Cadmium in the Human Environment:
Toxicity and Carcinogenicity
Ed. G.F. Nordberg, R.F.M. Herber & L. Alessio
Lyon, International Agency for Research on Cancer

Factors influencing the cadmium body burden in a population study

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Summary. The cadmium body burden, as estimated from 24-h urinary cadmium (Cd-U), was determined in 1523 non-occupationally exposed subjects living in five areas of Belgium. It increased with age until 55–65 years in both sexes and thereafter decreased slightly. It was higher in smokers but was inversely associated with alcohol consumption and social class. In men only, it was also positively correlated with body mass index. After the menopause, women showed a significant increase in 24-h Cd-U independently of the other factors. In addition, the cadmium body burden was independently associated with place of residence in both sexes. Highest levels of Cd-U were found in subjects living in an area with soils heavily polluted by cadmium.

Résumé. La charge corporelle en cadmium, estimée à l'aide de la concentration du cadmium dans les urines de 24 heures, a été déterminée chez 1523 sujets, non exposés professionnellement, vivant dans cinq régions de Belgique. La charge corporelle en cadmium augmente avec l'âge jusqu'à 55–65 ans et ensuite diminue. Elle est plus élevée chez les fumeurs, mais est inversement associée à la consommation d'alcool et au niveau social. Chez les hommes, elle est corrélée avec l'indice de Quetelet tandis que chez les femmes, elle augmente après la ménopause, indépendamment de tout autre facteur. Enfin, l'accumulation de cadmium varie avec le lieu de résidence tant chez les hommes que chez les femmes: les concentrations les plus élevées de cadmium dans les urines de 24 heures ont été observées chez des sujets résidant dans une région où les sols sont fortement pollués par le cadmium.

Introduction

A large-scale epidemiological study (Cadmibel) was carried out in Belgium from 1985 to 1989 to assess whether environmental pollution by cadmium leads to an increased uptake of cadmium by the human body and possibly to health effects. The present paper deals with the factors influencing the internal dose of cadmium in non-occupationally exposed subjects investigated in the Cadmibel survey.

Methods

The design of this cross-sectional study has been described in detail elsewhere (Lauwerys *et al.*, 1990). A stratified random sample of 2327 subjects was identified in two urban (Liège and Charleroi) and two rural (Hechtel-Eksel and Noorderkempen) areas. Subjects residing in the Liège area were subdivided into those living near a large zinc and cadmium producing plant that was in operation until 1981 (Engis, 20 km south-west of Liège) and those residing in the centre of the city or in the suburbs (Liège). Charleroi is an industrial city with iron foundries but without important industrial sources of cadmium emissions. Two non-ferrous smelters are in operation in Noorderkempen. No local source of environmental pollution by cadmium has been identified in Hechtel-Eksel.

Each participant was visited at home and invited to collect a 24-h urine sample. A self-administered questionnaire inquired about their current and past occupations, social class, duration of residence, current and past smoking habits, alcohol consumption and possible exposure to heavy metals both at work and during leisure time. Women were also asked for information on menstrual status and contraceptive pill intake. Subjects were excluded from the present analysis when they reported that they had been exposed to heavy metals (cadmium, zinc, lead, and mercury) at work (n = 372), when 24-h urine samples were judged under- or overcollected by previously published criteria (Staessen *et al.*, 1988) (n = 33) or when not all relevant biological measurements or questionnaire data could be obtained (n = 399).

Serum was analysed among other things for zinc, ferritin and γ-glutamyltransferase activity and urine (24-h collection) for cadmium (Lauwerys *et al.*, 1990). Heavy metals were measured by electrothermal atomic absorption spectrometry with Zeeman background correction (Claeys, 1982). Stringent international quality-assurance schemes were established during the survey and strict criteria were applied to ensure the accuracy and consistency of the analytical results[1]. Cd-U is given in µg/24 h, where 1 µg cadmium is 8.9 nmol. It is also given in µg/g of creatinine, as is usual for urinary spot samples.

Significant determinants of Cd-U ($p < 0.05$) were identified by step-wise multiple regression analysis. They were selected from a set of independent variables including place of residence, age, age squared, body mass index, social classes (low, intermediate, high), smoking habits (never, past and current smokers), current and past quantity of tobacco smoked (g per day), alcohol consumption habits (never, past and current consumers), current and past alcohol intake (g per day), serum ferritin, zinc and γ-glutamyltransferase activity. In women, menopause and contraceptive pill intake were also considered for entry into the regression model. The different categories of the nominal variables were coded 0,1 with the use of dummy variables (Kleinbaum *et al.*, 1988). The distributions of Cd-U, serum ferritin, zinc and γ-glutamyltransferase activity were normalized by a logarithmic transformation.

1. See p. 83–92

The influence of a given determinant on the urinary excretion of cadmium was assessed after accounting for the other confounding determinants. Adjustment and standardization were carried out with the regression coefficients obtained from the subset of confounding determinants.

Results

Mean age (± standard deviation) was 47.9 ± 16.3 years in men (n = 603) and 47.5 ± 16.3 years in women (n = 920) with a range of 18–88 years for both sexes. Current smoking was reported by 46 % of men and 34 % of women, with a mean daily consumption of 19 g of tobacco per day in both sexes. Regular alcohol consumption was reported by 37 % of men and 13 % of women, with a higher daily intake in men than in women (30 versus 20 g per day). The geometric mean of the Cd-U was 0.9 μg/24 h in men (range : 0.08–3.8 μg/24 h) and 0.80 μg/24 h in women (range : 0.06–8.0 μg/24 h).

Table 1 summarizes the results of the step-wise multiple regression analysis performed to identify the determinants significantly and independently influencing the 24-h Cd-U. In both sexes, age was the most important determinant in accounting for the observed variance. Place of residence came next, before smoking, social class and current alcohol consumption. Body mass index in men and menopause in women also accounted for a small but significant part of the variance of the 24-h Cd-U. These combined factors accounted for up to 47 % of the variance of Cd-U in men and 44 % in women.

Table 1. Determinants of 24-h Cd-U (in μg/24 h) ranked by decreasing percentage of explained variance[a]

Determinant	Men	Women
Age (linear and quadratic terms)	26.8	29.0
Place of residence	7.4	9.4
Current smoking and quantity smoked	6.3	3.3
Social class	3.3	0.7
Past quantity smoked	2.7	ns
Current alcohol consumption	0.4	1.3
Body mass index	0.4	ns
Menopause	–	0.3

[a] Values are percentages of variance explained by the determinant (squared partial correlation coefficient); ns = not significant

The geometric mean of the 24-h Cd-U in each 10-year age group was computed after standardization for place of residence, smoking, alcohol consumption, social class and, in men only, for body mass index (Table 2: SGM). It increased with age until 55 years in men and until 65 years in women and decreased thereafter. After standardization, Cd-U excretion was also significantly higher in women than in men.

The urinary excretion of cadmium was adjusted for age (50 years) after eliminating the confounding effects of smoking, alcohol consumption and social class in order to estimate the impact of place of residence on the cadmium body burden (Table 3). In Noorderkempen, the 24-h Cd-U of 50-year-old men never smokers amounted on the

Table 2. Geometric means of 24-h Cd-U by age in both sexes[a]

Age (years)	Men			Women		
	n	GM	SGM	*n*	GM	SGM
20–29	91	0.45 (0.24)	0.31	134	0.38 (0.31)	0.35
30–39	123	0.69 (0.38)	0.43	204	0.65 (0.52)	0.55 *
40–49	112	1.04 (0.57)	0.65	159	0.88 (0.72)	0.80 *
50–59	99	1.27 (0.77)	0.78	175	1.10 (0.96)	1.04 *
60–69	115	1.18 (0.77)	0.77	145	1.16 (1.10)	1.09 *
70–79	54	1.13 (0.82)	0.71	71	1.14 (1.26)	1.00 *
≥ 80	7	0.94 (0.82)	0.63	26	0.88 (0.99)	0.90

[a] GM = geometric mean in μg/24 h (and in μg/g creatinine in parentheses); SGM = standardized geometric mean (geometric mean computed after standardization for the other significant determinants mentioned in Table 1). An asterisk indicates a significant difference between the SGM found in men and women ($p < 0.001$).

average to 167% of that found in similar subjects living in Charleroi and Liège (Table 3). This cadmium overload is equivalent to the effect of smoking 20 cigarettes per day as explained hereafter. Subjects living in Engis and Hechtel-Eksel had a 20–25% greater cadmium body burden by comparison with that found in Charleroi and Liège. The following figures were obtained in women by comparison with those living in Liège : + 69% in Noorderkempen, + 36% in Hechtel-Eksel and + 42% in Engis.

Table 3. Geometric means of 24-h Cd-U by place of residence[a]

Area	Men			Women		
	n	GM	AGM	*n*	GM	AGM
Charleroi	106	0.83 (0.50)	0.76 (a)	165	0.65 (0.55)	0.99 (a)
Liège	194	0.75 (0.46)	0.76 (a)	249	0.64 (0.57)	0.86 (b)
Engis	66	0.95 (0.57)	0.92 (b)	93	0.89 (0.77)	1.22 (c)
Hechtel	151	1.01 (0.59)	0.94 (b)	197	0.89 (0.75)	1.17 (c)
Noorderkempen	86	1.12 (0.64)	1.27 (c)	216	1.09 (0.96)	1.45 (d)

[a] GM = geometric mean in μg/24 h (and in μg/g creatinine in parentheses); AGM = geometric mean adjusted for age (50 years) after standardization for the other significant determinants mentioned in Table 1. Means with the same letter in parentheses do not differ at the 5% probability level (pair-wise comparisons between areas for each sex separately)

The results of the multiple regression analysis showed in addition that:

1. Cd-U was higher in current smokers and increased in proportion to the quantity of tobacco smoked per day. From the regression coefficients it was estimated that the urinary excretion of cadmium due to smoking 20 cigarettes per day increases by about 63 % at age 45. The 24-h Cd-U in men past-smokers was also dependent on the quantity of tobacco smoked daily. This correlation was, however, not found in women past-smokers who had smoked less tobacco than men (16.6 cigarettes per day in women versus 22 cigarettes per day in men past-smokers) and for a shorter time.

2. Current alcohol consumers had lower 24-h Cd-U since a negative multiple regression coefficient was found for this determinant. The decrease predicted by the regression model amounted respectively to 8.9 % in men and to 17.4 % in women.
3. Men belonging to the highest of the three social classes and women of intermediate social class had lower 24-h Cd-U.
4. In men only, Cd-U increased with body mass index.
5. Postmenopausal women had a significantly higher 24-h Cd-U independent of age.
6. In both sexes Cd-U was not correlated with ferritin, zinc or γ-glutamyltransferase.

Each of these factors independently influenced Cd-U since the confounding effect of the other significant determinants was taken into account by the multiple regression procedure.

Discussion

One explanation for the age-dependent change in Cd-U excretion is a decrease in the cadmium body burden of elderly people due to the progressive loss of functional nephrons and hence of the ability of the kidneys to reabsorb and store circulating cadmium. A reduction of the cadmium intake via food might also contribute to this lowering of cadmium body burden after the age of 55–65 years.

With regard to the sex difference, it is possible that in menstruating women cadmium is taken up more avidly from the gastrointestinal tract than in men, resulting in a higher cadmium body burden at older age. Indeed, it has been suggested that iron deficiency stimulates the gastrointestinal uptake of cadmium (Flanagan *et al.*, 1978). However, in the present study, Cd-U was not correlated with serum ferritin.

The dependence of the cadmium body burden on place of residence probably reflects the impact of different degrees of environmental exposure to cadmium. High concentrations of cadmium have been found in sandy soils sampled in Noorderkempen, namely, up to 24 mg/kg (dry weight), with 41% of the samples having cadmium levels above 3 mg/kg (dry weight) (Lauwerys *et al.*, 1990). Well-water was also regularly used as drinking-water in this area and 25% of 2410 water samples collected in 1983 and 1984 had cadmium concentrations in the range 10–400 μg/l (Lauwerys *et al.*, 1990). The high levels of Cd-U observed among subjects living in Noorderkempen probably result from the consumption of locally grown vegetables and well-water up to 1985. Cadmium concentrations in soil samples collected from the kitchen gardens of 36 participants living in Liège were in the range 3–10.5 mg/kg (dry weight) (Sartor, unpublished data), whereas concentrations in the range 0.5–1 mg/kg soil (dry weight) were obtained in Charleroi (Lauwerys *et al.*, 1990). Mean levels of Cd-U were, however, similar in these two towns (Table 3). The intake of cadmium via food is therefore not influenced by current environmental exposure to cadmium in Liège. This does not preclude the possibility that environmental pollution by cadmium in Liège might have greatly enhanced the oral daily intake of cadmium in the past when the consumption of locally grown vegetables was higher. In Engis, clay soils are also heavily contaminated by cadmium (range: 7–39 mg/kg; $n = 29$; Sartor, unpublished data). Cd-U levels were, however, significantly lower than those found in Noorderkempen (Table 3). This could be explained partly by a higher uptake of cadmium in plants grown on sandy soils. In Hechtel-Eksel, the cadmium concentrations in soil (63 homes) were in the range 0.2–5.5 mg/kg (dry weight) but the mean levels of the 24-h Cd-U in subjects living in this area were higher than expected

(Table 3). The possible causes of the cadmium body overload among inhabitants of this rural area need further investigation.

The pollution of soils by cadmium in Liège, Engis and Noorderkempen is obviously the consequence of the release of cadmium in past and present non-ferrous industrial activities in these areas. In Hechtel-Eksel, an additional possible cause of soil pollution might be the use of materials contaminated by cadmium for road making.

In conclusion, environmental exposure to cadmium in certain areas of Belgium is an important determinant of the cadmium body burden in both men and women. The public health implications of the present results need to be interpreted in the light of the effects of cadmium on renal function and calcium metabolism.

Acknowledgements

The Cadmibel Study was supported by the Ministry of Health and Social Affairs, the Ministry of the Flemish Community, the Ministry of the Brussels Region, the Belgian National Fund for Medical Research, and the International Lead Zinc Research Organization.

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