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Relationship of Cadmium Levels Among Blood, Urine, and Diet in a General Population

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It has been established that the diet is the major source of exposure to cadmium (Cd) among general population, and that cigarette smoking will be an additional source of non-occupational exposure to this metal (Watanabe et al. 1985). For biological monitoring of exposure, the Cd level in blood has been evaluated as an indicator of exposure especially at occupational levels (e.g., Alessio et al. 1983). Attention has also been paid to urinary Cd as an indicator of occupational Cd exposure, probably because urine specimens are more readily available than blood samples, even though urinary excretion is a very minor route of elimination of cd from the body (Friberg et al. 1974). From the viewpoint of evaluation, it was stated that Cd in blood should be considered primarily as an indicator of recent exposure (Lauwerys et al. 1979), while urinary Cd mainly reflects Cd body burden when Cd exposure is low and kidney impairment is absent, but may be influenced by current Cd exposure when Cd exposure is intense (Alessio et al. 1983).

Although a few experimental studies have been reported on the quantitative relation among the indicators of Cd exposure (e.g., Suzuki and Lu 1976), reports which establish and evaluate the correlations among these parameters in a general population are scarce. The present study was initiated to examine the relation of the Cd level in blood (Cd-B) with the Cd intake through diet (Cd-D) and the excretion of Cd into urine (Cd-U) among those with no known exposure to Cd. The Cd-U was examined both in terms of the level in the spot urine (Cd-Us) and as the amount in the 24-hr urine sample (Cd-U24).

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MATERIALS AND METHODS

37 healthy female farmers, at the ages of 28 to 54 years and without any apparent kidney dysfunction, volunteered to participate in the study; they lived for years in 3 rural regions of Karakuwa, Kannari and Watari (where no heavy metal pollution has ever been known) in a prefecture of Miyagi, Japan. There have been no remarkable changes in their life circumstances in recent years. Blood from cubital vein and spot urine were collected at 10:00 am to 12:00 noon of the day of study. The collection of the 24-hr duplicates of diet (Yamagata and Iwashima 1975; Acheson et al. 1980) was initiated at the lunch of the previous day, and included as much plain drinking as consumed by the subject (Watanabe et al. 1985). In some cases, urine samples were collected for 24 hrs from the first urine in the morning of the previous day. Sampling was repeated up to 4 times from the summer of 1980 to the summer of 1982 (Table 1).

Diet duplicates (Watanabe et al. 1985), blood (Watanabe et al. 1983) and urine (Abe et al. 1986) were analyzed for Cd by the block wet digestion—automatic sample injection—flameless atomic absorption spectrometry (Watanabe et al. 1982) so that the results were strictly comparable. Cd-Us was corrected for a specific gravity of urine (Kowal and Zirkes 1983) of 1.016 (Rainsford and Lloyd Davies 1965). All glass- and plastic-ware except the sterile blood sampling devices were washed to be metal-leakage free. Acids for wet digestion (specified grade for pollutant metal analysis) and the cadmium standard solution were purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan). A log-normal distribution (Watanabe et al. 1983 and 1985) was assumed for statistical analyses, and the results were expressed in terms of the geometric mean (GM) and the geometric standard deviation (GSD). The statistical significance of the difference in means was examined by paired t-test and analysis of variance, when necessary.

RESULTS AND DISCUSSION

It was possible to collect blood samples on all of the 4 occasions of examination, spot urine samples on 3 occasions out of 4, and 24-hr diet duplicates twice in Karakuwa and once in Kannari and Watari. The 24-hr urine samples were available only in Karakuwa where the collections were made on 2 occasions. The results of Cd analyses are summarized in Table 1. The GM of Cd-B distributed in a narrow range from the lowest of 2.92 ng/ml in Watari in summer of 1981 to the highest of 5.34 ng/ml in Kannari in summer of 1982. The GSD was

Table 1. Cadmium levels in blood, spot and 24-hr urine, and 24-hr duplicates of diet.

Region	Biological sample (unit)	1980 (Summer)	1981 (Winter)	1981 (Summer)	1982 (Summer)
Karakuwa (n=11)	Blood (ng/ml)	3.64 (1.34)	3.19 (1.37)	4.15 (1.25)	3.97 (1.35)
	Spot urine (ng/ml)		4.75 (1.53)	2.26 (1.42)	3.60 (1.66)
	24-hr urine (ug/day)		2.70 (1.57)	2.80 (1.72)	
	24-hr diet (ug/day)		49.00 (1.78)	32.83 (1.25)	
Kannari (n=16)	Blood (ng/ml)	5.15 (1.36)	4.64 (1.57)	4.79 (1.40)	5.34 (1.45)
	Spot urine (ng/ml)		2.64 (1.59)	3.11 (1.49)	3.60 (1.66)
	24-hr diet (ug/day)		35.39 (1.32)		
Watari (n=10)	Blood (ng/ml)	3.33 (1.25)	4.63 (1.28)	2.92 (1.34)	3.40 (1.24)
	Spot urine (ng/ml)		1.29 (1.34)	4.17 (1.65)	2.19 (1.65)
	24-hr diet (ug/day)		37.75 (1.31)		
Total (n=37)	Blood (ng/ml)	4.13 (1.40)	4.15 (1.49)	4.02 (1.43)	4.32 (1.44)
	Spot urine (ng/ml)		2.60 (1.89)	3.06 (1.60)	2.79 (1.67)
	24-hr diet (ug/day)		39.67 (1.50)		

The value in the table is the geometric mean followed by the geometric standard deviation in parentheses. Cadmium concentrations in spot urine samples are corrected for a specific gravity of urine of 1.016.

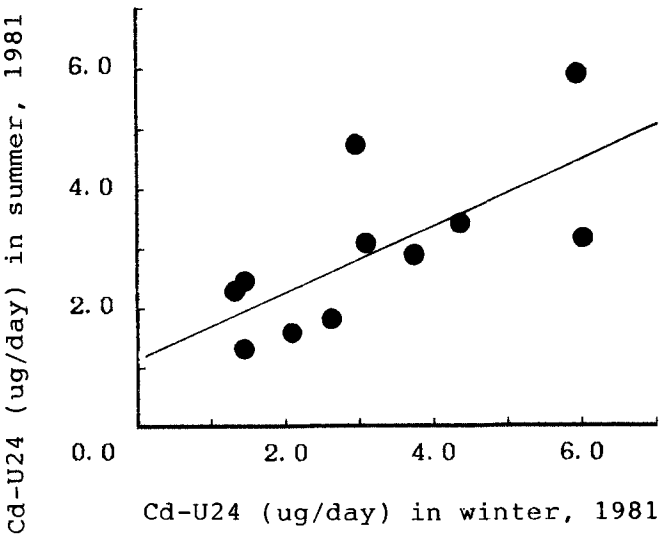

Figure 1. Correlation between Cd-U24 in winter and in summer, 1981. The line in the figure is a calculated regression line. For details, see the text. Cd-U24 means the amount of Cd in 24-hr urine.

Table 2. Correlation coefficients in cadmium concentrations between various biological samples

	24-hr diet (Cd-D)	Spot urine (Cd-Us)	24-hr urine (Cd-U24)
Blood (Cd-B)	-0.202 (48)	-0.026 (111)	0.633**(22)
24-hr urine	0.169 (22)	0.318 (22)	
Spot urine	0.356*(48)		

The value in the table is the correlation coefficient followed by the number of the paired cases in parentheses. Asterisks indicate statistical significance of the coefficient (* for $p<0.05$ and ** for $p<0.01$).

also small (less than 1.57). No statistically significant ($p>0.05$) difference was detected when the variances in Cd-B of the total 37 subjects as measured on the 4 occasions were analyzed, suggesting that Cd-B is a reliable indicator.

The GM of Cd-Us varied from the lowest of 1.29 ng/ml in Watari in winter of 1981 to the highest of 4.75 ng/ml in Karakuwa on the same occasion, even when corrected for a specific gravity of urine of 1.016. The GSD of Cd-U was generally larger than the corresponding GSD of Cd-B. The range between the lowest and the highest Cd-Us among the individuals was as wide as 6.37 ug/l (0.77 and 7.14 ug/l as the lowest and the highest, respectively) in winter or 7.72 ug/l (1.09 and 8.81 ug/l) in summer. When observed on individual basis, the largest difference in Cd-Us as examined on the 3 occasions was 7.76 ug/l with the lowest of 1.05 ug/l and the highest of 8.81 ug/l. Such findings suggest that Cd-Us of the same individual may vary in a wide range depending on the occasion. In contrast, Cd-U24 appeared to be stable. When 11 pairs of Cd-U24 (one set measured in winter, 1981, and the other in summer of the same year) were compared, the calculated regression line was $y = 1.190 + 0.554\ x$; where x and y are Cd-U24 (ug/day) in winter and summer, 1981, respectively (Fig. 1). The correlation coefficient (0.689) was statistically significant ($p<0.05$).

In accordance with the previous observation (Watanabe et al. 1985), Cd-D was significantly ($p<0.05$) higher in winter (GM; 49 ug/day) than in summer (GM; 35 ug/day). The winter Cd-D was especially high in 3 subjects (74.6, 113.4 and 131.3 ug/day). Further perusal of the menus of their diet disclosed that the food items common to them but not taken by others nor by any in summer were small squids (cooked as a whole; no viscera eliminated) and small sea snails. It is known that the viscera, especially the liver, of such mollusca is rich in cadmium (Hosogai et al. 1985).

The correlation was examined between each pair out of Cd-B, Cd-D, Cd-Us and Cd-U24. The correlation coefficients and statistical significance are summarized in Table 2. Contrary to expectation, the correlation between Cd-D and Cd-U24 was low and insignificant. This is probably associated with the facts that day-to-day fluctuation in dietary cadmium intake is remarkable as stated above and that collections of diet duplicates and urine samples were made for the same 24-hr period. Thus chances may be small for Cd-D to reflect on Cd-U24. Even when the 3 cases of extremely high Cd-D were excluded, the correlation coefficient was not significant ($r=0.182$,

$p<0.10$, n=19). The poor correlation on individual basis of Cd-B with Cd-D was in agreement with the previous observation (Watanabe et al. 1985). The correlation of Cd-Us with Cd-U24 was statistically insignificant ($p>0.05$) possibly due to diurnal variation in urinary metal excretion (Araki et al. 1983; Subramanian and Méranger 1984). No explanation is currently available for low yet significant ($p<0.05$) correlation between Cd-D and Cd-Us. It may be worthy to note that the correlation between Cd-B and Cd-U24 was highly significant ($r=0.633$, $p<0.01$, n=22). Even though that the number of cases investigated was still limited, this observation may suggest that there exists an quantitative correlation between Cd-B and Cd-U24. The regression line obtained was $y = -0.218 + 0.868\ x$; where x is Cd-B (ng/ml) and y is Cd-U24 (ug/day).

Although the correlation on individual basis is poor between Cd-D and Cd-U24, it may be feasible to make a quantitative evaluation of urinary Cd excretion as a route of Cd elimination among general (i.e., occupationally non-exposed) population. When the Karakuwa data of 11 cases each in winter and in summer of 1981 were pooled, the grand GM (n=22) for Cd-D was 40.92 ug/day and that for Cd-U24 was 2.75 ug/day. Thus, about 6.7% (=2.75/40.92) of Cd ingested will be excreted into urine in Japanese women who are not exposed to Cd occupationally and take about 40 ug Cd through diet daily. This rate of excretion is very close to the figure given as the absorption rate of Cd through the gastrointestinal tract [i.e., 4.4 to 5% (Kitamura, 1972; Yamagata et al. 1975; McLellan et al. 1978) or less than 10% (World Health Organization (1980)].

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