$	33 (11–750) $n = 100$
Ery-Hg (μg/L)	3.8 (0.71–18) $n = 100$	2.8 (<0.20–38) $n = 100$	2.1 (0.23–41) $n = 100$	3.6 (<0.20–60) $n = 99$	2.6 (0.64–11) $n = 100$	2.2 (0.21–7.3) $n = 100$
Smoking (%)						
Never	46	52	51	59	49	50
Ex	27	35	36	19	28	24
Current	27	13	13	22	23	26
Cigarettes per day In daily smokers[a]	17 (4–40) $n = 27$	15 (5–20) $n = 12$	12 (2–35) $n = 13$	12 (2–20) $n = 22$	11 (3–25) $n = 23$	10 (5–25) $n = 26$
Alcohol intake (times/week)[a]	0.74 (0–3.0) $n = 99$	0.79 (0–5.5) $n = 99$	1.2 (0–12) $n = 88$	0.38 (0–2.0) $n = 99$	0.44 (0–7.5) $n = 98$	0.64 (0–3.6) $n = 93$
Fish intake (times/week)[a]	1.3 (0–3.5) $n = 100$	0.89 (0.05–3.0) $n = 99$	0.95 (0.05–6.0) $n = 91$	1.2 (0–5.0) $n = 99$	0.92 (0.05–5.0) $n = 100$	1.1 (0–10) $n = 93$
S-ferritin (mmol/L)[b]	126 (4.2–830) $n = 98$	NA	140 (11–980) $n = 99$	44 (1.6–240) $n = 97$	NA	50 (4.9–380) $n = 100$

Note: n, number of subjects; NA, not analyzed.
[a]Mean.
[b]Median.

Table 2
Median cadmium (Cd), lead (Pb), and mercury (Hg) concentrations (μg/L) in erythrocytes grouped according to sex, age, lifestyle factors, and concentrations of ferritin in serum

	n		Ery-Cd		Ery-Pb		Ery-Hg	
	Men	Women	Men	Women	Men	Women	Men	Women
All	300	299	0.39	0.56	63	44	2.9	2.8
Age								
25–34	64	69	0.22	0.34	58	38	2.1	2.3
35–44	78	73	0.46	0.45	62	46	2.6	3.0
45–54	75	72	0.43	0.87	71	46	3.5	2.9
55–64	51	58	0.56	0.63	68	52	3.8	2.9
65–74	32	27	0.42	0.56	52	38	3.7	4.0
Smoking								
Never			0.25	0.43	57	44	2.5	2.8
Ex			0.47	0.49	67	37	3.6	2.6
Current			2.3	2.5	75	51	2.7	3.0
Alcohol intake								
<median			0.34	0.53	55	40	2.4	2.7
⩾median			0.44	0.58	73	49	3.2	3.0
Fish intake								
<median			0.30	0.58	57	40	2.0	2.5
⩾median			0.47	0.55	68	46	3.6	3.1
S-ferritin								
<median			0.48	0.56	62	42	3.1	2.8
⩾median			0.32	0.55	63	45	3.0	3.0

Table 3
Associations between cadmium (Cd), lead (Pb), and mercury (Hg) concentrations in erythrocytes and age and potential determinants

	Screening year[a]	Sex[a]	Age	Smoking[a]	Cigarettes per day[b]	Alcohol intake	Fish intake	Ery-Cd	Ery-Pb
Smoking	NS	NS	NS	X					
Cigarettes per day[b]	$\tau = -0.24$ $P = 0.001$ $n = 123$	$\tau = -0.25$ $P = 0.001$ $n = 123$	NS	X	X				
Alcohol intake	$\tau = 0.068$ $P = 0.043$ $n = 576$	$\tau = -0.23$ $P<0.001$ $n = 576$	$r_s = -0.17$ $P<0.001$ $n = 576$	$\tau = 0.14$ $P<0.001$ $n = 576$	$r_s = 0.19$ $P = 0.040$ $n = 117$	X			
Fish intake	$\tau = -0.15$ $P<0.001$ $n = 582$	NS	$r_s = 0.25$ $P<0.001$ $n = 582$	NS	NS	NS	X		
Ery-Cd	$\tau = -0.089$ $P = 0.005$ $n = 597$	$\tau = 0.15$ $P<0.001$ $n = 597$	$r_s = 0.25$ $P<0.001$ $n = 597$	$\tau = 0.50$ $P<0.001$ $n = 597$	$r_s = 0.45$ $P<0.001$ $n = 123$	NS	$r_s = 0.11$ $P = 0.007$ $n = 580$	X	
Ery-Pb	$\tau = -0.30$ $P<0.001$ $n = 598$	$\tau = -0.29$ $P<0.001$ $n = 598$	NS	$\tau = 0.12$ $P<0.001$ $n = 598$	$r_s = 0.31$ $P = 0.001$ $n = 123$	$r_s = 0.32$ $P<0.001$ $n = 575$	$r_s = 0.11$ $P = 0.006$ $n = 581$	$r_s = 0.15$ $P<0.001$ $n = 597$	X
Ery-Hg	$\tau = -0.27$ $P<0.001$ $n = 599$	NS	$r_s = 0.24$ $P<0.001$ $n = 599$	NS	NS	$r_s = 0.12$ $P = 0.004$ $n = 576$	$r_s = 0.39$ $P<0.001$ $n = 582$	NS	$r_s = 0.26$ $P<0.001$ $n = 598$

Note: *n*, number of subjects; NS, not statistically significant.
[a]Bivariate analyses by Kendall's tau (τ), all other by Spearman's rho (r_s).
[b]Daily smokers only.

In the whole data set, decreasing S-ferritin was associated with a significant rise of Ery-Cd. When men and women were analyzed separately, this correlation was statistically significant only in men ($r_S = -0.18$, $P = 0.014$, $n = 196$ and $r_S = -0.09$, $P = 0.216$, $n = 197$, respectively). However, there was an association for nonsmoking women

Table 4
Time trends given in percent annual change (%/yr) for cadmium (Cd), lead (Pb), and mercury (Hg) concentrations in erythrocytes in 1990–1999 in relation to gender and smoking habits

	Change							
	All		Never-smokers		Ex-smokers		Current	
	%/yr	CI	%/yr	CI	%/yr	CI	%/yr	CI
Ery-Cd[a]								
Men	−6.4	−3.3; −9.4	—	NS	—	NS	−8.7	−4.2; −12
Women	—	NS	—	NS	—	NS	—	NS
All	−4.1	−1.9; −6.2	NA	—	NA	—	NA	—
Ery-Pb[b]								
Men	−6.4	−4.8; −8.0	−7.1	−4.7; −9.4	−5.8	−3.1; −8.4	—	NS
Women	−5.8	−4.5; −7.0	−6.3	−4.4; −8.1	−5.2	−2.5; −8.0	−5.1	−2.6; −7.5
All	−6.3	−5.2; −7.3	NA	—	NA	—	NA	—
Ery-Hg[c]								
Men	−5.1	−3.1; −7.0	NA	—	NA	—	NA	—
Women	−6.1	−4.3; −7.8	NA	—	NA	—	NA	—
All	−5.8	−4.4; −7.0	NA	—	NA	—	NA	—

Note: CI, 95% confidence interval; NA, not analyzed; NS, not statistically significant (95% CI including 1.0).
[a]Adjusted for age.
[b]Adjusted for age and alcohol intake.
[c]Adjusted for age and fish intake.

younger than 55 years ($r_S = -0.46$, $P \leqslant 0.0001$, $n = 68$). An unexpected positive significant correlation appeared with fish intake (Table 3).

In the multivariate analyses, there were significant decreases with time in the combined group of all men and in male smokers, while the levels in women did not decrease significantly in any category (though there was a nonsignificant decrease in smokers with 3.6% per year, CI = −7.4;0, $P = 0.053$). The decrease in number of cigarettes per day among daily smokers explained part of the decreasing time trend for Ery-Cd; when number of cigarettes smoked per day was included in the multivariate analysis for Ery-Cd, the annual decrease in male smokers was 6.7% as compared with 8.7% when not included.

3.3. Lead

Ery-Pb decreased over time in both men and women (Table 1). Men had higher concentrations than women (Tables 1 and 2). There was a tendency toward an increase with age (Table 2), although this was not significant (Table 3). Smokers had higher Ery-Pb levels than ex-smokers and never-smokers (Table 2), and there was a significant correlation between Ery-Pb and number of cigarettes smoked per day in daily smokers (Table 3). Intake of alcohol and fish correlated with Ery-Pb. In the multivariate model, Ery-Pb decreased by 6.3% per year (Table 4).

3.4. Mercury

Ery-Hg decreased in both men and women over the time period (Table 1). There were no differences by sex or smoking, but Ery-Hg rose with age (Tables 2 and 3). There were positive correlations with fish intake and intake of alcohol. In the multivariate approach, Ery-Hg decreased by 5.8% per year (Table 4).

3.5. Sensitivity analysis

Since the age group of 65–74 years was included only in 1994 and 1999, we investigated the effect of this age group on the multivariate analyses. Exclusion of this age group changed the results of Table 4 only marginally: estimated annual decline did not change more than 0.8%. All statistical significances and nonsignificances remained unchanged.

4. Discussion

The main findings were that Ery-Pb and Ery-Hg decreased by 5–6% per year in the general population of northern Sweden, whereas for Ery-Cd, there was a decrease in smoking men only.

4.1. Methodological aspects

In the health surveys, which were the basis for the samples, the participation rate was 77% (Stegmayr et al., 2003). Hence, the results may be generalized to the adult population of the area.

We used samples from the MONICA Project, stored in a biobank, which had been taken into tubes without guarantee of metal sterility. However, if the samples had been contaminated, this would most likely have caused a deviation toward the null hypothesis and true associations would have been obscured. We had no such indications.

Later checks of the batches of tubes have indicated no significant contamination. Further support for the data reliability is given by the strict quality control and the fact that there was no indication of drying of samples during storage.

The age distribution differed somewhat between the different years of sampling. The reasons were (i) subjects aged 65–74 years were not invited to the 1990 study and (ii) the procedure used in selecting samples for this study stratified for attained age at sampling, while in the statistical analyses we used age as calculated only from year of birth and not exact date. The second deviation should not affect the overall conclusion on time trends, and neither should the first, since the analyses for time trends were adjusted for age.

4.2. Cadmium

Since Cd in blood is present almost entirely in the cells, Ery-Cd is as good a biomarker as blood Cd. The present Ery-Cd levels were in accordance with findings of blood Cd in the same area during the same period (Jakobsson Lagerkvist et al., 1993) and with concentrations in other parts of Sweden and effects of the determinants gender, age, and smoking (Bárány et al., 2002a–c, 2003; Nordberg et al., 2000a; Olsson et al., 2002; Skerfving et al., 1999). The levels in Swedes are low in an international perspective (Skerfving et al., 1999).

Previous data on time trends of Cd in humans are sparse. The concentrations of Cd in the present study were much lower than in 1981 in the same area (Elinder et al., 1982). In Belgium, blood Cd levels declined during the 1980s (Decoffre et al., 1992), probably because of a decrease in environmental pollution. It has been suggested that the concentration in kidneys of Swedes has decreased over time (Friis et al., 1998), although this has been questioned (Vahter et al., 1998).

Cigarette smoking is a major source of Cd (Skerfving et al., 1999). The number of smokers decreased in the present population during the time period studied, especially among men (Stegmayr et al., 2005) and this partly explains the overall Ery-Cd decrease among men. However, there was also a decrease in Ery-Cd among current smokers. That decrease can partly be explained by a decrease in the number of cigarettes per day. The reduction in number of cigarettes per day cannot be the full explanation of decreasing Ery-Cd among current smokers, since the decrease in Ery-Cd remained even after adjusting for number of cigarettes per day. Moreover, the magnitude of the decrease in number of cigarettes per day (3.9% annual decrease) was too small to explain the decrease in Ery-Cd in smoking men (8.7% annual decrease). Therefore, we believe that the Cd content in cigarettes in Sweden has decreased over time. We have not found any data on time trends for Cd in Swedish cigarettes but the Cd concentration in snuff has decreased (Swedish Match, unpublished data). It may be argued that Cd in tobacco would decrease only if the concentrations in the general environment decrease. However, different changes in Cd levels in fertilizers and in selection of which tobacco ends up in the cigarettes could also influence the Cd levels in cigarettes. The reduction of smoking has not been as successful in women as in men (Stegmayr et al., 2005), which may, at least in part, explain the smaller and not significant decrease in Ery-Cd.

Except for Cd in tobacco, it seems that Cd exposure has not changed significantly. This is not surprising when the available information is scrutinized. There is a local source of Cd emission from a primary smelter. Its emissions have decreased over time but the influence of that is limited, since the main part of the local deposition comes from airborne emissions transported long distances (Elinder et al., 1982; Jakobsson Lagerkvist et al., 1992). The deposition of Cd in Sweden increased during most of the 20th century (Johansson et al., 2001) but may have decreased to some extent in the 1990s (Gusev, 2004; IVL, 2004). The use of Cd-containing phosphate fertilizers in agriculture has caused an increase of Cd in soil, although during the past decade the Cd content in fertilizers has again decreased (Johansson et al., 2001). Furthermore, the acidification of water and soil by acid precipitation, which is a major problem in many parts of Sweden, mobilizes heavy metals (Bensryd et al., 1994). All these factors have affected the Cd content in vegetables and animal foods in a complicated pattern. The Cd content in the Swedish diet and in Swedish herring and pig kidney has increased over time (Skerfving et al., 1999). The same was true for wheat during the first part of the 1900s, although during the past decade, there are indications of a decrease (Jorhem et al., 2001). Taken together, we believe that the observed decrease in Ery-Cd is caused by decreased Cd exposure from cigarettes, probably for a longer time than just the past decade. We do not believe that the decrease in Ery-Cd indicates a significant reduction in environmental exposure to Cd in Sweden. Note also that the rate of a change in Ery-Cd may be different from that of the Cd exposure, since the body burden of Cd has a very slow decay (Skerfving et al., 1999); this will attenuate the effects of any change of the external exposure.

We had not expected any correlation between Ery-Cd and fish intake. In the studied population, a fish meal generally replaces a meat meal. In Sweden, fish Cd levels are in the same order as Cd levels in meat (SCOOP 3.2.11., 2004). In view of this we find it hard to explain the association between Ery-Cd and fish intake. It may be a result of chance or of other explanations, e.g., confounding related to life-style.

With regard to S-ferritin, there was a significant negative correlation with Ery-Cd in women before menopause, which is in accordance with previous findings (Bárány et al., 2005; Olsson et al., 2002; Skerfving et al., 1999) and indicates an enhanced Cd absorption parallel to iron. However, postmenopause there was no such association, probably because the iron status then improves with a

degree that varies between individuals. Among men a weak association was found. This is not in conflict with the lack of association among postmenopausal women; it is reasonable to assume that a man's current iron status reflects iron status previously in life better than the current iron status of a postmenopausal woman. We do not believe that changes in iron status over time significantly affected the time trends for Ery-Cd.

4.3. Lead

Pb in blood is present almost entirely in the cells. The present Ery-Pb levels were in accordance with other data from the same area (Jakobsson Lagerkvist et al., 1993) and with known effects of the determinants gender, age, alcohol intake, and smoking (Bárány et al., 2002a–c; Bensryd et al., 1994; Nordberg et al., 2000b; Skerfving et al., 1999). However, we have no good explanation for the positive correlation between Pb and fish intake.

The rapid decrease in Ery-Pb over time was very consistent; it occurred in both men and women and in both smokers and nonsmokers. Since the reported alcohol intake increased over time in the present population (in accordance with the general trend in Sweden), the decrease of Ery-Pb cannot be explained by changes in intake of alcohol, which was also seen in the multivariate analysis. The time pattern of blood Pb is consistent with reports from other areas in Sweden (Bárány et al., 2002b; Strömberg et al., 2003) and elsewhere (Skerfving et al., 1999). Furthermore, the present concentrations are (as would be expected) much lower than in samples taken in 1981 in the same area (Elinder et al., 1982).

The decrease is easily explained. The deposition of Pb in Sweden has decreased over the past decade (Gusev, 2004; IVL, 2004; Johansson et al., 2001), mainly due to the elimination of Pb as an additive in automobile gasoline, which essentially ended in 1994. However, our data show that there was also a decrease of Ery-Pb after that year, which is probably due to a widespread contamination of the environment, including crop fields. Accordingly, Pb in Swedish wheat bran has also continued to decrease (Jorhem et al., 2001). Some of the present reduction of Ery-Pb may be due to a change from soldered to welded food cans. Hence, there are strong reasons to believe that the intake through food, which is the major source in Sweden, has decreased. In other parts of the world, exposures through paint and drinking water are a problem (Skerfving et al., 1999); however, such exposures have always been very low in Sweden. The actual time trend of Pb exposure may have a pattern somewhat different from that of Ery-Pb, since the skeletal Pb burden, which reflects earlier uptake, has a slow decay and will affect Ery-Pb.

4.4. Mercury

The Ery-Hg levels were in accordance with data from the present area (Hallgren et al., 2001) and with other parts of Sweden (Bárány et al., 2002a–c, 2003; Johansson et al., 2001; Skerfving et al., 1999). Ery-Hg decreased rapidly over time. This is in accordance with limited and scattered observations (Skerfving et al., 1999). A main source of Hg in Sweden is fish. Hence, we observed a fairly close association between Ery-Hg and fish intake, in accordance with previous findings (Bárány et al., 2003; Bensryd et al., 1994; Bergdahl et al., 1998; Hallgren et al., 2001; Skerfving et al., 1999). The increase of Ery-Hg with rising age is probably because young subjects have a lower fish intake than older subjects (Swedish means: women, 27 g/day at age 25–34 years vs. 48 g/day at >65 years; men, 25 g/day vs. 43 g/day, respectively; Becker and Pearson, 2002).

To some extent, the present decay of Ery-Hg may be explained by lower fish intake. Hence, there was a decrease in fish intake in men. However, the decrease was also present when adjustment was made for fish intake, and fish intake did not change significantly in women. The explanation may thus be the lower concentrations of Hg in locally caught fish (Fellbrink, 2002) due to a decrease of pollution (Johansson et al., 2001; Gusev, 2004; IVL, 2004) or a change to other fish species with lower Hg content.

Another explanation to consider is a decrease in inorganic Hg. Ery-Hg is mainly present as MeHg; its content in plasma is low. In contrast, inorganic Hg is mainly present in plasma, although there is also some in the erythrocytes. Twenty-three of the present samples were analyzed for total and inorganic Hg (median inorganic Hg 0.5, range <det.lim–7.5 μg/L; H.M. Custodio et al., unpublished). The inorganic Hg made up only 8% (range 2–57%) of the total Hg.

A major source of inorganic Hg is dental amalgam fillings (Åkesson et al., 1991; Bergdahl et al., 1998; Skerfving et al., 1999). The use of amalgam has decreased dramatically in Sweden (National Swedish Board of Social Welfare, 2002; Sundberg et al., 2000), including the present region (Wännman et al., 2004). However, considering its low fraction in the erythrocyte samples, the change in odontological practice has probably had less impact than MeHg in fish. In the long run, of course, the decreased use of Hg for dental fillings should contribute to a decrease in environmental pollution of Hg.

There was a positive correlation between Ery-Hg and alcohol intake. It is known that ethanol affects the metabolism of Hg (Clarkson, 1997). However, the expected effect should be in the opposite direction and thus we have no explanation for this observation.

5. Concluding remarks

There was a remarkable decrease of Pb and Hg levels, partly due to changes of life-style, but apparently the main reason is decreased intake through food. Thus, for Pb and maybe also Hg the actions against pollution during recent decades have caused a rapid decrease of exposure. Still, the highest concentrations were in the range suspected to cause toxic effects (Skerfving et al., 1999). Also, slight toxic

effects of Cd on the kidneys (Åkesson et al., in press-a; Järup et al., 2000; Olsson et al., 2002) and bone (Åkesson et al., in press-b; Alfvén et al., 2000) have been recorded in the Swedish general populations. Hence, reduction of pollution by all three elements is warranted, but efforts against Cd pollution seem particularly urgent.

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