Int Arch Occup Environ Health (1993) 65:57–63

International Archives of
Occupational and Environmental Health

Cadmium, zinc, copper, and metallothionein levels in the kidney and liver of inhabitants of Upper Silesia (Poland)*

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Received February 16, 1993 / Accepted April 4, 1993

Summary. The levels of Cd, Zn, Cu and metallothionein (MT) were determined in renal cortex and liver of 75 subjects deceased in the period 1986–1989 in the area of Upper Silesia (Katowice). The mean age of the population studied was 53.6 ± 14.6 years. The determined levels (mean ± SD) were: 43.1 ± 23.5 µg Cd/g; 52.5 ± 17.4 µg Zn/g; 2.2 ± 0.7 µg Cu/g; 0.80 ± 0.36 µmol Hg/g in renal cortex and 3.5 ± 2.5 µg Cd/g; 82.8 ± 34.3 µg Zn/g; 4.5 ± 2.6 µg Cu/g; 0.69 ± 0.44 µmol Hg/g in the liver. The level of Cd in renal cortex was 40% higher in smokers compared to nonsmokers and was independent of the gender. Whole-body retention of Cd was 34.1 ± 18.5 mg; smoking elevated the value from 27.1 to 38.2 mg. Compared with a similar study made in central Poland (Łódź), a significant difference was found only regarding the level of Zn and MT in the liver, pointing to the possibility that exposure to this element in the region of Upper Silesia may be higher.

Key words: Cadmium – Zinc – Kidney – Liver

Introduction

Cadmium is a well-known toxic metal occurring in the environment from natural and anthropogenic sources. It accumulates in the human organism during practically the whole life span, the kidneys and the liver being the main sites of accumulation. A 20-fold increase in the anthropogenic cadmium emission during the twentieth century has caused a five-fold increase in whole-body retention in humans [13].

Long-term low-level exposure to cadmium leads to tubular renal dysfunction [42]. The dysfunction is irreversible [18] and may be considered the first symptom of further renal, damage [45]; it is predictive of an exacerbation of the age-related decline in the gomerular filtration rate.

The best method for evaluation of cadmium exposure is biological monitoring, i.e., determining cadmium levels in the renal cortex (CdK), urine (CdU), and blood (CdB). However, critical values for the general population are still uncertain. The generally accepted critical concentrations of 200 µg/g and 10 µg/g creatinine for CdK and CdU, respectively, concern professional exposure [19]. International monitoring studies of cadmium levels in the blood, urine, and renal cortex of humans initiated in 1978 by UNEP/WHO have shown [55] great geographical differences in the levels of cadmium in humans (e.g., for renal cortex: Japan 61.1 mg/kg; Sweden 18.3 mg/kg) caused by the differences in daily intake. They have also proved the need for quality control along with monitoring studies.

Poland is considered one of the most polluted countries in Europe. Ecologically endangered regions constitute about 10% of the country's surface area and are inhabited by one-third of the population [40]. Upper Silesia, the most industrialized region of the country, is also the most polluted. It constitutes 1% of the country's surface area but is inhabited by 3 million people, almost 8% of the whole population [20]. It is in Upper Silesia that cadmium production was started in 1829, and in 1910 10% of the world's cadmium still came from Upper Silesia [11]. The following information characterizes the recent situation in this region.

Katowice, with a population of 366000, is the capital of Upper Silesia, and a centre for heavy industry in Poland. The mean monthly cadmium concentration in the air of the Katowice area (GOP) in 1982 was 17.0–110.0 ng Cd/m^3 [16]. Jaworowski et al. [27] give a mean daily concentration in the centre of Chorzow (1981–1982) of 28.9 ng/m^3 [1]. The fallout of cadmium was in the range of

*This work has been supported by the grant CPBR 11.12(C-56/86) from the Institute of Rural Medicine, Lublin, Poland
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[1] The maximum allowed concentration (yearly mean) according to Polish regulations [43] is 100 ng/m^3, and the corresponding value recommended by the WHO [56] is 10–20 ng/m^3

2.2 kg/km^2 per month in Gliwice to 7.2 kg/km^2 per month in Katowice [33]. The cadmium concentration in the soil in GOP varies from 1.2 to 51.7 mg/kg [21][2]. The concentration of cadmium in drinking water in GOP is 0.58–4.51 µg/dm^3 [16][3].

Cadmium exposure of humans in Poland has been the subject of a number of investigations [1, 2, 5–7, 25–27, 30, 41, 47, 48]. The aim of this study was to obtain data on exposure to cadmium of the general population in Upper Silesia and to compare them with those for Central Poland.

Materials and methods

Subjects. The investigations were carried out on people who died in the years 1985–1989 as inhabitants of Katowice or its close surroundings. Autopsies were performed at the Department of Pathology, Silesian Medical University, Katowice, on average 32 ± 17.5 h after death. Renal cortex and liver samples were collected from persons not exposed to cadmium professionally who had no history of liver or kidney diseases and in whom no macroscopic lesions were found in these organs at autopsy. The information about the patient (taken from the case history) was included in a questionnaire concerning sex, age, body weight, kidney and liver weights, profession, place of residence, and smoking history. Unfortunately, full information was not always available.

The samples were obtained from 75 persons (42 women and 33 men) with a mean age of 53.6 years. Samples (ca. 20 g) of tissues were collected from the lower left pole of the kidney after separating the cortex from the medulla, and from the upper part of the left lobe of the liver. The samples were placed in acid-washed (10% HNO_3, 48 h) polyethylene containers, which were then closed tightly and stored until analysis at −20°C.

Measurements. Metals (cadmium, zinc, and copper) were measured by flame AAS (Pye-Unicam SP-192) with deuterium background correction after tissue digestion with a mixture of acids (HNO_3, H_2SO_4, $HClO_4$, Merck, Suprapure) as described elsewhere [4]. Three samples were always prepared from each tissue. The detection limits were: 0.02 µg Cd/ml, 0.01 µg Zn/ml, and 0.04 µg Cu/ml. The relative standard deviation for ten determinations at 0.2 µg/ml was 5%, 2%, and 5% for cadmium, zinc, and copper respectively.

Metallothionein was determined in full homogenates using the ^{203}Hg method [58], giving a relative standard deviation of 5%. Levels of metallothionein were expressed in µmol Hg/g wet tissue to enable easy comparison with metallothionein levels determined by different methods.

Analytical quality assurance. Analyses of metals were performed under strictly defined conditions alongside analyses of internal laboratory control samples based on a CL-1 standard (lyophilized cabbage leaves) supplied by AGH (Poland) with certified metal levels. We also participated in the interlaboratory analytical quality control program conducted by the Institute of Veterinary Science (Poland). In three received samples our results were within 4% of the correct values. In addition, three samples of the renal cortex were analyzed by us (AAS method) and then using neutron activation analysis in the Institute of Chemistry and Nuclear Techniques in Warsaw; the maximum differences between the methods were 4%, 17%, and 20% for cadmium, zinc, and copper respectively.

[2] The maximum allowed level in Poland is 3 mg Cd/kg soil [34]
[3] The maximum allowed level in drinking water in Poland is 5 µg/dm^3 [17]

Statistical analysis. All the determined values revealed log-normal distributions. In Table 1 all the parameters for each distribution are given along with the arithmetic mean and standard deviation for easier comparison with the results of other authors. Student's *t*-test was used to evaluate statistical differences between groups. The whole-body retention of cadmium was calculated assuming that the kidney and liver contain half of the total cadmium content of the organism and that the ratio of cadmium concentration in the cortex to that in whole kidney is 1.25 [51].

Results and discussion

Cadmium

Cadmium levels in the renal cortex (CdK) and the liver (CdL) for the whole investigated population are shown in Tables 1–3. The dependence of CdK on age is shown in Fig. 1. We observed, in agreement with other data [48], a great range of concentrations (7.4–107.5 µg/g) with upper values in individual age groups increasing until about 50 years of age and then decreasing, in accordance with the well-known age dependence [19]. The upward trend with age is not evident, however, from the mean values (Table 3).

The CdK levels in Upper Silesia for nonprofessionally exposed persons (GM 36.1 µg/g) are the highest in Europe [22, 46, 53–55] (Fig. 2). Unexpectedly, however, these levels do not differ from the values found by us in Central Poland (GM 35.5 µg/g) [7]. A higher concentration can only be found in Japan [23, 55].

Smoking greatly increases the cadmium level in the organism [55]. In smokers CdK levels (47.7 µg/g) were ca. 40% higher than in nonsmokers (34.7 µg/g) (Tables 1, 2). The results are in agreement with literature data [22, 46, 54, 55]. The high mean CdK level (43.1 ± 23.5 µg/g), as well as the value for the 90th percentile (73.6 µg/g), is the result of smoking practised by the majority of the studied population. The tobacco produced in Poland contains high amounts of cadmium (1.3–3.2 µg Cd/cigarette) [8, 57] that exceed the cadmium levels in imported cigarettes (0.5–1.0 µg/cigarette) [57]. No effect of sex on CdK has been found (Table 2).

The mean CdK level in Upper Silesia is lower than the generally accepted "critical concentration" of 200 µg/g [19]. It is, however, very close to the value 50 µg/g, at which "renal risk" was observed in 10% of general population in Belgium. Also Lindqvist et al. claim [32] that the critical value for the general population should be lower than the hitherto accepted value and they suggest 30 µg/g. One should also bear in mind the groups at particular risk, e.g., diabetes mellitus patients and people with calcium or iron deficiency, for whom the critical value may be even lower.

The levels of cadmium in the renal cortex should reflect the daily intake of cadmium with food. The daily cadmium intake with food averages 27.5 µg in Poland, and values as high as 77.8 µg have been reported [3]. Data for nonsmokers are of special value for the evaluation of the dependence between cadmium intake in food and its tissue levels. High CdK levels close to 30 µg/g in nonsmokers correspond to daily intakes of 15 µg (Belgium [9]) or nearly 30 µg (Poland [3]). The discrepancy

Table 1. Statistical characterization of the investigated population and determined monitoring parameters

	Age	Renal cortex			Liver		
		Cd (μg/g)	Zn (μg/g)	MT (μmol Hg/g)	Cd (μg/g)	Zn (μg/g)	MT (μmol Hg/g)
Total							
No.	75	75	75	72	75	75	71
$\bar{X}$	53.6	43.1	52.5	0.80	3.5	82.8	0.69
SD	14.6	23.5	17.4	0.36	2.5	34.3	0.44
GM	51.5	36.1	49.4	0.72	2.7	76.2	0.58
GSD	1.3	1.9	1.4	1.61	2.2	1.5	1.83
Median	49.7	32.8	49.1	0.66	2.3	72.9	0.53
90%	72.5	73.6	75.1	1.27	6.8	127.3	1.26
Smokers							
No.	46	46	46	44	46	46	44
$\bar{X}$	50.3	47.7*	52.9	0.93**	3.7	78.5	0.68
SD	13.1	23.4	18.4	0.37	2.6	32.0	0.37
GM	48.6	41.0	49.4	0.85	2.9	72.1	0.58
GSD	1.3	1.8	1.5	1.57	2.1	1.5	1.8
Median	46.9	39.6	48.8	0.78	2.7	68.6	0.53
90%	67.3	78.2	76.8	1.42	7.2	120.1	1.16
Nonsmokers							
No.	27	27	27	26	27	27	25
$\bar{X}$	59.7	34.7*	50.8	0.58**	2.9	90.5	0.72
SD	15.6	22.4	15.9	0.22	2.0	38.4	0.56
GM	57.1	28.5	48.3	0.54	2.3	83.7	0.58
GSD	1.4	1.9	1.4	1.51	2.2	1.5	1.95
Median	53.9	25.4	45.6	0.50	2.0	77.9	0.53
90%	79.9	63.8	71.4	0.87	5.6	140.3	1.45

* $P<0.05$; ** $P<0.001$
$\bar{X}$, Mean; SD, standard deviation; GM, geometric mean; GSD, geometric standard deviation

between these figures probably results from differences in the average age of the populations under study.

CdL levels in the investigated population (0.30–11.9 μg/g) conform with our preliminary results [6] and other data for the region [48]. They are close to the levels found for Central Poland [7] and polluted areas in Belgium [31], Germany [54], and Northeastern Hungary [53]. Higher CdL levels were only found in Japan (10 and 60 μg/g for nonpolluted and polluted areas, respectively) [37]. As for CdK, the levels of CdL do not depend on sex. They are also independent of age, which points to differences in turnover rates in the liver and kidneys. Unexpectedly, the values of CdL for smokers and nonsmokers do not differ significantly. This may reflect differences caused by routes of entry and the subsequent disposition of the metal. Despite the above discrepancies, a correlation was found between CdK and CdL (Table 4). The monitoring value of CdL could become evident in the case of high exposure, when kidney levels decrease due to kidney damage [37]. In the case of low and moderate environmental exposure, as in our study, the monitoring value of CdL is considered small.

The whole-body cadmium retention in the inhabitants of Upper Silesia is 34.1 ± 18.5 mg. Smoking increases retention by 40% (from 27.1 ± 38.2 mg). Whole-body retention of cadmium in inhabitants of Upper Silesia is practically the same as in Central Poland [7], but much higher than in Southern Bavaria (21.9 mg) [14].

Zinc

Zinc levels in the cortex (ZnK) show a high scatter of individual values (7.4–107.5 μg/g) in agreement with other data [48]. The mean ZnK level 52.5 μg/g (Table 1) is similar to that in Central Poland [7] and slightly higher than that in Canada 40.1 μg/g [12] and India 36.4 μg/g [39]. No effect of smoking or sex on ZnK levels was found.

Similar changes in CdK and ZnK with age (Table 3) result from the correlation between these values (Table 4). A correlation between ZnK and CuK was also observed (Table 4).

The observed wide scatter of individual ZnL values (29.0–221.6 μg/g) confirms previous data [48] for this region. The mean zinc level in the liver (82.8 ± 34.3 μg/g) is markedly higher than in Central Poland ($P<0.02$) [7], Canada [12], and Japan [38, 49], and, like ZnK, does not depend on sex. In smokers, there is a downward tendency of ZnL, but this appeared nonsignificant. The high ZnL levels may reflect an especially high environ-

Table 2. Cadmium levels (µg/g) in renal cortex (CdK) and liver (CdL) in relation to smoking and gender (arithmetic mean ± SD)

	Total	Females	Males
Total			
No.	75	42	33
Age	53.6 ± 14.6	56.1 ± 15.6	50.3 ± 12.7
CdK	43.1 ± 23.5	41.4 ± 23.4	45.2 ± 23.8
CdL	3.5 ± 2.5	3.5 ± 2.3	3.5 ± 2.9
Smokers			
No.	46	17	29
Age	50.3 ± 13.1	51.5 ± 14.4	49.5 ± 12.5
CdK	47.7 ± 23.4*	49.8 ± 23.9	46.5 ± 23.4
CdL	3.7 ± 2.6	4.3 ± 2.4	3.4 ± 2.8
Nonsmokers			
No.	27	24	3
Age	59.7 ± 15.6	59.9 ± 15.8	58.0 ± 16.6
CdK	34.7 ± 22.4*	35.5 ± 22.2	27.7 ± 27.9
CdL	2.9 ± 2.0	3.0 ± 2.1	2.2 ± 1.7

* $P < 0.05$

Table 3. Cadmium, zinc, and metallothionein concentration[a] in renal cortex and liver in relation to age and smoking

	20–40 yr	41–60 yr	> 60 yr
Total			
No.	12	36	26
Age	34.7 ± 4.4	49.7 ± 6.6	69.2 ± 7.3
CdK	47.2 ± 19.1	47.8 ± 23.7	36.0 ± 23.3
ZnK	52.6 ± 22.1	54.4 ± 15.9	50.7 ± 17.1
MTK	0.83 ± 0.28	0.93 ± 0.37	0.64 ± 0.31
CdL	3.4 ± 1.6	3.6 ± 2.8	3.4 ± 2.6
ZnL	65.4 ± 28.0	76.4 ± 25.0	100.4 ± 41.4
MTL	0.57 ± 0.39	0.62 ± 0.31	0.85 ± 0.57
Smokers			
No.	10	26	10
Age	34.1 ± 4.4	49.4 ± 6.7	68.5 ± 7.6
CdK	48.0 ± 19.7	51.9 ± 23.8	36.6 ± 24.3
ZnK	54.3 ± 24.1	53.3 ± 16.7	50.4 ± 18.4
MTK	0.83 ± 0.30	1.01 ± 0.37	0.81 ± 0.40
CdL	3.3 ± 1.6	3.9 ± 2.8	3.7 ± 3.3
ZnL	63.5 ± 30.5	74.7 ± 25.1	103.6 ± 38.1
MTL	0.57 ± 0.41	0.61 ± 0.29	0.94 ± 0.45
Nonsmokers			
No.	2	8	16
Age	–	51.5 ± 6.5	69.2 ± 7.3
CdK	–	35.6 ± 23.4	30.8 ± 13.9[b]
ZnK	–	55.3 ± 14.8	50.8 ± 16.8
MTK	–	0.70 ± 0.26	0.53 ± 0.17
CdL	–	2.3 ± 1.8	3.2 ± 2.2
ZnL	–	81.6 ± 29.1	98.4 ± 44.4
MTL	–	0.64 ± 0.43	0.80 ± 0.65

[a] Metals (Cd, Zn) are expressed as µg/g) wet weight (mean ± SD); metallothionein (MT) is expressed as µmol Hg/g wet weight (mean ± SD)
[b] One subject eliminated on the basis of statistical criteria

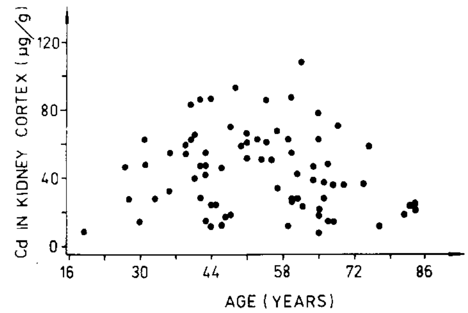

Fig. 1. Cadmium in kidney cortex in relation to age in deceased persons from Upper Silesia

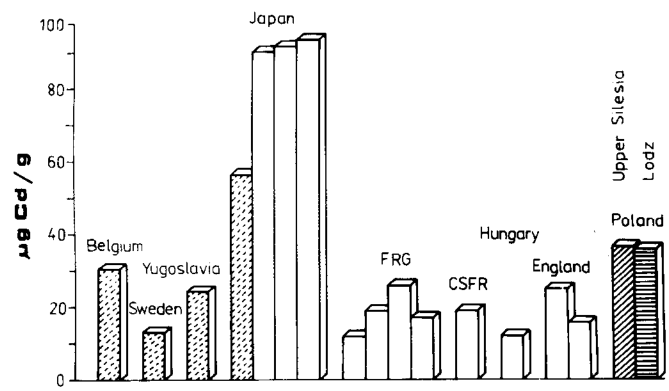

Fig. 2. Cadmium levels in renal cortex in humans from various countries: Belgium [55], Sweden [55], former Yugoslavia [55], Japan [55, 37, 28, 23], Germany [54, 50, 22], former Czechoslovakia [22], Hungary [53], England [35, 46], and Poland (Lodz) [7]

mental exposure to zinc in inhabitants of the Silesian region [16]. There appears to be a correlation between Zn levels in the renal cortex and in the liver (Table 4).

Metallothionein

It is known that cadmium in the human kidney is mainly bound to metallothionein (MT) [52], a protein induced by several heavy metals. The tissue level of MTK has been suggested as an index of exposure to these metals [12].

MTK levels in the inhabitants of Upper Silesia varied within the range 0.20–2.10 µmol Hg/g. The dependence of MTK on age, like that of CdK, reached its maximum at around 55 years of age, after which the level decreased (partially shown in Table 3), in agreement with literature data [12, 15]. As in Central Poland [7], the mean MTK level was 0.80 ± 0.36 µmol Hg/g and, like CdK, it was about three times higher than in Canada [12]. Smoking increases the MTK level by about 60% while sex has no effect on it. Kidney MT in humans is a cadmium- and zinc-binding protein, which is reflected in the observed correlations between MT and these metals (Table 4).

The difficulty of comparing MT levels given in various papers, discussed previously [5, 6] means that MTK levels are of limited monitoring value.

The mean MTL level was 0.69 µmol Hg/g and was 50% higher than the values for Central Poland [7]. We

Table 4. Correlation coefficients in renal cortex and liver

	No. of subjects	r	Regression equation
Renal cortex			
Zn-Cd	75	0.40*	Zn (μg/g) = 0.29 · Cd (μg/g) + 39.8
MT-Cd	72	0.53*	MT (μmol Hg/g) = 0.91 · Cd (μmol/g) + 0.45
MT-Zn	72	0.46*	MT (μmol Hg/g) = 0.63 · Zn (μmol/g) + 0.29
Cu-Zn	75	0.46*	Cu (μg/g) = 0.018 · Zn (μg/g) + 1.3
Liver			
MT-Zn	71	0.85*	MT (μmol Hg/g) = 0.72 · Zn (μmol/g) − 0.24
MT-age	71	0.34**	MT (μmol Hg/g) = 0.011 · years + 0.12
Zn-age	75	0.39*	Zn (μg/g) = 0.014 · years + 0.52
Kidney/liver			
CdL-CdK	75	0.51*	CdL (μg/g) = 0.055 · CdK (μg/g) + 1.1
ZnK-ZnL	75	0.33**	ZnL (μg/g) = 0.65 · ZnK (μg/g) + 48.7

* $P < 0.001$; ** $P < 0.005$

did not observe an increase in MTL with age, nor did we notice any effect of smoking and sex on it. Liver MT is a zinc-thionein [10, 24], which is reflected in the correlation between ZnL and MTL, while there is no correlation between CdL and MTL. However, a correlation is observed between MTK and MTL (Table 4).

Copper

Copper levels in the renal cortex and liver were 2.2 μg/g and 4.51 μg/g, respectively, and were close to the values for Central Poland (2.4 and 4.3 μg/g) [7]. These levels are not correlated with other parameters (sex, smoking).

Conclusions

Cadmium levles (CdK, CdL, retention) in inhabitants of Upper Silesia are the highest in Europe; this is true for the smoking and nonsmoking subgroups as well as the entire population. Unexpectedly, these values do not differ from those found previously in the inhabitants of Central Poland [7]. This is especially evident in nonsmokers. The parameter that is significantly different between the two investigated regions, especially in nonsmokers, is ZnL, which is suggestive of contamination of the Silesian region with zinc.

Although in Upper Silesia the average life span is a year shorter than elsewhere in Poland [44], it is claimed that this is due mainly to circulatory system diseases and neoplastic diseases without any connection with cadmium. The existing health status report [44] does not suggest an excessive frequency of kidney diseases, as has been reported among people living in a lead- and cadmium-polluted region of the United States [36]. Nevertheless, considering the high contamination of Upper Silesian soil, the problem of food supplied from local small gardens should be given attention, as was previously done in Kempen, Holland [29].

The lack of any significant difference between the level of cadmium in the inhabitants of the most polluted region of Poland (Upper Silesia) and the inhabitants of Central Poland suggests that similar levels may exist in the whole population. This hypothesis requires verification in further studies.

Acknowledgements. The authors wish to express their gratitude to Mrs. M. Skrzypińska-Gawrysiak, MSc, for intralaboratory quality control and to Mr. A. Debicki for his assistance in the determinations.

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