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REVIEW

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Critical evaluation and review of cadmium concentrations in blood for use in occupational health according to the TRACY protocol

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Abstract Cadmium in blood (B-Cd) may be used to assess recent exposure to cadmium in the working or general environment. In a paper published elsewhere pooled reference values using meta-analysis of B-Cd values in general-population studies were calculated. In the present study tentative reference intervals were described which can be used for comparison with data from occupationally exposed groups or individuals. The selection of studies was done according to criteria as published by the international project TRACY. For this purpose, 800 publications covering the period 1983–1992 were reviewed on their suitability for establishing tentative reference intervals. From these 800 publications, four finally met the selection criteria. Most important criteria for selection were the check for contamination during sampling of the blood, the storage and pretreatment procedures, and the existence of internal and external quality control programs. Also, stratifications into sex, smoking habits and occupation were important selection criteria. It turned out that for non-smoking white-collar workers in the age range of 19–65 years, B-Cd values were below 0.8 µg/l for most areas. All other groups within this age group, e.g., white collar workers in Japan, blue-collar workers, and smokers tend to have higher B-Cd values in these sequences. Blue-collar workers not clearly exposed to Cd have higher values than white-collar workers, indic-

ating still some minor exposure. It is not clear if this small exposure has an occupational or lifestyle (e.g., diet) origin. Geographic regions also show an influence on B-Cd levels, e.g., values in Japan are higher than elsewhere. This influence may be due to differences in diet. The conclusion will be that reference values for B-Cd in fact are area-dependent.

Key words Blood · Cadmium · Reference intervals · Occupational health

Introduction

Cadmium (Cd) is toxic for many plants and invertebrates, e.g., bacteria, algae, protozoa, and arthropods. Toxicity for fish, amphibians, birds, and wild small mammals has been well established (WHO 1992a).

The daily human intake of Cd obviously depends on the personal diet. In “uncontaminated” areas the average daily intake is between 10 and 16 µg/day for a person of 70 kg. The average total daily intake of Cd in Germany (Müller 1993), in most other European countries, in the United States and in New Zealand is very likely in the 10–30 µg/day range (Schelenz 1983; Elinder 1985; Herber 1993).

The most important lifestyle factor regarding Cd intake is tobacco smoking, especially self-rolled cigarettes. Smoking of one cigarette, containing 1–2 µg of Cd, results in the inhalation of about 0.1–0.2 µg Cd (Friberg et al. 1986).

In the working environment levels of Cd can be up to 0.5 mg/m³ in battery factories, but generally not higher than 100 µg/m³ (Friberg et al. 1986). Some figures for exposure limit values are: Sweden, 0.02 mg/m³ (respirable dust as Cd); UK, 0.05 mg/m³ (fumes as Cd); USA, 0.002 mg/m³ (respirable fraction as Cd); Australia 0.01 mg/m³ (as Cd). All values are time weighted averages (TWA). Respirable dust is defined as the airborne particulate that may reach the alveolar compartment.

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The critical organ for chronic Cd exposure is the kidney. In the case of short-term peak exposure of workers, the lung may be the critical organ (WHO 1992b). Kidney dysfunction is the most characteristic sign of exposure of Cd (Friberg et al. 1986). The renal dysfunction induced by Cd is tubular, but claims have been made that Cd can also cause early glomerular effects (Lauwerys et al. 1974; Bernard et al. 1976, 1979). This, however, remains controversial (Piscator 1988). In the working environment at high exposure levels, workers have developed proteinuria, renal glucosuria, aminoaciduria, hypercalciuria, phosphaturia, and polyuria (WHO 1992b).

Cd in blood (B-Cd) can be used as a biological monitoring measure for recent exposure in occupation or general environment. B-Cd mainly reflects the exposure during recent weeks or months (WHO 1992b). If the exposure remains during longer periods (months) stable, and the exposure is not too high, B-Cd also reflects the body burden.

Determination of B-Cd was a problem in many laboratories, at least until the early 1980s (Herber 1990; Herber et al. 1990). The goal of the project TRACY (a EUREKA project), is the establishment of reference values, which are especially important in occupational health. This study is based on earlier criteria developed by the Scientific Committee on Toxicology of Metals of the International Commission on Occupational Health (ICOH), and the Commission on Toxicology of the International Union of Pure and Applied Chemistry (IUPAC) (Vesterberg et al. 1993). Earlier publications have constructed a framework for these criteria; mercury in blood was the first subject of review (Brune et al. 1991); a paper was published on chromium in blood, serum and urine (Brune et al. 1993); and the latest paper concerned nickel in blood, serum and urine (Templeton et al. 1994).

In view of the toxicity of cadmium, and of the problems inherent in the determination of B-Cd, establishment of reference values for this element is also needed.

In an earlier study, meta-analysis of B-Cd values in the general population was performed (Alessio et al. 1994). The meta-analysis study reported pooled reference values based on data from the literature. Weighting factors were used for smoking, dietary habits, country, indirect occupational exposure, age, sex, residence, medication and hobbies. Data were used from the general population; one country (Japan) was excluded from the meta-analysis study because it showed heterogeneity compared with other countries. Reference values obtained in this study are thus applicable for the general population of European and North American countries. It was remarked that the gain from pooling of the populations was negligible and that study of the heterogeneity of the populations will be more useful.

Another approach will be the stratification of the population according to variables causing the hetero-

geneity. This means that the TRACY criteria for the "Analytical and statistical details" will be similar to the meta-analysis study. With respect to "Population and sampling" different criteria compared with the meta-analysis study will be applied for "Description of individuals". In the present study an attempt was made to estimate reference intervals for use in occupational health. This means that the population was selected from healthy adults of working age; that stratification into males and females was necessary, and that selection into different occupations was made. The reference intervals established in this way can be used in occupational health for comparison with data from exposed groups or individuals.

Literature search

Literature searches were performed using the POLTOX, OSH-ROM Silver Platter, and MEDLINE CD-ROMs for the period 1983–1992. Altogether about 800 references were gained. After a first search on title alone 400 abstracts seemed useful; after a second search of abstracts, 80 remained. From these 80 full papers seven environmental studies in the general population and 60 occupational studies were finally selected. The selection criteria were "analytical factors", "occupation known", and "age range 19–65".

Suitability for occupational health studies, and stratification

Population and sampling

Description of individuals

Smoking habits Smoking of cigarettes, and especially self-rolled cigarettes, enhances B-Cd levels (WHO 1992b). Thus stratification has to be according to the classes "smokers" and "nonsmokers". B-Cd depends on the number of cigarettes, the length of the cigarettes, tobacco brand, etc. As an example it was reported that for every cigarette smoked per day, the level of B-Cd increases 1.6% (Wibowo et al. 1982). Therefore, only values for nonsmokers were given. Values for smokers can be calculated with linear regression.

Occupation It is known that blue-collar workers have higher values than white-collar workers (Brockhaus et al. 1983). Thus, as a first approach a stratification had to be made between "blue collars", and "white collars", and if possible, a stratification along specific occupations.

Sex B-Cd differs between sexes (Watanabe et al. 1989a). Gastrointestinal absorption of Cd is higher in females than in males, due to differences in iron stores

(Andersen et al. 1992). On the other hand, men might be slightly more exposed by occupation, if compared with, e.g., housewives. Therefore, stratification according to sex is also important. Separate reference values for men and women is common practice.

Age It is reported that B-Cd increases with age (Ikeda 1992). Thus, stratification according to age was necessary.

Medication Medication may disturb the metabolism, as may certain diseases. Data from patients have to be excluded, while medication (for instance use of chelators in workers exposed to several metals) has to be known. Thus, studies without mentioning medication were excluded.

Hobby Some hobbies do have the risk of exposure to Cd, e.g., welding, pottery making, etc. Hobbies of this kind have to be known. Studies without mention of hobbies were excluded.

Country, area, urban/rural Levels in Japan were twice as high as in the USA within one study (Friberg and Vahter 1983), probably due to differences in diets. Stratification according to countries and rural/urban habitation was needed. In addition the area can be given.

Sampling design

Blood sampling avoiding contamination had to be mentioned. Blood samples must be taken with regular precautions regarding contamination and the pre-analytical factors carefully evaluated including test specimen handling before determination.

Statistics

Sufficient individuals to get an impression of the distribution were needed. The International Federation of Clinical Chemistry (IFCC) recommends that at least 120 values are measured. This number, however, is based on a heterogeneous population; with stratification a more homogeneous population is formed and thus fewer stringent requirements for the number were required. The number was dependent on the skewness, but 40 was sufficient (Vesterberg et al. 1993).

Preanalytical and analytical factors

Storage and pretreatment

Addition of anticoagulants, check for contamination of used containers, tubes and chemicals must be men-

tioned and a cleaning procedure for the utensils must be described. All chemicals and utensils may contain Cd in concentrations up to 1000-fold the concentration in blood. Colored stoppers are especially suspect. Checking for contamination is very important and papers that did not describe a procedure for this item or mention the blank of the procedure were rejected.

Analytical factors

Analytical method Requirements were the mentioning of the standard deviation of the within-run, between-run (between-day) (or repeatability and reproducibility), sensitivity, determination limits, etc. It has been shown that if a method is used with a determination limit low enough to determine levels of Cd in blood of 0.1 µg/l, discrepancies between methods are less important than those between laboratories (Herber et al. 1990). Thus, mention of the type of analytical method is not required, other than the instrumental technique. The most common method now used for the determination of B-Cd is graphite furnace atomic absorption spectrometry.

Quality assurance

Requirements for quality assurance were the internal quality control by pooled test substances, or (preferably) certified reference materials with concentration levels comparable to the level of test substances (accuracy). External control had to be shown by assessment of an independent laboratory or participation in collaborative studies or intercomparison programs, all during the period that the test substances were determined. The bias from agreed values should be given.

Statistical data treatment

A proof of normality of the distribution by statistical testing had to be given. If the distribution is not Gaussian, adequate transformation had to be done (preferably the geometric mean had to be calculated).

Selection of data for establishment of reference values

Publications solely with the following factors were selected:

- Contamination was clearly checked during, storage and pretreatment procedures
- Figures were given for the precision, etc.
- Internal quality control was done by using pooled samples and/or reference samples
- External quality was checked by participation in an external quality control program

- Blood sampling was clearly mentioned under circumstances avoiding contamination
- Sufficient individuals were studied to verify the distribution ($n \geq 40$)
- A nonsmoker group was included
- Stratification into white-collar and blue-collar workers was done
- Stratification into sex was done
- Age class was within the range 19–65 years
- The country mentioned as well as urban, rural, industrialized, or nonindustrialized areas

Results and discussion

A common reason for rejection was a poor description of the analytical factors regarding checking for contamination, missing method description, and lack of quality control. It should be remarked that papers with a poor definition of the analytical factors be rejected.

It turned out that nearly all the occupational studies were dose-effect studies or were lacking control groups that could be used for reference values. Dose-effect studies as such are of course of value. However, these studies cannot be used for reference values as a distinct control group, with a corresponding mean B-Cd, is missing in such studies. Control groups in studies where two groups were compared were sometimes defined as “healthy individuals”, “laboratory workers”, or “administrative workers”. The values of such white-collar worker groups cannot be used for tentative reference values for blue-collar workers. The reason is that blue-collar workers have higher B-Cd values compared with white-collar workers (Brockhaus et al. 1983). It is not clear if blue-collar workers have higher values because there still exists a small occupational exposure, or that a different lifestyle or diet pattern is responsible for the three differences. In the bulk of the environmental studies, occupation was not mentioned and/or the age range was not of use for the present reference value purposes.

From the previously mentioned 67 publications, four were finally selected as suitable for defining tentative reference values according to the procedure described. The first publication, by Friberg and Vahter (1983), dealt with a general population study in different countries in Europe, Asia, and America. This study was mentioned in the meta-analysis study (Alessio et al. 1994) as well. Aspects particularly relevant in the suitability of this paper for reference intervals are: (i) the quality control, and (ii) occupation. The quality control was checked, by both internal and external programs. A design was presented for quality control using a program for a different participating laboratories for sampling, storage, transport and analysis. Internal quality control samples were used with concentrations of metals known to the laboratories, and external quality control samples with different concentrations not

known to the laboratories. A statistical procedure was given for the criteria of acceptance of laboratory performance. Results of the external quality control program were also given in the paper. The occupation studied with limited to teachers because this is a homogeneous group of white-collar workers; for the same reason tentative reference intervals were restricted in the underlying study to such populations. Blood sampling was checked for contamination; the number of individuals was generally sufficient. Stratification by occupation was not needed because only teachers were studied, nonsmokers were present, male and female groups were stratified for age, country, and areas were reported. Table 1 shows the results of this study as

Table 1 Reference values from a study in the general population in Europe, Asia, and America (Friberg and Vahter 1983). Values given are for nonsmokers. Occupation: Schoolteachers. Age groups ≤ 19 to ≥ 60 years. Values of cadmium in blood ($\mu\text{g/l}$). GM geometric mean, GSD geometric standard deviation, n number of teachers

Country/area		Males	Females
Belgium/Brussels	GM	1.0	0.9
	GSD	1.64	1.72
	n	50	39 ^a
Croatia/Zagreb	GM	0.5	0.4
	GSD	2.11	2.07
	n	30 ^a	84
China/Beijing	GM	0.5	0.7
	GSD	1.88	1.77
	n	43	118
India/Ahmedabad	GM	0.9	0.8
	GSD	1.46	1.50
	n	76	100
India/Bangalore	GM	0.8	0.8
	GSD	1.94	1.50
	n	9 ^a	44
India/Calcutta	GM	0.8	0.7
	GSD	1.45	1.52
	n	31 ^a	50
Israel/Jerusalem	GM	0.4	0.4
	GSD	1.80	1.81
	n	92	51
Japan/Tokyo	GM	0.9	1.1
	GSD	1.66	1.62
	n	17 ^a	77
Mexico/Ciudad	GM	0.3	0.3
	GSD	3.49	3.20
	n	17 ^a	30 ^a
Peru/Lima	GM	0.6	0.8
	GSD	1.53	1.50
	n	12 ^a	89
Sweden/Stockholm ^b	GM	0.1	0.3
	GSD	1.99	1.99
	n	31 ^a	45
USA/Baltimore	GM	0.6	0.5
	GSD	1.89	1.85
	n	24 ^a	64

^a Insufficient number of individuals to calculate a distribution

^b Random population sample

stratified by country and sex. Some cells of these stratification groups contain too few individuals to calculate a distribution ($n \leq 40$) and thus cannot be used for TRACY. The concentration of B-Cd ranged from 0.3 µg/l (Sweden, females) to 1.1 µg/l (Japan, females), which points to considerable differences, probably in diet.

Another study, performed in Germany and also published in 1983, was by Brockhaus et al. Contamination was checked, figures for the precision were given, and internal quality was checked, using commercial control specimens. External quality was checked by participation in the Health and Safety Directorate (European Commission) program for B-Pb and B-Cd. Blood sampling was checked for contamination, and the number of individuals was mostly sufficient. A nonsmoker's group was included, and stratification into "white collars", and "blue collars" was made. Male and female groups were existent, the age group was 60–65 years, country and area were mentioned, and health status was asked for in the study. Results suitable for TRACY are shown in Table 2. From this study only the values for the white-collar workers can be used because the number of blue-collar workers was too low. Levels in this study for white-collar workers were comparable with the levels in the teacher study (Friberg and Vahter 1983), and in particular with levels in China, Israel, Croatia and the USA. For both females and males a geometric mean (GM) of 0.44 µg/l B-Cd was reported.

The other two studies suitable for TRACY were published in 1989 and were performed by the same group of investigators. The first study was done in factory workers within cities in China (Watanabe et al. 1989a), while the second study was performed in factory workers in Korea and Japan (Watanabe et al. 1989b). Contamination was checked as mentioned in a separate publication, and figures for precision were given in a separate publication. It was mentioned that when a difference over 10% between replicate determinations existed, determinations were repeated. The external quality was assessed by participation in a quality assurance program of the Japanese Ministry of Labour. Additional figures were given for the external

quality performance, but not for the internal performance. Blood sampling was carried out under circumstances avoiding contamination, as mentioned in a separate publication. Mostly, enough individuals were studied, and a nonsmoking group was included. Stratification into different occupations was done, and male and female groups were present. The age group for the Chinese study was ≤ 16 to ≥ 60 years, and for the Korean and Japanese study ≤ 19 to ≥ 60 years. Countries and areas were mentioned and the subjects had no known occupational exposure to Cd or other metals. Table 3 shows the results from the study in China. Levels of B-Cd in this study (1.26 µg/l B-Cd for males and 1.21–1.38 µg/l B-Cd for females) were higher than in both earlier mentioned studies; in the teacher study (Friberg and Vahter 1983) for males 0.5 µg/l (Table 1) and for females 0.7 µg/l were reported. This difference might be due either to the difference in occupation (white-collar workers vs blue-collar workers), or in lifestyle factors (e.g., different diets). Another possibility may be the difference in age distribution between the two studies additional to these points. In the fourth study (Watanabe et al. 1989b) the same trends can be observed (Table 4).

From these four papers, tentative reference intervals can be constructed. As stratification parameters as a first approach, nonsmokers in the age group 19–65 years, divided into white-collar workers and blue-collar workers, can be chosen. The white-collar worker levels are then 0.3–2.07 µg/l GM (the teachers and the German studies), and the blue-collar worker levels 0.53–2.22 µg/l (GM, the German, Chinese, Korean and Japanese studies). Thus, blue-collar workers seem to have slightly elevated B-Cd values as compared with white-collar workers. A closer look, however, reveals that more strata are visible, i.e., geographic areas, and different occupations within the blue-collar worker group. Differences in geographic areas again may be due to differences in diet, e.g., it is well known that Japanese rice contains more Cd than rice from other areas. The occupation stratum is clearly not homogeneous because between the different blue-collar workers a small exposure to Cd still exists, reflected in B-Cd value.

In conclusion, it can be said that it will be difficult to construct general B-Cd values. The easiest stratum is that of nonsmoking white-collar workers in the age range 19–65 years. Here, values will be < 0.8 µg/l (Friberg and Vahter 1983). It is likely that values in Japan, and perhaps in other countries with higher oral intake of Cd, will be higher. Also values for blue-collar workers will be higher, because of some small exposure. For all these remaining strata, no reliable reference intervals can be constructed. A very few papers could be selected, it will also be clear that for cadmium in blood (the second most studied element) the need of reliable reference intervals in future is an important topic.

Table 2 Reference values from a study in the general population in Germany (Brockhaus et al. 1983). Values given are for nonsmokers. Age groups 60–65 years. Urban population: Cologne area. Values of cadmium in blood (µg/l). GM geometric mean, n number of individuals, *White-collar workers* clerks, office workers, pensioners, and housewives, *Blue-collar workers* not specified

Occupation		Males	Females
White-collar workers	GM	0.44	0.44
	n	165	234
Blue-collar workers	GM	0.53	0.38
	n	13 ^a	2 ^a

^a Insufficient number of individuals to calculate a distribution

Table 3 Reference values from a study in factories in China (Watanabe et al. 1989a). Values given are for nonsmokers. Age groups: ≤16 to ≥60 years. Urban population: Hefei, Shenyang, and Jinxi. Occupation: blue-collar workers. Values of cadmium in blood (µg/l). *GM* geometric mean, *GSD* geometric standard deviation, *n* number of individuals

Area/occupation		Males	Females
Hefei/shoemakers	GM	1.26	1.21
	GSD	1.768	1.579
	<i>n</i>	47	176
Shenyang/degreasing workers	GM	1.15	1.33
	GSD	1.361	1.081
	<i>n</i>	13 ^a	6 ^a
Jingxi/solvent synthesis workers	GM	1.28	1.38
	GSD	1.081	1.704
	<i>n</i>	28 ^a	43

^a Insufficient number of individuals to calculate a distribution

Table 4 Reference values from studies in factories in Korea and Japan (Watanabe et al. 1989b). Values given are for nonsmokers. Age groups: ≤19 to ≥60 years. Urban population: Masang and Miyagi. Occupation: blue-collar workers. Values of cadmium in blood (µg/l). *GM* geometric mean, *GSD* geometric standard deviation, *n* number of individuals

Area/occupations		Males	Females
Masan/degreasers ^a	GM		1.58
	GSD		1.54
	<i>n</i>		161
Miyagi/shoemakers	GM	1.78	2.22
	GSD	1.73	1.54
	<i>n</i>	62	113

^a Also office workers, age upto 49 years

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References

Alessio L, Apostoli P, Braga M, Duca PG, Herber RFM, Nordberg G, Vesterberg O (1994) Estimation of pooled reference values for cadmium in blood using meta-analysis and TRACY criteria. *Sci Total Environ* 152:69–177

Andersen O, Nielsen JB, and Nordberg GF (1992) Effects of dietary factors on intestinal cadmium uptake. In: Nordberg GF, Herber RFM, Alessio L (eds) *Cadmium in the human environment*. International Agency for Research on Cancer, Lyon

Bernard A, Roels H, Hubermont G, Buchet JP, Masson PL, Lauwereys RR (1976) Characterization of the proteinuria in cadmium-exposed workers. *Int Arch Occup Environ Health* 38:19–30

Bernard A, Buchet JP, Roels H, Masson P, Lauwereys R (1979) Renal excretion of proteins and enzymes in workers exposed to cadmium. *Eur J Clin Invest* 9:11–22

Brockhaus A, Freier I, Ewers U, Jermann E, Dolgner R (1983) Levels of cadmium in blood in relation to smoking, sex, occupation, and

other factors in an adult population of the FRG. *Int Arch Occup Environ Health* 52:167–175

Brune D, Nordberg GF, Vesterberg O, Gerhardsson L (1991) A review of normal concentrations of mercury in human blood. *Sci Total Environ* 10:235–282

Brune D, Aitio A, Nordberg GF, Vesterberg O, Gerhardsson L (1993) Normal concentrations of chromium in serum and urine-a TRACY project. *Scand J Work Environ Health* 19 [Suppl 1]:39–49

Elinder CG (1985) Cadmium, uses, occurrence and intake. In: Friberg L, et al. (eds) *Cadmium and health: a toxicological and epidemiological appraisal vol 1*. Exposure, dose and metabolism. CRC Press, Boca Raton, pp 23–63

Friberg L, Vahter M (1983) Assessment of human exposure to lead and cadmium through biological monitoring; results of a UNEP/WHO global study. *Environ Res* 30:95–128

Friberg L, Kjellström T, Nordberg GF (1986) *Cadmium In: Friberg L, Nordberg GF, and Vouk VB (eds) Handbook on the toxicology of metals, vol 2*. Elsevier, Amsterdam, p 130ff

Herber RFM (1990) The World Health Organization study on health effects to cadmium. *Toxicol Environ Chem* 28:1–10

Herber RFM (1993) Cadmium. In: Seiler H, Sigel A, Sigel H (eds) *Handbook on metals in clinical and analytical chemistry*. Marcel Dekker, New York, pp 283–297

Herber RFM, Stoeppler M, Tonks DB (1990) Cooperative inter-laboratory surveys of the determination of cadmium in whole blood. *Fresenius J Anal Chem* 338:269–278

Ikeda M (1992) Biological monitoring of the general population for cadmium. In: Nordberg GF, Herber RFM, Alessio L (eds) *Cadmium in the human environment*. International Agency for Research on Cancer, Lyon

Lauwereys RR, Buchet JP, Roels H, Brouwers J, Stanescu D (1974) Epidemiological survey of workers exposed to cadmium. *Arch Environ Health* 28:145–148

Müller M (1993) *Cadmium Aufnahme und Cadmium Ausscheidung Erwachsene nach der Marktkorb- und Duplikatmethode (Dissertation in German)*. Friedrich-Schiller University, Jena

Piscator M (1988) Some views on metabolism, toxicity and carcinogenicity of cadmium. In: Stoeppler M, Piscator M (eds) *Cadmium (3rd IUPAC Cadmium Workshop, Jülich, August 1985)*. Springer, Berlin Heidelberg New York, pp 3–12

Schelenz R (ed) (1983) *Essentielle und toxische Inhaltsstoffe in der tägliche Gesamtnahrung*. Report BFE-R-83-02 (in German), Bundesforschungsanstalt für Ernährung, Karlsruhe

Templeton DM, Sunderman FW, Herber RFM (1994) Tentative reference values for nickel concentrations in human serum, plasma, blood, and urine: evaluation according to the TRACY protocol. *Sci Total Environ* 148:243–251

Vahter M (1982) Assessment of human exposure to lead and cadmium through biological monitoring. National Swedish Institute of Environmental Medicine and Karolinska Institute, Stockholm

- Vesterberg O, Alessio L, Brune D, Gerhardsson L, Herber R, Kazantzis B, Nordberg G, Sabbioni E (1993) International project for producing reference values for concentrations of trace elements in human blood and urine: TRACY. *Scand J Work Environ Health* 19[Suppl 1]:19–26
- Watanabe T, Qu JB, Jin C, Liu YT, Yin SN, Nakatsuka H, Seiji K, Inoue O, Ikeda M (1989a) Blood cadmium levels in the populations of 3 Chinese cities. *Toxicol Lett* 47:145–153
- Watanabe T, Nakatsuka H, Seiji K, Ioue O, Cho KS, Lee KM, Lee BK, Lee SH, Ikeda M (1989b) Blood cadmium levels in the populations of Masan, Korea, and Miyagi, Japan: an inter-regional comparison. *Toxicol Lett* 47:155–163
- Wibowo AAE, Herber RFM, Deyck W van, Zielhuis RL (1982) Biological assessment of exposure in factories with second degree usage of cadmium compounds. *Int Arch Occup Environ Health* 49:265–273
- World Health Organization (1992a) Cadmium: environmental aspects (Environmental health criteria 135). WHO, Geneva
- World Health Organization (1992b) Cadmium (Environmental health criteria 134). WHO, Geneva