The Relationship Between Bone Lead and Hemoglobin

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Objective.—To determine whether the concentration of lead in bone constitutes a biological marker that is more sensitive for chronic toxicity than blood lead levels.

Design.—Survey.

Setting.—A construction trade union with members who engage in carpentry, demolition, and other construction activities.

Participants.—Members of the construction trade union.

Main Outcome Measures.—We measured blood pressure, serum creatinine, hematocrit, and hemoglobin. We measured blood lead by anodic stripping voltametry and used a cadmium 109 K x-ray fluorescence instrument to make in vivo measurements of lead in the tibia (a heavily cortical bone) and the patella (a heavily trabecular bone). Information was also collected on medical history, smoking, and alcohol ingestion.

Results.—Bone lead levels in the patella were found to be significantly correlated with a decrease in hemoglobin and hematocrit, even after adjusting for age, blood lead, body mass index, cigarette smoking, and alcohol ingestion and removing outliers. Blood lead levels were low (mean=0.40 μmol/L [8.3 μg/dL]) and were not correlated with either hemoglobin or hematocrit. In the final multivariate regression model that corrected for measurement error, an increase in patella bone lead level from the lowest to highest quintile in this study population (37 μg/g) was associated with a decrease in hemoglobin and hematocrit of 11 g/L (95% confidence interval [CI], 2.7 to 19.3 g/L) and 0.03 (95% CI, 0.01 to 0.05), respectively.

Conclusion.—We conclude that patella bone lead levels are associated with decreased hematocrit and hemoglobin levels despite the presence of low blood lead levels. This conclusion may reflect a subclinical effect of bone lead stores on hematopoiesis and is the first epidemiological evidence that bone lead may be an important biological marker of ongoing chronic toxicity.

(*JAMA*. 1994;272:1512-1517)

DESPITE the decline in occupational and environmental lead exposure that the United States and other countries have experienced in the last few decades, much concern remains regarding the toxicologic implications of lead exposure. Most of this concern has been driven by laboratory and epidemiological research linking ever lower levels of lead exposure, as reflected by blood lead levels, with deficits in neurobehavioral functioning and elevated blood pressure.[1]

An additional concern is that lead is known to accumulate in the skeleton, with a half-life of years to decades.[2,3] Bone serves as a long-lived repository of 75% and 90% to 95% of lead in children and adults, respectively.[4-6] Many studies have demonstrated that bone lead levels remain elevated despite declines in blood lead, raising the issue of whether bone lead may be a better biological marker of chronic toxicity. Indirect evidence has begun to mount that lead is released from these bone stores, particularly during times of increased bone turnover.[7,8]

Until recently, human studies on the toxicologic significance of bone lead stores have not been possible. However, with the development of in vivo K x-ray fluorescence (KXRF), it is now possible to conduct epidemiological studies using bone lead level as a measure of cumulative lead exposure.[9] This technique, under steady development during the last 10 years, measures stores of lead in bone.

The field is still young, however. Few studies have specifically examined the relationship between bone lead and outcomes indicative of toxicity. Most studies have concentrated on surveying bone lead levels among groups of subjects[10-14] and examining the kinetics of bone lead in relation to blood lead and chelatable lead.[15-17] Two investigations with an etiologic component were limited to assessing the relationship between KXRF-measured bone lead and indicators of kidney damage among occupational groups with very high exposures.[18,19] We report herein a cross-sectional investigation in which we measured blood lead and bone lead among workers with only moderate lead exposure histories and related these measures to blood pressure and indicators of renal function and hematologic status. We found a significant negative relationship of bone lead levels to hemoglobin and hematocrit, despite low blood lead levels.

METHODS

The International Brotherhood of Carpenters and Joiners (also known as the United Brotherhood of Carpenters) is one of the largest trade unions in the United States. Members of this union are en-

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gaged primarily in carpentry, but also work in a variety of other occupations and activities associated with building construction or renovation. Some work may involve lead exposure, such as demolition of surfaces coated with lead paint, welding, or working with plumbers who use lead solder, or scrap metal work.

In 1991, the United Brotherhood of Carpenters Health and Welfare Fund, with support from the National Institute for Occupational Safety and Health, arranged with us to conduct a screening of a sample of their members during their 1991 national convention in Atlantic City, NJ.

Selection of Subjects for Screening

Since the duration of the convention and the time requirements for each bone lead measurement protocol limited the number of subjects we could screen, we used the results from returned questionnaires to perform a stratified sampling procedure to increase the number of targeted subjects who were at the extremes of age (<35 years and >55 years), nonwhite, or female and the number of subjects who reported no activities with known exposures to lead. A total of 250 subjects were targeted for 132 screening slots and received a preconvention recruitment flyer inviting them to join the study. At the time of registration for the convention, participation by targeted subjects was confirmed, and those who consented were scheduled for the lead examination protocol.

Examination Protocol

Subjects in this protocol filled out a detailed questionnaire on occupational activities, medications, and lifestyle habits, including smoking and the ingestion of alcohol, and underwent bone lead examination by a KXRF instrument, blood pressure determination, and phlebotomy for determination of blood lead levels and other parameters.

Resting blood pressure was determined using a standard sphygmomanometer by a nurse. After each subject was seated and waited for 3 minutes, the systolic and fifth-phase diastolic blood pressure was measured to the nearest 2 mm Hg of pressure in the left arm.

Blood lead was measured by anodic stripping voltametry, using an ESA Inc, Chelmsford, Mass, model 3010. Of the samples, 8% consisted of blinded reference material from the New York State Department of Health. The coefficient of variation for analyses in this laboratory have been estimated as 10%, 8%, and 5% to 6% at blood lead concentrations of 0.05 to 0.48, 0.48 to 1.45, and 1.45 to 2.89 μmol/L (1 to 10, 10 to 30, and 30 to 60 μg/dL), respectively.

For each individual, a complete blood count and hematocrit, using an Argos ABX automated analyzer, and serum chemistries, using an Olympus AU5061 multichannel analyzer, were measured.

KXRF Bone Lead Measurements

Bone lead measurements were taken of each subject's midtibial shaft and patella using a KXRF instrument (Abiomed Inc, Danvers, Mass). The physical principles, technical specifications, and validation of this[20,21] and other KXRF instruments[22,23] have been described in detail elsewhere.[14] In short, this instrument uses a cadmium 109 (^{109}Cd) γ-ray source to provoke the emission of fluorescent photons from target tissue that are then detected, counted, and arrayed on a spectrum.[24] The net lead signal is determined after subtraction of Comptom background counts using a linear least-squares algorithm. The lead fluorescence signal is then normalized to the elastic or coherently scattered τ-ray signal, which arises predominantly from the calcium and phosphorus present in bone mineral. The unit of measurement so derived is micrograms of lead per gram of bone mineral (μg/g).

Since the instrument provides a continuous unbiased point estimate that oscillates around the true bone lead value, negative point estimates are sometimes produced when the true bone lead value is close to zero. The instrument also provides an estimate of the uncertainty associated with each measurement that is derived from a goodness-of-fit calculation of the spectrum curves and is equivalent to a single SD. Although a minimum detectable limit calculation of twice this value has been proposed for interpreting an individual's bone lead estimate,[25] retention of all point estimates makes better use of the data in epidemiological studies.[26]

By normalizing the measurement to calcium counts, the measurement is rendered insensitive to variations in the shape, size, density, and histomorphometry of bone, overlying tissue thickness, and movement.[22] Validation studies of the instrument we used have indicated a fairly high degree of precision and accuracy of the point and measurement uncertainty estimates in comparison with chemical analyses in studies of lead-doped phantoms and cadaveric legs[20,22] and studies involving repeated measurements.[27]

For our study, 12½-minute measurements were taken at the midshaft of the left tibia and at the left patella after each region had been washed with a 50% solution of isopropyl alcohol. The KXRF beam collimator was sited perpendicular to the bone surface for the tibia and at 30° in the lateral direction for the patella.

Position of the peak spectra on a lead target was checked three times daily for calibration. At the close of each day's measurements, the room housing the KXRF instrument was cleaned with a high-efficiency, particulate-air–filtered vacuum cleaner (Nilfisk Inc, model G580, Malvern, Pa), and the subject's test chair was wiped with isopropyl alcohol. A blank phantom was then positioned and measured 20 consecutive times overnight as an additional calibration check; analysis of means and SDs did not disclose any significant shift in accuracy or precision.

Data Analysis

The focus of these analyses was on bone lead and blood lead measurements as predictors and blood pressure, serum creatinine, serum uric acid, systolic and diastolic blood pressure, hematocrit, and hemoglobin as outcome variables. Age, body mass index (weight in kilograms divided by the square of height in meters), cigarette smoking (<1, 1 to 20, or >20 cigarettes smoked per day, on average), and alcohol consumption (<2 or ≥2 drinks per day, on average) were examined as covariates in these relationships. We have reported elsewhere our analyses of occupational, environmental, and lifestyle correlates of bone and blood lead levels from this study.[28]

Since age has been observed to be a strong correlate of bone lead levels from many previous investigations[14,21,29,30] and could confound the relationships between bone lead and outcome, we examined smooth plots of all variables against age. Both tibia and patella bone lead were found to have a strong positive relationship with age that was mostly linear.

To examine the form of the relationship between the outcome variables and predictors after controlling for age, we examined smooth plots of the residuals from the regression of the outcomes and predictors on age. (Smooth plots were performed with LOWESS,[31] which fits a nonparametric curve to a bivariate scatterplot using robust locally weighted regressions.) The smooth plots suggested that diastolic blood pressure, serum creatinine, serum uric acid, hematocrit, and hemoglobin were linearly associated with bone lead and blood lead, while a log transformation on bone lead was more appropriate for analyzing systolic blood pressure.

The analyses were performed using multivariate linear regression models. Covariates were selected for inclusion depending on whether enough evidence existed from previous investigations to include each covariate in the model. Table 1 summarizes the variables inserted in each outcome model. Model selection was performed separately for each outcome

Table 1.—Covariates Included in the Initial Saturated Regression Models for Blood Pressure, Serum Uric Acid, Serum Creatinine, Hematocrit, and Hemoglobin

Outcomes of Interest	Age	Body Mass Index	Smoking	Alcohol Intake	Hypotensive Medications
Blood pressure (systolic and diastolic)	x	x	x	x	x
Serum creatinine	x	x	x		
Serum uric acid	x	x		x	x
Hemoglobin	x	x	x	x	
Hematocrit	x	x	x	x	
Hypertension*	x	x	x	x	

*Defined as taking medications for hypertension on a regular basis, systolic blood pressure greater than 160 mm Hg, or diastolic blood pressure greater than 95 mm Hg.

Table 2.—Range, Mean (±SD), and Median of Age, Lead Biological Markers, and Outcomes of Interest Among Carpenters (n=119)*

Variable	Range	Mean (±SD)	Median
Lead Biomarkers and Other Covariates			
Age, y	23-67	48.6 (9.6)	49
Blood lead, μmol/L (μg/dL)	0.09-1.20 (2-25)	0.40 (0.19)(8.3 [4.0])	0.38 (8)
Tibia bone lead, μg/g†	−15-39	9.8 (9.5)	9
Tibia bone lead Measurement error, μg/g	5-14	7.1 (1.4)	7
Patella bone lead, μg/g†	−11-78	13.9 (13.6)	12
Patella bone lead, μg/g Measurement error, μg/g	3-15	8.0 (1.6)	8
Outcomes of Interest			
Systolic blood pressure, mm Hg	106-186	135 (18)	130
Diastolic blood pressure, mm Hg	60-112	85 (9)	84
Body mass index	19.5-45.9	29.9 (4.6)	29.1
Serum creatinine, μmol/L (mg/dL)	79-203 (0.9-2.3)	110 (16) (1.25 [0.18])	106 (1.2)
Serum uric acid, μmol/L	214-714	381 (83)	387
Hemoglobin, g/L	123-190	151 (10)	151
Hematocrit	0.38-0.55	0.45 (0.03)	0.45

*Of the 119 carpenters, 90 were normotensive and 29 were hypertensive, which was defined as taking medications for hypertension on a regular basis, systolic blood pressure greater than 160 mm Hg, or diastolic blood pressure greater than 95 mm Hg.

†Bone lead is measured in micrograms of lead per grams of bone mineral. Negative bone lead values sometimes result because the curve-fitting measurement procedure of the K x-ray fluorescence instrument produces estimates that fluctuate around the true value; if the true value is close to zero, and there is a relatively large error associated with the measurement, multiple measurements will produce some estimates that are positive and some that are negative.

variable by the method of backward elimination starting with a model that included all predictors and covariate variables transformed as suggested by the smooth plots. The elimination of variables terminated when no additional variable could be discarded without a decrease in the total model R^2 of at least 10%.

Measurement uncertainty in an independent variable biases the ordinary least-squares estimate of its effect toward the null. Adjusted parameter estimates that are approximately unbiased can be obtained when there is information about the measurement error variability using the method of Fuller.[32] Fuller's method is approximately equivalent to multiplying the ordinary least-squares estimate, β_{OLS}, of the regression parameter corresponding to the mismeasured covariate by an estimate of the reliability ratio. Namely, the corrected $\beta \approx \lambda\ \beta_{OLS}$, where $\lambda = \Sigma$ (measured bone lead^2)/Σ (measured bone lead^2–estimated measurement error variance). Using the estimates of measurement uncertainty associated with each bone lead measurement, we applied this method to the final regression models for each outcome variable to calculate adjusted parameter estimates and 95% confidence intervals (CIs).

In models of systolic and diastolic blood pressure, analyses were examined both with and without subjects who indicated they took daily medications with a hypotensive effect. To further examine the relationship of lead to blood pressure, subjects were classified as hypertensive if they indicated regular ingestion of at least one medication to treat hypertension (diuretic, centrally acting hypotensive agent, vascular smooth-muscle relaxant, angiotensin-converting enzyme blocker, β-blocker, or calcium channel blocker) or had a systolic blood pressure of greater than 160 mm Hg or a diastolic blood pressure of greater than 95 mm Hg. Using a logistic regression model of hypertensive vs nonhypertensive and including covariates listed in Table 1, we then performed the backward-elimination procedure described herein.

Table 3.—Smoking and Alcohol Consumption Among Carpenters (n=119)

Variable	No. (%)
Usual cigarette smoking, No. of cigarettes per day	
0	95 (80)
1-20	11 (9)
>20	13 (11)
Usual alcohol consumption, No. of drinks per day	
0	30 (25)
1-2	25 (21)
3-7	34 (29)
>7	30 (25)

Results of all models were run both with and without data identified as outliers by the extreme studentized residuals method.[33]

RESULTS

We completed KXRF measurements of bone lead, blood pressure, complete blood cell counts, and serum chemistry on 119 subjects. As a check on the quality of the bone lead data, the median and distribution of the individual measurement uncertainty estimates were examined for the tibia and patella measurements. No measurement had an uncertainty estimate that was more than twice greater than the median uncertainty estimate.

Subjects ranged in age from 23 to 67 years with a mean (±SD) of 48.6 years (±9.6 years) (Table 2). All but two subjects were men, and there were only three blacks and one Asian. Blood lead levels were low, with a mean (±SD) of 0.40 μmol/L (±0.19 μmol/L) (8.3 μg/dL [±4.0 μg/dL]). Tibia bone lead levels had a mean (±SD) of 9.8 μg/g (±9.5 μg/g), whereas patella bone lead levels were somewhat higher with a mean (±SD) of 13.9 μg/g (±13.6 μg/g). The estimates of measurement uncertainty were distributed normally for both the tibia and patella and were not correlated with any of the outcome measures. Most subjects were nonsmokers (Table 3). Blood pressure, serum creatinine, uric acid, hematocrit, and hemoglobin levels were predominantly in the normal range.

Both tibia and patella bone lead levels had a strong positive correlation with age (Figure 1), with smooth plots indicating generally linear relationships.[28] In a matrix of Pearson correlations, both age-adjusted tibia and patella bone lead levels were correlated ($P<.15$ or below) with hematocrit and hemoglobin (Table 4). Blood lead level was not correlated with age or with any of the outcome variables of interest.

In the final step-wise multivariate regression models, patella bone lead was found to be the strongest predictor of both hemoglobin and hematocrit (Table 5). These relationships remained significant ($P<.05$) with or without two outliers identified by the extreme studen-

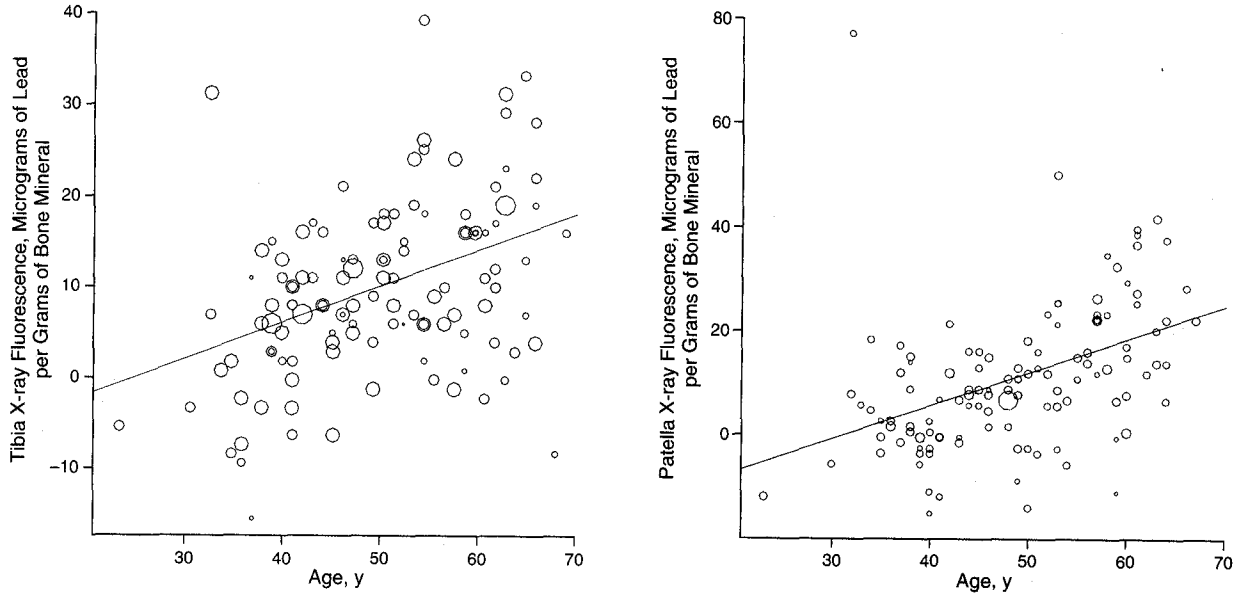

Figure 1.—Left, Scatterplot and regression line of tibia bone lead level vs age in 119 carpenters. Size of the diameter of each point is proportional to the inverse of the estimate of uncertainty for the bone K x-ray fluorescence measurement (the smaller the point, the larger the estimated measurement uncertainty). Univariate regression of bone lead on age was Y=0.41x−9.7, where Y=tibia bone lead (micrograms per grams of bone mineral) and X=age in years. Right, Scatterplot and regression line of patella bone lead level vs age in 119 carpenters, Y=0.68x−18.8.

Table 4.—Pearson Correlation Coefficients for Biological Markers of Lead, Smoking, Alcohol Consumption, and Outcomes of Interest*

Variable	Age	Blood Lead	Tibia Bone Lead	Age-Adjusted Tibia Bone Lead	Patella Bone Lead	Age-Adjusted Patella Bone Lead	Body Mass Index	Cigarettes Smoked	Alcoholic Drinks
Age	...	−0.04	0.41†	...	0.44†	...	0.32†	−0.07	−0.06
Blood lead	...	...	0.12	0.15‡	0.19§	0.24†	−0.01	−0.14‡	0.15‡
Tibia bone lead	...	...	...	...	0.55†	0.41†	0.14‡	0.15‡	−0.05
Age-adjusted tibia bone lead	...	...	...	...	0.40†	0.45†	0.01	0.14‡	−0.08
Patella bone lead	...	...	...	...	...	...	0.15‡	−0.09	0.08
Age-adjusted patella bone lead	...	...	...	...	...	...	0.01	−0.07	0.07
Body mass index	...	...	...	...	...	...	...	0.04	−0.02
Cigarettes smoked	...	...	...	...	...	...	...	...	−0.04
Hematocrit	−0.08	−0.05	−0.19§	−0.17‡	−0.23§	−0.22§	0.01	0.11	0.06
Hemoglobin	−0.05	−0.06	−0.17‡	−0.16§	−0.22§	−0.22§	0.11	0.16‡	0.09
Systolic blood pressure	0.29†	−0.08	0.19§	0.08	0.18‡	0.05	0.38†	−0.03	0.00
Diastolic blood pressure	0.12	−0.10	0.07	0.02	−0.02	−0.08	0.29†	−0.03	0.05
Serum creatinine	−0.03	−0.11	−0.01	0.00	0.02	−0.01	0.06	−0.07	−0.01
Serum uric acid	0.01	0.03	−0.08	−0.09	0.09	0.10	0.25†	−0.02	0.17‡

*Ellipses indicate no correlation.
†$P<.01$.
‡$P<.15$.
§$P<.05$.

tized residuals method, one of whom was 23 years of age and the other of whom had a patella bone lead level of 78 μg/g.

In the final model of hemoglobin, which included alcohol ingestion and body mass index, an increase in patella bone lead of 37 μg/g (the difference between the medians of the lowest and highest quintiles of patella bone lead) was predicted to be associated with a decrease in hemoglobin of 7 g/L. The total R^2 of the model was .078. In the final model of hematocrit, which included alcohol ingestion, an increase in patella bone lead of 37 μg/g was associated with a 1.9% decrease in hematocrit, and the total model R^2 was .061. A smooth plot of patella bone lead vs hemoglobin after adjustment for alcohol ingestion and body mass index revealed a fairly linear negative relationship (Figure 2). After correcting the analyses for the presence of measurement error in the bone lead variable, an increase in patella bone lead from the lowest to highest quintile in this study population (37 μg/g) was associated with a decrease in hemoglobin and hematocrit of 11 g/L (95% CI, 2.7 to 19.3 g/L) and 0.03 (95% CI, 0.01 to 0.05), respectively.

Patella bone lead, tibia bone lead, and blood lead were not found in the regression models considered to be significantly correlated with any of the other outcome variables of interest (serum creatinine, serum uric acid, systolic and diastolic blood pressure, and hypertension).

COMMENT

We previously reported a case study in which bone lead was found to be the source of recurrent lead toxicity long after environmental lead exposure had ceased in a 37-year-old woman who had developed increased bone turnover during thyrotoxicosis.[34] The present study, however, is to our knowledge the first epidemiological study to suggest that

Table 5.—Final Regression Models for Hemoglobin and Hematocrit*

Predictor Variable	Parameter Estimate	SE	P
	Hemoglobin		
Intercept	14.395	0.604	.001
Patella bone lead, μg/g	−0.019	0.0069	.008
Alcoholic drinks of >2 per d, yes/no	0.078	0.068	.257
Body mass index	0.031	0.020	.129
	Hematocrit		
Intercept	46.093	0.404	.001
Patella bone lead, μg/g	−0.052	0.019	.009
Alcoholic drinks of >2 per d, yes/no	0.173	0.193	.373

*Backward-selection procedure, beginning with saturated model that included age, patella and tibia bone lead, blood lead, current smoking (yes/no), alcoholic drinks of more than two per day (yes/no), and body mass index. The procedure was terminated when no additional variable could be dropped without a decrease in the total model R^2 of at least 10%. For hemoglobin, model R^2=.078; for hematocrit, model R^2=.061.

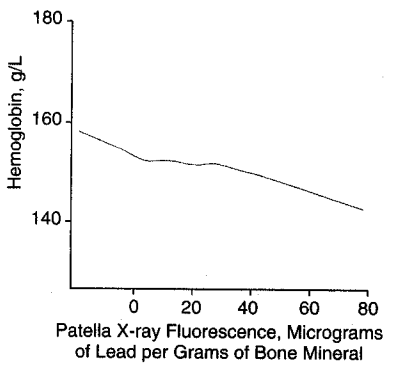

Figure 2.—Smooth plot of patella bone lead vs hemoglobin after adjustment for alcohol ingestion and body mass index.

accumulated bone lead exerts subclinical toxicity in a population of apparently normal men with low blood lead levels.

In our investigation, patella bone lead remained strongly associated with decreases in both hemoglobin and hematocrit before and after adjusting for age, tibia bone lead, blood lead, body mass index, cigarette smoking (which can lead to hemoconcentration), and alcohol ingestion (which can lead to hemoconcentration acutely and depress hematopoiesis chronically). The final model R^2 values were less than .10, reflecting weak explanatory power of the final models; however, the P values for patella bone lead were less than .01, and the true explanatory power of bone lead is probably higher when the error of our bone lead measurements is taken into account. Moreover, even though our final model corrected for measurement error associated with the KXRF technique, there is an additional error in attempting to estimate the entire body lead burden by measurement of a single site[35]; thus, the true relationship between entire body lead burden and hemoglobin and hematocrit is likely to be steeper.

Although it is clear from our previous report that these subjects had performed certain occupational activities, ie, welding, paint stripping, and demolition, that increased their lead exposure above that which would be expected in the general population, as carpenters they performed these activities only sporadically.[28] In comparison with four previous investigations of "normal" populations using the ^{109}Cd KXRF technique, the subjects in this study had bone lead levels that were only moderately elevated.[14,21,28,36]

The significance of patella bone lead exceeded that of the tibia despite the greater measurement error associated with the patella measurements. This occurrence may reflect the fact that unlike the tibia, which is made of dense cortical bone, the patella bone is a highly trabecular bone, which is know to have more dynamic turnover of lead.[17,24,37]

This investigation cannot elucidate the mechanism by which bone lead may exert a depressive effect on hemoglobin and hematocrit. Blood lead levels were low and not predictive of lower hemoglobin and hematocrit. This result is in keeping with a previous study suggesting that blood lead levels must exceed 1.21 μmol/L (25 μg/dL) before impaired hematopoiesis can be detected.[38] Decreased red blood cell survival has been associated with greatly elevated blood lead levels,[39,40] but is unlikely to be a factor among those men considering their low blood lead levels. It is possible that this association represents an inhibitory effect on hematopoiesis through depression of erythropoietin, as suggested by Graziano et al,[41] who found a negative association between serum erythropoietin levels and blood lead levels among adult women. Bone lead may serve as a proxy of elevated kidney lead burden, where erythropoietin synthesis takes place. Alternatively, bone lead may depress heme synthesis enough (through the inhibition of δ-aminolevulinic acid dehydratase and ferrochelatase) to have a direct effect on hematopoiesis. How this might occur in the presence of low blood lead is obscure; one possibility is that bone lead directly elevates serum ionized lead levels without a discernible increase in blood lead, a possibility suggested by some kinetic models of blood lead partitioning.[42,43] Finally, without a direct measure of iron stores, we cannot rule out the possibility that iron deficiency, which increases lead absorption and causes anemia, was an unmeasured confounder; however, iron deficiency would have had to be present in a number of our subjects for years to increase bone lead, a possibility that seems remote in a group of working men presumably ingesting a normal American diet.

This investigation had several limitations. Our sample size was relatively small. The 12½-minute KXRF measurements that were allotted to each bone site allowed us to evaluate many more research subjects than would have been possible with the 30-minute measurements we usually used for our studies; however, the shorter time significantly increased our measurement error. In addition, we were using a prototype KXRF instrument for this work; ongoing and future work will take advantage of newer KXRF designs that afford greater measurement precision.[22,27] We had no measure of δ-aminolevulinic acid dehydratase activity or serum erythropoietin, which may have allowed us to determine the mechanism of bone lead's effect. Our analysis of blood pressure suffered by the error associated with a single blood pressure measurement.

No relationship was found between bone lead and blood pressure, serum creatinine, serum uric acid, or hypertension, despite studies indicating an association between blood lead and these outcomes[44]; this may be a reflection of measurement error and the small sample size of our study, however.

In summary, this investigation provides new clues in understanding the full toxicologic implications of lead exposure and accumulation. Since bone lead may be a better biological marker than blood lead for chronic toxicity, further research should be directed at the relationship of bone lead to the outcomes explored in this study as well as others, such as cognitive functioning, peripheral nerve conduction, and reproductive outcomes.

This study was supported by the National Institute for Occupational Safety and Health, United Brotherhood of Carpenters (UBC), and National Institute of Environmental Health Sciences (NIEHS) Occupational and Environmental Health Center grants 2 P30 ES 00002, ES 05257-01A1, and P42-ES05947. The KXRF instrument used in this work was developed by Abiomed Inc, Danvers, Mass, with support from National Institutes of Health grant SBIR 2R44 ES03918-02.

Many thanks to Doug Burger, PhD, for his technical assistance with the KXRF instrument. Many thanks also to a dedicated research team including Marisa Barr, MS, Scott Slater, Sudha Kotha, MPH, Sybil Wyatt, Frances Perez, and Lynn Ratkos, MS. Carrie Wager conducted all programming for data

analyses. This research would not have been possible without Edward Gorman III, JD, director of the UBC Health and Welfare Fund, Michael Buchet, JD, policy coordinator, UBC, and the UBC members who participated in this study.

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Conversion From Système International (SI) Units to Traditional Units (Modified From *The SI Manual in Health Care*)

System	Component	SI Reference Interval*	SI Unit	Conversion Factor (Divide by)	Traditional Reference Interval*	Traditional Unit
Serum	Urate (as uric acid)	120-420	μmol/L	59.48	2.0-7.0	mg/dL

*This reference value is not intended to be definitive since each laboratory determines its own values. It is provided for illustration only.