Cadmium and Lead in Blood in Relation to Low Bone Mineral Density and Tubular Proteinuria

Tobias Alfvén, Lars Järup, and Carl-Gustaf Elinder

Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden; Department of Epidemiology and Public Health, Imperial College School of Medicine, London, United Kingdom; Department of Renal Medicine, Huddinge University Hospital, and Department of Medical Epidemiology, Karolinska Institutet, Stockholm, Sweden

Long-term exposure to cadmium may cause kidney and bone damage. Urinary cadmium is commonly used as the dose estimate for the body burden of cadmium. However, elevated levels of cadmium in the urine may reflect not only high levels of cadmium dose but also renal dysfunction. In this study we used blood cadmium as the dose estimate. In addition, we analyzed blood lead. We examined 479 men and 542 women, ages 16–81 years, who were environmentally or occupationally exposed to cadmium and lead. We used urinary protein α1-microglobulin as a marker for tubular proteinuria and measured forearm bone mineral density using dual-energy X-ray absorptiometry. The relationship between blood cadmium and tubular proteinuria was strong, even when we excluded occupationally exposed participants. The subgroup with the highest blood cadmium levels had a 4-fold risk of tubular proteinuria compared to the subgroup with the lowest blood cadmium levels. In the older age group (age ≥ 60), the risk of low bone mineral density (z-score < −1) for the subgroup with the highest blood cadmium levels was almost 3-fold compared to the group with lowest blood cadmium levels. We found no similar associations for lead. The observed effects may be caused by higher cadmium exposure in the past. This study strengthens previous evidence that cadmium exposure may affect both bone mineral density and kidney function.

Methods

This study is part of the OSCAR (Osteoporosis—cadmium as a risk factor) study, performed in the southeastern part of Sweden in two communities with environmental cadmium and lead pollution (2,3). A total of 1,465 subjects, ages 16 to 80, who had resided near the battery plant for at least 5 years between 1910 and 1992, were asked to participate, and 904 of them (62%) agreed to do so.

Several workers with previous or current occupational exposure from the two battery plants in the study area were also included.

Out of 242 occupationally exposed workers, 117 (48%) agreed to participate in the examinations.

Thus, 1,021 individuals (60%) agreed to take part in the study and gave their informed consent to the investigation. Among the nonparticipants, a telephone survey of a random sample including 5% of the nonparticipants gave no indication that they differed from the examined group in a systematic way with regard to age, sex, or morbidity.

Each study subject received a questionnaire including questions regarding employment, residence, smoking, and food habits, as well as medical history, especially regarding kidney diseases and diseases related to osteoporosis. Specially trained nurses collected urine and blood samples and measured bone mineral density (BMD), height, and weight.

The presence of cadmium and lead in blood was determined by inductively coupled plasma mass spectrometry (ICP-MS). A quadrupole spectrometer (VG PQ2+; Fisons Elemental, Winsford, Cheshire, UK) equipped with an autosampler (Gilson 222; Gilson, Villiers, France) was used. We used commercial reference samples to check the method accuracy.

We used urinary protein HC (human complex-forming glycoprotein, formerly called α1-microglobulin) to detect early renal damage using single radial immunodiffusion for the determinations. The sensitivity of the method was 1.7 mg/L, and its total analytic imprecision (intra-assay and interassay) was 6% (18). The analyses were made at the Department of Clinical Chemistry at Lund University.

Address correspondence to T. Alfvén, Institute of Environmental Medicine, Karolinska Institutet, Box 210, SE-171 77 Stockholm, Sweden. Telephone: +46-8-728-75-08. Fax: +46-8-30-45-71. E-mail: tobias.alfven@student.ki.se

We thank all the participants in the study and the other team members in project OSCAR: D. Carlsson, L. Hellström, B. Persson, C. Petersson, and G. Spång. We also thank A. Grubb, Department of Clinical Chemistry in Lund, who analyzed the protein HC; the late A. Schütz, Department of Occupational and Environmental Medicine in Lund, who analyzed the cadmium and lead; A-C. Palmqvist and A-K. Blomberg for entering data into computer files.

The study was supported by a grant from the Swedish Environmental Protection Agency.

Received 20 September 2001; accepted 15 January 2002.

Environmental Health Perspectives • VOLUME 110 | NUMBER 7 | July 2002 699
University Hospital. Morning urine was voided in acid-washed polyethylene bottles and stored frozen (−20°C) until transfer to Lund University Hospital. At the laboratory, the sample was thawed and 10 mL urine was poured into a polypropylene tube. Subsamples for the determination of protein HC were pipetted from the sampling bottle into separate tubes and freeze stored until analysis. A preservative solution was added to the subsample for protein HC determination according to Tencer et al. (19). Protein HC was then adjusted to urinary creatinine to account for differences in dilution of the urine. Creatinine was measured using an enzymatic colorimetric method using a Hitachi Modular-P (Roche Diagnostics, Mannheim, Germany).

The cut-off points used for tubular proteinuria were 0.8 mg protein HC/mmol creatinine for men and 0.6 mg/mmol for women, which reflects the upper 95% limit in a Swedish reference population (18).

We measured bone mineral density (BMD) in the forearm, with an ambulant instrument (Osteometer DTX-200; Meditech A/S, Redovre, Denmark), using dual energy X-ray absorptiometry (DXA), which is commonly used to evaluate BMD (20). We measured the nondominant arm with the patient in a supine position. We measured the BMD in the distal site in the forearm, which includes both the radius and the ulna from the 8-mm point (point where the radius and ulna are separated by 8 mm) and 24 mm proximally. The distal site contains 10–20% trabecular bone (21). We checked the internal variation by daily calibration using a phantom. We compared the measured BMD to a reference population furnished by the instrument supplier (Osteometer; Meditech). The reference population did not have any previous or present diseases known to influence calcium metabolism. No restrictions were made on smoking or other lifestyle habits. The ambulant instrument was used and validated in a previous study (22).

The degree of osteoporosis can be assessed by computing an age- and sex-standardized z-score (23). A common definition of low bone mineral density is z-score < −1 (24), which indicates one standard deviation below a sex- and age-standardized mean, which is used in the present study.

Variables with a skewed distribution were log transformed (log e) to achieve normal distribution when appropriate.

Multiple regression was used for the multivariate analysis. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were computed using logistic regression. All the statistical analyses were performed using the STATA 7.0 software (Stata Corp., College Station, TX, USA).

**Results**

Characteristics of the study population regarding sex, age, blood cadmium, blood lead, urinary excretion of protein HC, BMD, and smoking are presented in Table 1. The smokers had been smoking regularly for at least 1 year.

Table 2 shows the regression coefficients for the independent variables age, blood cadmium, blood lead, and smoking, with log-transformed protein HC as the dependent variable. There was a strong positive correlation between blood cadmium and age and protein HC. No similar effect was seen for blood lead. The results changed only marginally when analyzing blood cadmium and blood lead separately or when smoking was excluded. When the analyses were restricted to environmentally exposed persons, the results remained essentially the same.

Another way to examine the relation is to look at the dose–response relationship between blood cadmium and tubular proteinuria. A total of 171 people (128 environmentally and 43 occupationally exposed) had tubular proteinuria, using the above-mentioned cut off points. Figure 1 shows the odds ratios (with 95% CIs) for tubular proteinuria for different blood cadmium groups in the environmentally exposed group, after adjustment for age, sex, and smoking. The cut-off level for the lowest dose group was set at 5 nmol/L, and this group was used as the reference group (n = 658). The remaining subjects were divided into four groups of similar size (n = 84, 93, 80, 94). This produced cut-off-points for the different groups of 5, 7, 10, and 15 nmol/L. Excess risks for tubular proteinuria were found for all the groups exceeding 7 nmol cadmium/L blood.

As shown in earlier published data (2), BMD decreases more rapidly after 55–60 years of age in both men and women. The analyses of BMD thus focused on the older age group (> 60 years). In Table 3, a multiple linear regression is shown for the subgroup older than 60 years, with distal BMD as the dependent variable and age, weight, blood cadmium, blood lead, and smoking as independent variables. In both the whole group and the older subgroup there was a negative correlation between age and BMD and a positive correlation between weight and BMD. There was a negative correlation between cadmium dose, expressed as blood cadmium, for both men and women in the older age group—significant for women and close to significant for men. In contrast, we observed no significant trend for lead. In the whole group (all ages), no significant correlations could be found among blood cadmium, lead, and BMD. Smoking did not alter the analyses in a major way. The results only changed marginally if blood cadmium and blood lead were examined in separate analyses.

We conducted dose–response relationships for the bone effects in a similar way as for the renal effects. Table 4 shows the odds ratios (with 95% CIs) for low bone mineral density (z-score < −1) for three blood cadmium groups for people over 60 years of age, adjusted for weight and smoking. The z-score includes adjustment for age and sex as described above. The cut-off level for the lowest dose group was set at 5 nmol/L as above. The remaining subjects were divided into two groups of similar size (n = 177, 174). This produced cut-off points for the different groups of 5 and 10 nmol/L. Statistically significant differences were seen at blood cadmium levels > 5 nmol/L, and in the group with blood cadmium > 10 nmol/L the OR was 2.9 (95% CI = 1.4–5.8).

Table 1. Characteristics of the 1,021 individuals examined in the study.

| Characteristics | Men (n = 479) | Women (n = 542) |
|-----------------|---------------|-----------------|
|                 | Mean (10th, 90th percentiles) | Mean (10th, 90th percentiles) |
| Age (years)     | 54 (range 18–81) | 52 (range 16–81) |
| Blood Cd (nmol/L) | 7.5 (1.3, 17) | 5.5 (1.5, 12) |
| Blood Pb (μmol/L) | 0.16 (0.08, 0.25) | 0.11 (0.05, 0.17) |
| Urinary protein HC (mg/mmol creatinine) | 0.67 (0.16, 1.2) | 0.46 (0.15, 0.8) |
| Distal bone mineral density (g/cm²) | 0.56 (0.40, 0.67) | 0.44 (0.32, 0.54) |
| Smoking (ex or former) | 53 | 43 |

*Missing analyses for 5 men, 7 women. *Missing analyses for 8 men, 7 women. *Missing analyses for 9 men, 9 women. *Missing records for 3 men, 8 women.

Table 2. Multiple linear regression analysis for log transformed protein HC (mg/mmol creatinine) as a function of age, blood-cadmium, blood-lead, and smoking.

| Characteristics | Men (n = 480) | Women (n = 521) |
|-----------------|---------------|-----------------|
|                 | Regression coefficient | 95% CI | Regression coefficient | 95% CI |
| Age (years)     | 0.023 | 0.019–0.028 | 0.017 | 0.013–0.020 |
| Blood Cd (nmol/L) | 0.016 | 0.009–0.023 | 0.015 | 0.0049–0.025 |
| Blood Pb (μmol/L) | 0.015 | 0.058–0.083 | 0.19 | 0.09–0.80 |
| Smoking (ever or former/current) | -0.042 | -0.18–0.096 | 0.028 | -0.030–0.15 |

R² = 0.26. R² adj = 0.17.
Discussion

Our results show that there is a relationship between blood cadmium and tubular proteinuria and low bone mineral density. We found no similar associations for lead. The relationship between cadmium and tubular proteinuria is strong, even when the occupationally exposed participants are excluded. The subgroup with the highest cadmium levels had a 4-fold increased risk of having tubular proteinuria compared to the subgroup with the lowest blood cadmium levels. In the older age group (age > 60), the risk of low bone mineral density (z-score < −1) for the subgroup with the highest blood cadmium levels was almost three times that of the group with lowest blood cadmium levels.

It is difficult to find a perfect dose estimate for cadmium and lead, as with many other toxic agents. The dose estimate most often used for cadmium is urinary cadmium. However, renal damage may lead to a higher excretion of cadmium, as has been shown both in animal (1,5) and in human studies (1,6,25,26). It has been shown that blood cadmium can be a better dose estimate when tubular proteinuria is present (27). Examination of cadmium-exposed workers more than 15 years after the cessation of exposure showed a stronger association between blood cadmium and tubular proteinuria than between urinary cadmium and tubular proteinuria (27).

During high cadmium exposure, for example through occupational exposure, the cadmium concentration in blood increases relatively rapidly. After some months, cadmium in blood reaches a concentration that corresponds to the intensity of the exposure. If the exposure stops, the blood cadmium concentration decreases fairly rapidly, with an initial half-time of 2–3 months (4,7). However, cadmium accumulated in the body will influence the blood cadmium concentration. Therefore, after exposure ceases, the concentration in blood will not decrease to the preexposure level. Thus, cadmium in blood may serve as a good estimate of the accumulated body burden of cadmium.

Also, in the general population, blood cadmium is influenced largely by the body burden of cadmium. One study on the influence on blood cadmium concentrations from various dietary factors showed no significant association between cadmium concentrations in blood and duplicate diets, while body burden, measured as urinary cadmium and S-ferritin (measure of body iron stores) were the main determining factors for blood cadmium (28). A study of environmentally exposed women in Japan also showed that blood cadmium correlated closely with urinary cadmium. Both blood and urinary cadmium correlated in this study with cadmium in food duplicates (copies of the food eaten by participants during the study) (29).

In nonsmoking, nonoccupationally exposed individuals in Sweden, the blood cadmium levels are usually between 0.9 and 7 nmol Cd/L, but in smokers the concentrations are often considerably higher (30). A Swedish study on an elderly population with a mean age of 87 years showed blood cadmium concentrations of 3.9 nmol/L in nonsmokers and 7.5 nmol/L in current smokers (31). A Japanese study on adult women in an area not defined as cadmium polluted showed mean cadmium levels in blood of 18.9 nmol/L (32). The mean blood cadmium levels in this study (7.6 nmol/L for men and 5.5 nmol/L for women) are in the upper normal limit of the general Swedish population, but lower than in Japan. It is important to remember that it is not possible to directly compare the blood levels in the present study with other groups with another exposure history. Most occupationally exposed and many of the environmentally exposed people in the current study had a much more pronounced exposure earlier when the battery plant was still operating. It is difficult to estimate which blood cadmium levels they had, for example, 30 years ago, although most probably they were higher. Another problem is that the prevalence, rather than the incidence, of tubular proteinuria and low BMD is being analyzed. It is not possible to say how high the exposure was at the time when the tubular proteinuria or the low BMD appeared.

In a Belgian study (33) on environmentally cadmium-exposed individuals, there was a negative correlation between urinary cadmium and forearm bone density in postmenopausal women. The results from the present study are in agreement with the Belgian report, with an effect especially in older people. In our earlier report from project OSCAR, using urinary cadmium as the dose estimate, the effect on the bone mineral density was more pronounced among men than women (2). This is in contrast to the present study where the effect is slightly more pronounced in women. However, it is not only the dose estimate that differs between the two studies; in the previous report an additional 41 occupationally highly exposed men and 2 women were included. These subjects were excluded from the present study because data were missing on blood cadmium and lead.

The effect of cadmium on bone mineral density is much more pronounced in older people (> 60 years) in the present study. This may reflect that the bone is more sensitive to cadmium as the bone ages. Another possible explanation is that it takes a couple of decades for cadmium to affect the bone. The infamous itai-itai disease in Japan, characterized by severe osteoporosis and osteomalacia, was most likely caused by cadmium and was found almost exclusively in older women (4).

In contrast to our findings on cadmium, we found no associations between blood lead and tubular proteinuria measured as protein HC excretion. The mean blood lead levels in

Table 3. Multiple linear regression analysis of BMD for the subgroup ages 60 years and older, as a function of age, weight, blood cadmium, blood lead, and smoking.

| Characteristics | Regression coefficient | 95% CI | Regression coefficient | 95% CI |
|-----------------|------------------------|--------|------------------------|--------|
| Age (years)     | 0.0035                 | 0.0058–0.0013 | 0.0055                 | 0.0074–0.0035 |
| Weight (kg)     | 0.0022                 | 0.0011–0.0032 | 0.0026                 | 0.0017–0.0035 |
| Blood Cd (nmol/L) | 0.00044               | 0.0002–0.0035 | 0.0030                 | 0.0054–0.0066 |
| Blood Pb (µmol/L) | 0.048                | 0.20–0.10   | 0.078                  | 0.057–0.21 |
| Smoking (never or former/current) | 0.020                | 0.044–0.0035 | 0.019                  | 0.0077–0.045 |

* R² = 0.21, R² = 0.28.

Table 4. Logistic regression model for low BMD (z-score < −1) including blood cadmium and smoking as categoric variables and weight as a continuous variable, for the subgroup older than 60 years.

| Variable          | OR | 95% CI |
|-------------------|----|--------|
| Blood Cd < 5 nmol/L (mean 2.5) | 1  | —      |
| Blood Cd ≥ 5 nmol/L and <10 nmol/L (mean 7.2) | 2.0 | 1.1–3.9 |
| Blood Cd ≥ 10 nmol/L (mean 21) | 2.9 | 1.4–5.8 |
| Smoking           | 0.62 | 0.46–1.5 |
| Weight            | 0.96 | 0.94–0.98 |
our study were 0.16 µmol/L for men (range 0.08, 0.25) and 0.11 µmol/L for women (range 0.05–0.17). The levels that appeared to be the threshold for proximal tubular injury in both animal and human studies have been around 3 µmol/L ([7]). In concordance with the present results, other studies with lower lead blood levels have shown negative relations between blood lead kidney function ([26]).

Neither could we find any associations between lead and distal forearm bone mineral density. Different experimental and some human studies have shown that lead also may affect the bone. Studies on children have shown negative correlations between lead in bone and the levels of 1,25-dihydroxyvitamin-D ([34,35]). Experimental studies have shown different possible mechanisms on how lead may affect bone ([13]). It is possible that bone effects from lead exposure can occur at higher levels than in the present study.

Lead is often and most easily measured in blood, and it is a commonly used indicator of the total body burden ([9]). However, the half-life of lead in blood is short, about 36 days ([9]), so it typically represents mostly, but not only, recent exposure. Lead in blood is derived from levels in the environment and from lead stored in tissues, mostly bone, that reenters the blood. Maybe the results would have been different if the total body burden could have been better measured. Methods for detecting low lead levels in bone with in vivo X-ray fluorescence are now available ([36,37]), but are not easily accessible.

Thus, this report in combination with our earlier studies ([2,3]) show that cadmium exposure is related to early renal and bone effects regardless whether urinary or blood cadmium is used for dose estimation. The possible effect of tubular damage on the excretion of cadmium does not appear to confound these findings. Lead does not seem to be a confounder.

It is still debated whether early renal effects such as tubular proteinuria have any clinical effects. However, a newly published study from the area where this study was performed shows that the age-standardized rate ratio for end stage renal disease increased from 1.4 in the low-exposure group to 1.9 and 2.3 in the moderate- and high-exposure groups, respectively ([15]).

To summarize, we found a relationship between low blood cadmium and tubular proteinuria and low bone mineral density. These associations may be caused by higher cadmium exposure in the past. We found no such associations for blood lead. This study strengthens previous evidence that environmental cadmium exposure may affect both BMD and kidney function.

REFERENCES AND NOTES

1. Friberg L, Elinder C-G, Kjellström T, Nordberg GF. Cadmium and Health: A Toxicological and Epidemiological Appraisal. Boca Raton, FL: CRC Press Inc, 1985.
2. Alfvén T, Elinder C-G, Carlsson MD, Grubb A, Hellström L, Persson B, Pettersson C, Spång G, Schütz A, Järup L. Low level cadmium exposure and osteoporosis. J Bone Miner Res 15:1579–1586 ([2000]).
3. Jarup L, Hellström L, Alfvén T, Carlsson MD, Grubb A, Persson B, Pettersson C, Spång G, Schütz A, Elinder CG. Low level exposure to cadmium and early kidney damage: the OSCAR study. Occup Environ Med 57:668–672 ([2000]).
4. Elinder C-G, Friberg L, Nordberg GF, Kjellström T, Överdöster G. Biological Monitoring of Metals. Geneva: World Health Organization, 1994.
5. Nordberg G, Piscator M. Influence of Long-term cadmium exposure on urinary excretion of protein and cadmium in mice. Environ Physiol Biochem 23:47–49 ([1972]).
6. Mason HJ, Williams N, Armitage S, Morgan M, Green S, Perrin B, Morgan WD. Follow up of workers previously exposed to silver solder containing cadmium. Occup Environ Med 55:553–556 ([1999]).
7. Jarup L, Rogfenfelt A, Elinder CG, Nogawa K, Järup L. Biological half-time of cadmium in the blood of workers after cessation of exposure. Scand J Work Environ Health 9:327–331 ([1983]).
8. Jarup L, Elinder CG, Spång G. Cumulative blood-cadmium and tubular proteinuria: a dose-response relationship. Int Arch Occup Environ Health 60:223–229 ([1988]).
9. WHO. Inorganic Lead. Geneva: World Health Organization, 1995.
10. Stæssen JA, Lauwereys RR, Buchet JP, Bullpit CJ, Rondia D, Vanrenterghem Y, Amery A. Impairment of renal function with increasing blood lead concentrations in the general population. The Cadmiubul Group. N Engl J Med 327:151–156 ([1992]).
11. Loghman-Adham M. Renal effects of environmental and occupational lead exposure. Environ Health Perspect 105:928–939 ([1997]).
12. Barry PS. A comparison of concentrations of lead in human tissues. Br J Ind Med 32:119–139 ([1975]).
13. Gouy R, Estévez, Bhattacharjya M, Korch K, Poussaint J. Environmental risk factors for osteoporosis. Environ Health Perspect 102:390–394 ([1994]).
14. Bergbäck B, Carlsson M. Heritage of cadmium and lead. A case study of a Swedish accumulator factory. Sci Total Environ 166:35–42 ([1995]).
15. Hellström L, Elinder C-G, Dahlberg B, Lundberg M, Jarup L, Persson B, Axelsson O. Cadmium exposure and end-stage renal disease. Am J Kidney Dis 38:1001–1008 ([2001]).
16. Kjellström N, Efron PE, Schütz A. Biological monitoring of metals. Geneva: World Health Organization, 1994.
17. Jarup L, Elinder CG, Nordberg G, Vahter M. Cumulative blood-cadmium and tubular proteinuria: a dose-response relation-ship. Int Arch Occup Environ Health 36:275–285 ([1976]).
18. Buchet JP, Roels H, Bernard A, Lauwereys R. Assessment of renal function of workers exposed to inorganic lead, cad-mium or mercury vapor. J Occup Med 22:741–750 ([1980]).
19. Jarup L, Persson B, Elinder CG. Blood cadmium as an indicator of dose in a long-term follow-up of workers previously exposed to cadmium. Scand J Work Environ Health 23:31–36 ([1997]).
20. Berglund M, Axelson O, Nenmell B, Vahter M. Intestinal absorption of dietary cadmium in women depends on body iron stores and fiber intake. Environ Health Perspect 102:1058–1066 ([1994]).
21. Shimbo S, Zhang ZW, Moon CS, Watanabe T, Nakatsu H, Matsuda-Inoguchi N, Higashikawa K, Ikeda M. Depression of renal function with increasing blood lead concentrations, and dietary intake of cadmium and lead among women in the general population of Japan. Int Arch Occup Environ Health 72:163–170 ([2000]).
22. Jarup L, Berglund M, Elinder CG, Nordberg G, Vahter M. Health effects of cadmium exposure—a review of the litera-ture and a risk estimate. Scand J Work Environ Health 24 Suppl 1:81–98 ([2000]).
23. Nordberg M, Winblad B, Basun H. Cadmium concentra-tion in blood in an elderly urban population. Biometals 13:311–317 ([2000]).
24. Ikeda M, Zhang ZW, Higashikawa K, Watanabe T, Shimbo S, Moon CS, Nakatsu H, Matsuda-Inoguchi N. Background exposure of general women populations in Japan to cadmium in the environment and possible health effects. Toxicol Lett 108:161–168 ([1999]).
25. Stæssen JA, Roels HA, Emelison D, Kuznetsova T, Thijis L, Vangronsveld J, Fager R. Environmental exposure to cadmium, forearm bone density, and risk of fractures: prospective population study. Public Health and Environmental Exposure to Cadmium (Pheeco) Study Group. Lancet 352:1140–1144 ([1998]).
26. Koo WW, Suppan PA, Bomschein RL, Krug-Wispe SK, Stoneberg JJ, Tsang RC, Berger DG. Serum vitamin D metabolites and bone mineralization in young children with chronic low to moderate lead exposure. Pediatrics 97:680–687 ([1996]).
27. Mahaffey KR, Rosen JF, Chesney RW, Peeler JT, Smith CM, Deluca HF. Association between age, blood lead concentration, and serum 1,25-dihydroxycholecalciferol levels in children. Am J Clin Nutr 55:1327–1331 ([1992]).
28. Hu H, Milder FL, Burger DE. X-ray fluorescence measure-ments of lead burden in subjects with low-level commu-nity lead exposure. Arch Environ Health 45:199–206 ([1994]).
29. Lilley J, Walters BG, Heath DA, Droz Z. In vivo and in vitro precision for bone density measured by dual-energy X-ray absorptiometry. Osteoporos Int 1:141–146 ([1991]).
30. Schlenker RA, VonSeggen WW. The distribution of corti-cal and trabecular bone mass along the lengths of the radius and ulna and the implications for in vivo bone mass measurements. Calcif Tissue Res 20:31–52 ([1976]).
31. Nordberg M, Winblad B, Basun H. Cadmium concentr-a-tion in blood in an elderly urban population. Biometals 13:311–317 ([2000]).