¹⁰⁹Cd K α ray fluorescence measurements of tibial lead content in young adults exposed to lead in early childhood

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Abstract

Objectives—Tibial lead measurements were performed in a population of 19–29 year old people who had been highly exposed to lead in childhood to find whether lead had persisted in the bone matrix until adulthood.

Methods—¹⁰⁹Cd K α ray fluorescence was used to measure the tibial lead concentrations of 262 exposed subjects and 268 age and sex matched controls. Questionnaire data allowed a years of residence index to be calculated for exposed subjects. A cumulative blood lead index was calculated from the time weighted integration of available data of blood lead.

Results—The mean (SEM) difference between exposed and control men was 4.51 (0.35) $\mu\text{g Pb/g bone mineral}$, and between exposed and control women was 3.94 (0.61) $\mu\text{g Pb/g bone mineral}$. Grouped mean bone lead concentrations of exposed subjects were predicted best by age. When exposed and control subjects' data were combined, grouped mean bone lead concentrations were predicted best by cumulative blood lead index. The years of residence index was neither a good predictor of bone lead concentrations for exposed subjects nor for exposed and control subjects combined. Finally, exposed subjects had increased current blood lead concentrations that correlated significantly with bone lead values.

Conclusion—Bone lead concentrations of exposed subjects were significantly increased compared with those of control subjects. Lead from exposure in early childhood had persisted in the bone matrix until adulthood. Exposed subjects had increased blood lead concentrations compared with controls. Some of this exposure could be related to ongoing exposure. However, some of the increase in blood lead concentration in adult exposed subjects seemed to be a result of endogenous exposure from increased bone lead stores. The endogenous exposure relation found for men was consistent with reported data, but the relation found for women was significantly lower. Further research is needed to find whether the observed differences are due to sex, or pregnancy and lactation.

(Occup Environ Med 2000;57:465–471)

Keywords: lead; environment; childhood

In 1994 a cross sectional neurotoxicity study was performed on a population of young adults who had been exposed to lead in early childhood and on a group of age and sex matched control subjects. The control subjects lived in the Spokane area, and were randomly selected from drivers' licence records. The exposed subjects in the study were a subset of a larger cohort of 917 young adults who had lived in one of the five towns of the Silver Valley, Idaho, during childhood. Exposed subjects were between the ages of 9 months and 9 years old during the period 1 January 1974 to 31 December 1975, which was the period during which the emissions from the Bunker Hill lead smelter, in the Silver Valley, were highest. A fire at the smelter damaged the air emission controls and dramatically increased the lead emissions from the smelter until repairs were completed. Monthly lead emissions from the smelter averaged 8.3 metric tonnes in 1955–64, 11.7 metric tonnes in 1965–73, and 35.3 tonnes from October 1973 to the end of September 1974. In 1974, the mean blood lead concentration among children from 9 months to 9 years of age residing in the Silver Valley was 50 $\mu\text{g/dl}$, and in 1975 it was 39.6 $\mu\text{g/dl}$. The Bunker Hill smelter was closed in 1981.

Two hundred and eighty one of the exposed subjects and 287 age and sex matched controls underwent medical testing in August and September of 1994 at Sacred Heart Medical Center, Spokane, Washington. Informed consent was obtained from all of the study participants. The results of the neurotoxicity testing have been previously reported.¹ This paper is intended to describe in much greater detail the bone lead data which were obtained as part of the wider study.

Methods

BONE LEAD MEASUREMENTS

Of the 281 exposed subjects and 287 controls who underwent medical testing, 262 exposed subjects and 268 controls had their tibial lead content measured by ¹⁰⁹Cd K α ray fluorescence. The number who had their tibial concentration assessed was lower than the total study participation because subjects were excluded from bone lead testing if they reported possible pregnancy. The 530 subjects had their tibial lead concentration measured by one of two α ray fluorescence systems, one from the University of Maryland² and one from McMaster University, Ontario.³ A section of the left midshaft tibia about 3 cm long from each subject was measured. The skin surface of

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Accepted 8 February 2000

this area was cleaned before measurement with an isopropyl alcohol solution to remove any possible lead contamination. Subjects were seated in a chair, and measurements were made for 1800 seconds live time, about 40 minutes true time. The radiation exposure from a single measurement was extremely low; the effective dose was 40 nSv.⁴ The median (range) individual measurement uncertainty for this radiation dose and time was 4.26 (2.2–21.3) $\mu\text{g Pb/g bone mineral}$. Defining the in vivo detection limit as twice the median uncertainty resulted in an overall in vivo detection limit of 8.52 $\mu\text{g Pb/g bone mineral}$.

The two systems were calibrated with one set of plaster of Paris standards containing known amounts of added lead. Plaster of Paris that was certified lead free was not available, so the plaster of highest guaranteed purity was used to construct the blanks. This plaster was contaminated with lead to a concentration of 1–2 $\mu\text{g Pb/g plaster}$.

Both centres analysed bank and in vivo spectra by the Marquardt method⁵ to obtain x ray intensities. The lead x ray intensities were normalised to the coherent scatter peak found in ¹⁰⁹Cd bone lead spectra and calibration lines were constructed of x ray coherent intensity against concentration. The normalisation resulted in a measure of lead in $\mu\text{g Pb/g bone mineral}$ and rendered the accuracy of the measurement independent of tissue overlay thickness, bone shape, size, mass, and subject motion.^{6–9} Two estimates of bone lead content were made for each subject, one from the α x ray region of the spectrum and one from the β x ray region. This allowed the accuracy of the data to be confirmed; the mean α - β estimate was calculated for the population and was zero to within uncertainties. The final bone lead result for each subject was calculated as being the inverse variance weighted mean of the α and β estimates.

MARKERS OF EXPOSURE

Demographic data were collected from the subjects who underwent a range of medical tests—for example blood lead concentration at the time of x ray fluorescence. Also, the defining difference between exposed and control subjects was residential proximity to the lead smelter. Information as to exposed subjects' residence in the Silver Valley area was obtained and a years of residence index was calculated for each subject.

CUMULATIVE BLOOD LEAD INDEX

A simple cumulative exposure model was created for each 1 year age group of both the exposed and control populations as occupational exposure studies have found that bone lead concentrations are correlated with cumulative blood lead index.^{10–17} The available data on blood lead were extremely limited in this study, as is often the case in research into environmental exposures, and so the model was of necessity simple. The model was too crude to be applied to individual people and was only applied to group mean data. Figure 1 illustrates a hypothesised variation of blood lead concen-

trations over time for both exposed and control subjects.

There are three sets of blood lead measurements that form the basis of the model of exposure of the exposed subjects. Blood lead measurements of exposed children were taken in 1974 and 1975 and blood lead measurements were taken of exposed subjects in adulthood in 1994. As well as the blood lead data, there is some information about the output from the smelter. The output of the lead smelter was 11.7 tonnes a month in 1965–73 and 33.5 tonnes a month in 1974–5. Data from leaded gasoline use have shown that group blood lead concentrations were related to the leaded gasoline used,^{18,19} which implies that group blood lead concentrations are related to the concentration of lead in automobile exhaust fumes. The assumption was made here that group blood lead concentrations would depend on the concentration of lead being emitted from the smelter. The model assumed that blood lead concentrations were 50 $\mu\text{g/dl}$ from late 1973 to the end of 1974, when the output was 33.5 tonnes a month, and were consequently 16.7 $\mu\text{g/dl}$ from 1965–1973 when the smelter output was 11.7 tonnes a month. Exposure was assumed to have ended at the end of 1974, and blood lead concentrations were then modelled as declining exponentially until 1994 to a baseline blood lead concentration of 2 $\mu\text{g/dl}$. This model estimate of a baseline concentration compares with a measured mean (SD) blood lead concentration in the exposed subjects of 2.95 (0.19) $\mu\text{g/dl}$ in 1994. The exponential decline was assumed to follow the physiologically determined half life of lead in blood of 45 days.²⁰ This assumption of the 45 day half life was based on the decline of measured group blood lead concentrations from the end of 1974 to mid-1975 from 50 $\mu\text{g/dl}$ to 39.6 $\mu\text{g/dl}$.

The exposure pattern for control subjects assumed that mean blood lead concentrations had declined in the past few decades.^{18,19,21} The model assumed that the mean blood lead concentrations of control subjects were twice as high in the early 1980s as in 1994, and four times as high as those in the 1960s. An exponential model with a decay time of 13 years was used to project the measured mean control blood lead concentration of 1.60 $\mu\text{g/dl}$ back to 1965. A cumulative blood lead index was calculated for each age group of control and exposed subjects by integrating the area

Figure 1 Variation of blood lead concentrations with time used to construct a cumulative blood lead index for exposed and control subjects.

Table 1 Group inverse variance weighted (IVW) mean bone lead results for exposed and control men and women

	Bone lead contents (µg Pb/g bone mineral)	
	Exposed group IVW mean (SEM)	Control group IVW mean (SEM)
Men	4.54 (0.31)	0.03 (0.31)
Women	5.61 (0.43)	1.67 (0.43)

under the appropriate blood lead curve, from birth to 1994.

STATISTICAL METHODS

Inverse variance weighted group mean data for exposed male, female, and control subjects were compared to determine whether there were any significant differences in bone lead content. The term variance is used here to mean (individual measurement uncertainty)². Inverse variance weighted group mean bone lead values were used, as poor precision bone lead data can affect population mean estimates, and the inverse variance weighting reduces this effect.

Relations between group mean bone lead concentrations and group mean age, years of residence index, and cumulative blood lead index were investigated for both exposed and control subjects to find which markers of exposure predicted bone lead content. Linear regressions were performed of group mean bone lead data versus age, versus years of residence, and versus cumulative blood lead index for exposed and control subjects. Scatter plots, residual plots, and normal probability plots of the residuals were investigated to find whether the assumption of linearity was valid. All subset regression was performed and Mallows' C_p and adjusted R² criteria were applied to choose which of the possible multiple regression models best predicted exposure. The possible collinearity of predictor variables was investigated; the extent to which the variances of regression coefficients were inflated by collinearity was studied by calculating a variance inflation factor. The variance inflation factor was defined as (1-R²)⁻¹ where R²_i is the coefficient of determination of B_i due to regression X_i on the remaining predictors X_j in the model.

POSSIBLE ENDOGENOUS EXPOSURE

Studies of occupationally exposed subjects have shown that increased bone lead concentrations can result in increased blood lead concentrations after the end of exposure as a result of endogenous exposure from bone lead stores. The relation between blood lead concentration at the time of x ray fluorescence measurement and bone lead content was therefore investi-

gated for men and women in this population. Group mean blood lead values were linearly regressed against group mean bone lead values to find whether subjects in this population were experiencing endogenous exposure.

Results

Table 1 contains the group inverse variance weighted mean bone lead contents for exposed and control men and women. The bone lead contents of the exposed group were significantly higher than bone lead contents of the control group for both men and women. For men, the difference between exposed and control subjects mean (SEM) was 4.51 (0.44) µg Pb/g bone mineral (p<0.001), whereas for women the difference between the exposed and control subjects was 3.94 (0.61) µg Pb/g bone mineral (p<0.001). The group mean bone lead concentrations for exposed men and women were not significantly different, but concentrations for control men and women were significantly different (p<0.001). This difference was no longer significant, however, when age was taken into account. When control men and women were stratified into 1 year age groups, for each age group, the difference between them was not significant.

LINEAR REGRESSIONS

There was no significant correlation (at the 95% confidence interval) with age for either control men or control women. However, bone lead concentration was significantly correlated with age both for exposed men and for exposed women (table 2 contains regression data).

The results of the regressions for exposed men and women were the same, to within uncertainties; therefore the data for men and women were combined. For the combined data, group bone lead concentration and age were not significantly correlated for control subjects. Bone lead was significantly correlated with age for exposed and control subjects combined (fig 2), and there was no evidence of a difference in correlation between group bone lead concentration and age (table 2). Exposed subjects were found to have group bone lead concentrations that were significantly higher (p<0.005) than those of control subjects for seven out of the 11 age groups (fig 3). The regression for exposed subjects of mean bone lead concentration versus years of residence was also found to be significant (table 2).

Group mean bone lead value was significantly correlated with group mean cumulative

Table 2 Results of the regression of bone lead content versus different variables

	r ²	n	p Value
Correlations of bone lead with:			
Age (control men)	0.19	11	0.2>p>0.1
Age (control women)	0.30	11	0.1>p>0.05
Age (exposed men)	0.83	11	p<0.001
Age (exposed women)	0.69	11	0.005>p>0.001
Age (exposed men and women)	0.86	11	p<0.001
Years of residence (exposed men and women)	0.41	23	p<0.005

Figure 2 Bone lead concentration versus age for exposed and control subjects.

Figure 3 Difference in bone lead concentration between exposed and control subjects for each 1 year age group.

blood lead index for exposed subjects, for control subjects, and for control and exposed subjects combined. The regression results were the same for the three groups. Regression data are presented in table 3, and a plot of the regression of bone lead versus cumulative blood lead index is presented in figure 4.

MULTIPLE REGRESSION ANALYSIS

All subset regression indicated that a multiple regression analysis which included all three variables (age, years of residence, and cumulative blood lead index) was the best model to apply for exposed subjects. The results of the multiple regression (standard and backward stepwise) of the data for exposed subjects are presented in table 4. Standard multiple regression indicated that age and years of residence were significant predictors of bone lead concentration in control subjects. However, backward stepwise multiple regression ($\alpha=0.05$, f to remove=4) indicated that age was the only significant predictor of bone lead concentration in exposed subjects. This result seems surprising, given that both age and years of residence were significant at the 90% level in the full model. Further analysis of the different models applied to the data indicated, however, that there was substantial collinearity among the explanatory variables. As the variables age, years of residence, and cumulative blood lead index are all estimates that include time as a variable, this result is hardly surprising. Large changes were found in regression coefficients as variables were included or removed in the models. Calculation of the variance inflation factor indicated that models that included two or three variables had regression coefficients that were poorly estimated because of collinearity. The most adequate model was where only one variable was used to predict bone lead content. An analysis of the linear regression data concluded that for exposed subjects, age was the best predictor of bone lead, corroborating the results of the stepwise regression.

Table 3 Results of the regression of bone lead versus cumulative blood lead index for the different groups

	Slope ($\mu\text{g Pb/g bone mineral}/\mu\text{g/dl y}$)	Intercept ($\mu\text{g Pb/g bone mineral}$)	r^2	n	p Value
Exposed	0.039 (0.005)	-2.52 (1.03)	0.86	11	<0.001
Control	0.038 (0.016)	-2.39 (1.31)	0.38	11	<0.05
Combined	0.039 (0.003)	-2.47 (0.46)	0.89	22	<0.001

Figure 4 Bone lead versus cumulative blood lead index for exposed and control subjects.

When data from exposed and control subjects were combined the regression of years of residence index against bone lead failed tests of the assumption of linearity. This was because every age group of control subjects had zero years of residence in the Silver Valley and the data were therefore clustered. All subset regression was performed on the three possible models of age against bone lead, cumulative blood lead index against bone lead, and cumulative blood lead index and age against bone lead. The variance inflation factor indicated that collinearity between regressor variables was not a problem in the model which combined age and cumulative blood lead index (variance inflation factor=1.53). However, a lower Mallows' C_p value was found for the model of cumulative blood lead index versus bone lead ($C_p=1.0$) than for the model which incorporated both age and cumulative blood lead index ($C_p=3.0$), indicating that cumulative blood lead index alone was the better predictor of bone lead content. This was corroborated by backward stepwise multiple regression (table 5) which selected cumulative blood lead index as the explanatory variable of lead ($\alpha=0.05$, f to remove=3).

Although the regression of years of residence index against bone lead for the exposed and control group combined had failed tests for linearity, it was incorporated into a three variable model of age, cumulative blood lead index, and years of residence against bone lead. This further confirmed the finding that cumulative blood lead index was the best predictor of bone lead when exposed and control subjects were studied together (table 5). Neither age nor years of residence were significant predictors of bone lead when the exposed and control groups were regressed together.

POSSIBLE ENDOGENOUS EXPOSURE

Group mean blood lead concentration at the time of x ray fluorescence measurement and group inverse variance weighted mean bone lead content were not significantly correlated for control men or women, but were significantly correlated for exposed men and women. (Regression data are presented in table 6, figure 5 presents a plot of blood lead versus bone lead for exposed and control men.) The regressions were significantly different for exposed men and women with the slope derived from women being 40% ($\pm 10\%$) of the slope derived from men. The exposed female

Table 4 Results of the multiple regression analysis for exposed subjects only

Group	Multiple regression method	Independent variable	β	p Value
Exposed only (n=11)	Standard	Age	1.63 (0.61)	=0.03
		Years of residence	0.88 (0.35)	=0.04
		Cumulative blood lead index	-1.46 (0.86)	=0.13
	Backward stepwise	Age	0.93 (0.13)	<0.001

Table 5 Results of the multiple regression analysis for exposed and control subjects combined

Group	Multiple regression method	Independent variable	β	p Value
Exposed and control combined (n=22)	Backward stepwise	Cumulative blood lead index	0.94 (0.18)	<0.001
		Age	0.09 (0.18)	=0.61
		Years of residence*	0.17 (0.31)	=0.60
	Standard	Cumulative blood lead index	0.74 (0.37)	=0.06

*Regression of years of residence index v bone lead failed tests of linearity.

Table 6 Results of the regression of blood lead versus bone lead for subgroups of exposed subjects

	Slope ($\mu\text{g/dl}/(\mu\text{g Pb/g bone mineral})$)	Intercept ($\mu\text{g/dl}$)	r^2	n	p Value
Men	0.126 (0.022)	3.33 (0.25)	0.72	14	p<0.001
Women	0.052 (0.011)	1.60 (0.12)	0.69	12	p<0.001
Parous women	0.055 (0.012)	1.70 (0.14)	0.67	12	0.005>p>0.001

Figure 5 Blood lead at the time of x ray fluorescence measurement versus bone lead for exposed and control men.

group was subdivided into parous and nulliparous groups to try and determine whether the difference between men and women was associated with pregnancy and lactation. Blood lead at the time of x ray fluorescence measurement and bone lead content were not significantly correlated for nulliparous exposed subjects, but were significantly correlated in the parous exposed subjects. The parous group data are presented in table 6; nulliparous data are not included because the results were not significant.

Discussion

NEGATIVE BONE LEAD VALUES

The Marquardt method of analysis produced results for low concentrations of bone lead that were negative. These results can cause confusion because it is obviously not physically the case. The negative results arose, however, from the inherent statistical processes associated with radiation detection and measurement. The method measures the magnitude of the spectral background under an x ray peak by fitting a combination of exponentials over a wide range of energies. The background is therefore predominantly predicted from regions on either side of the x ray peak. Poisson statistics dictate that for a signal of N counts, there is a

$\sqrt{N}$ uncertainty. At low concentrations, the situation can arise where the background under an x ray peak is predicted to be of a certain size from the spectral shape on either side of the peak area. However, because there is the $\sqrt{N}$ uncertainty in each spectrum channel, the integrated signal in the region of the peak is less than the predicted background size. The integrated signal minus the predicted background is therefore a negative number, and the bone lead content is predicted to be negative.

When multiple measures are made of a true zero concentration standard, it will be estimated to be negative, but zero to within twice the uncertainty, 47.5% of the time. However, the incidence of negative numbers in this population with low bone lead content was increased slightly above this because the calibration standards were contaminated at a concentration of 1 to 2 $\mu\text{g Pb/g}$ plaster. The contamination created a positive intercept on calibration lines, which were subtracted in the calculation of bone lead values. However, a single set of calibration standards was used throughout the study, and the bone lead values all had the same offset. Relative bone lead values were therefore accurate, and estimates of the slopes of regression lines of bone lead content were valid, but had intercepts offset from zero.

BONE LEAD RESULTS

In the overall population, exposed subjects were found to have significantly higher group mean bone lead concentration than controls even though the difference in concentration was small—about 4 $\mu\text{g Pb/g}$ bone mineral. This is an important finding, showing that childhood lead exposure has persisted in the bone matrix until adulthood.

Group bone lead concentration was significantly correlated with age in exposed subjects but not in controls. In seven out of 11 age groups, bone lead concentration were significantly higher in the exposed than in the control group. The oldest exposed subjects, therefore, had the greatest difference in bone lead concentration compared with controls; their bone lead concentrations were increased by about 8 $\mu\text{g Pb/g}$ bone mineral (figs 2 and 3).

These small differences were found in this population because bone lead and blood lead concentrations in control subjects were extremely low. The differences might not have been found in a heavily industrialised environment because adult lead exposure, or lead exposure during the 1970s and 1980s from gasoline, might have masked the difference.^{18 19}

Bone lead content in the exposed group was predicted best by age. However, when exposed and control subjects were combined it was found that the best predictor of bone lead content was cumulative blood lead index, with age no longer being significant. These data are interpreted as meaning that within the population of the Silver Valley, where exposure was relatively constant from 1965 to the beginning of 1973, age could predict exposed subjects' bone lead concentrations with respect to other exposed subjects. However, the level of

exposure was different in Silver Valley and Spokane residents, so when bone lead contents of exposed and control subjects were compared, cumulative blood lead index became the best predictor of bone lead content because it took the difference in exposures into account.

The fact that group bone lead contents of exposed subjects were predicted best by age was probably coincident on three factors; the smelter output was relatively constant between 1965 and the beginning of 1973, the residence of the population was relatively stable during childhood, and most exposure was over a short period in childhood with concentrations being much lower in early adulthood. This was partly suggested by the x axis intercept of the regression of group inverse variance weighted mean bone lead content with age. The intercept was at age 18 and this implied that the most recent 18 years of exposure were relatively insignificant compared with the earlier exposure period.

Although years of residence had been found to correlate with bone lead content in the exposed population, age was a better predictor of bone lead content for exposed subjects. This was probably because age provided a limit on exposure that was not always explicit in the measure years of residence. To cite an extreme, a 19 year old person could not have had high exposure, because he or she was not born at the time of high smelter output. Further, a 19 year old person and a 29 year old person could have had the same calculated 19 years of residence in the valley, but the 29 year old person might have resided for their first 19 years in the valley when exposure was higher, so the two subjects would have had different bone lead contents.

Age and years of residence are good as predictors of exposure when exposure is relatively constant and comparable between groups. However, better exposure indices could be used which include variations of exposure pattern and take physiological factors into account.

The simplified model of exposure used in this study to construct a cumulative blood lead index seemed to work well with group data. The incorporation rate of lead into bone was suggested to be 0.039 (0.003) ($\mu\text{g Pb/g bone mineral}/(\mu\text{g/dl year})$). This compares well with occupational exposure studies in which the rates have been found to be 0.05 – 0.1 ($\mu\text{g Pb/g bone mineral}/(\mu\text{g/dl year})$).^{10–17} Childhood rates should not actually be expected to correspond so well with adult occupational rates because bone turnover is much higher in young children than in adults.²² The rate of incorporation of lead into bone should, therefore, be higher. However, in this study group, there has been growth and bone turnover in the intervening period that would be expected to have reduced bone lead concentration. These two factors have possibly acted in opposite directions on bone lead concentration and cancelled each other out.

The intercept of the regression of group bone lead concentration against cumulative blood lead index was -2.5 $\mu\text{g Pb/g bone mineral}$. This converted to -1.6 $\mu\text{g Pb/g}$

plaster. This negative intercept on the regression of group bone lead against cumulative blood lead index was a result of the calibration lines having a positive offset due to contamination of the plaster.

This model of cumulative exposure works with group data, but it is an oversimplification. Better models of exposure need to be constructed and further studies should be performed incorporating the study data into physiologically based lead biokinetic models to find more accurately the exposure patterns and the retention of lead in the bone mineral matrix.

ENDOGENOUS EXPOSURE

Correlations between group mean blood lead at the time of x ray fluorescence measurement and group inverse variance weighted mean bone lead content for both exposed men and exposed women suggested that exposed subjects were experiencing endogenous exposure as a result of their increased bone lead stores.^{10–14 23} For exposed men, the slope of the regression was 0.126 (0.022) ($\mu\text{g/dl}/(\mu\text{g Pb/g bone mineral})$). This compares well with data obtained from occupationally exposed men which found the slope to be 0.13 – 0.17 ($\mu\text{g/dl}/(\mu\text{g Pb/g bone mineral})$).^{10–14} However, for exposed women, the slope was considerably lower (0.055 (0.011) ($\mu\text{g/dl}/(\mu\text{g Pb/g bone mineral})$)) and does not compare well with occupational data. When the exposed women were divided into parous and nulliparous groups, only the regression data from parous women were significant. The lack of a correlation among nulliparous women was probably due to low bone lead content in the nulliparous subjects and was an artifact of age. Nulliparous women had lower bone lead content because they tended to be younger. All of the 19 year old exposed women in the study were nulliparous, whereas only one of 14 women aged 29 years were nulliparous. The possible relation for endogenous exposure in women was therefore dominated by measurements of parous subjects. It was not possible to determine from these data whether the difference in endogenous exposure was a result of sex differences or differences due to physiological changes as a result of pregnancy and lactation. Further studies are required to find whether possible endogenous exposure differences between men and women were a result of changed metabolism of lead during pregnancy and lactation.

Conclusion

The bone lead measurement systems were able to discern small differences, of about 4 $\mu\text{g Pb/g bone mineral}$ in exposed populations. Young men and women who were exposed to lead in early childhood were found to have significantly increased group bone lead concentrations compared with controls.

Multiple regression analysis indicated that bone lead concentration in the exposed group was predicted best by age. When exposed and control subjects were combined it was found that the best predictor of bone lead concentration was cumulative blood lead index.

The persistence of lead in the bone matrix of exposed subjects compared with controls was found to result in increased blood lead concentrations in the exposed group, possibly as a result of endogenous exposure. In men, the increased blood lead concentrations were found to compare well with data for occupational studies. In women, the relation between blood and bone was lower than in men, but the relation in women was dominated by data from parous women. It was not established if differences between men and women were sex differences or due to physiological changes caused by pregnancy or lactation.

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Open reviewing

Many journals, including the BMJ, have moved to a system of open reviewing, whereby authors know the names of reviewers of their papers. Research has shown that named reviews, although not of better quality than anonymous reviews, are not of worse quality either. Therefore in the interests of transparency, it seems fair to let authors know who has reviewed their paper. At *Occupational and Environmental Medicine* we have considered the issue carefully. There are some concerns that reviewers, especially those who are more junior, might feel intimidated and not wish to make negative comments about papers submitted by senior people in the field. On the other hand, some reviewers might hide behind the cloak of anonymity to make unfair criticisms so as to reduce the chances of publication by rivals. We have decided to introduce initially a system of open reviewing if the reviewers agree explicitly. So when a reviewer is sent a paper, he or she is asked to indicate whether we can disclose their name or not when sending the authors their comments. We will be monitoring this to see how many of our reviewers are happy to be named. If it is most of them, we will move to a system of open reviewing as the norm, with a possible “opt out” clause for reviewers.