

Seasonal Variation in Bone Lead Contribution to Blood Lead during Pregnancy¹

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Population blood lead level (PbB) often shows seasonal variation, frequently being higher in summer and lower in winter. As vitamin D metabolites also show seasonal variability, and the metabolites are associated with bone metabolism, some authors have posited a role for bone lead release in seasonal PbB changes. We made third trimester and post-delivery PbB measurements on 414 immigrant women (98% Latina) in Los Angeles. We measured *in vivo* tibia and calcaneus (heel) lead concentration postdelivery via K-shell X-ray fluorescence. We saw evidence of seasonal variation in prenatal PbB, but not postnatal PbB. PbB was highest in spring and lowest in autumn. Tibia lead concentration was associated with prenatal PbB, as reported before. The contribution of tibia lead to prenatal PbB varied seasonally, with the greatest contribution occurring in the winter quarter and the least in the summer quarter. The temporal pattern of bone lead contribution to PbB follows the seasonal alteration of insolation. There was no seasonal component in prenatal PbB associated with calcaneus lead, nor were there seasonal variations in either calcaneus or tibia lead contributions to postnatal PbB. Bone turnover in the third trimester of pregnancy may be higher in winter months than in summer months, resulting in greater fetal lead exposure in spring than at other times of the year. © 2001 Academic Press

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INTRODUCTION

Many studies of nonoccupationally exposed groups have described seasonal variation in blood lead levels, most often in children (Baghurst *et al.*, 1992; McMichael *et al.*, 1985; Rabinowitz *et al.*, 1985; Rothenberg *et al.*, 1996; Schell *et al.*, 1997; Stark *et al.*, 1980). Typically, blood lead levels are higher in summer months than in winter months. Explanations for the effect range from seasonal variation in exposure factors (greater opportunity for airborne lead to enter houses in warm weather when windows are open, more outdoor activity in summer when especially children may be exposed to contaminated soil or dust in streets, yards, etc.) to seasonal variation in Vitamin D metabolism.

In a recent study of maternal blood lead during pregnancy, we described a seasonal variation in blood lead (Rothenberg *et al.*, 1999). We present additional data from this data set of combined blood lead and bone lead measurements. Subjects entered the study in the third trimester of pregnancy and were studied again 2 months after delivery. These data suggest that there is seasonal variation of bone lead influence on blood lead, at least during pregnancy.

MATERIALS AND METHODS

Complete information on methods has been previously described (Rothenberg *et al.*, 2000, 1999). Here we summarize our procedures.

We recruited outpatients attending prenatal clinics at the King-Drew Medical Center in Los Angeles, California. Subjects read and signed an

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informed consent approved by the Institutional Review Board of Drew University of Medicine and Science.

We present data only on immigrant subjects ($N = 414$), as there were significant differences in blood lead levels in nonimmigrants and immigrants (nonimmigrant geometric mean (GM) = 1.8 $\mu\text{g/dL}$, geometric standard deviation (GSD) = + 1.4/ - 0.8; immigrant GM = 2.2 $\mu\text{g/dL}$, GSD = + 2.4/ - 1.2; $P = 0.006$) and significant differences in age, education, and other variables that could be confounded with lead (Rothenberg *et al.*, 1999). We did not analyze nonimmigrant bone lead data, as there were less than 150 subjects available over the 4-year period.

Blood was drawn for blood lead analysis in the third trimester of pregnancy and again 60 days after delivery. Blood lead levels were analyzed by atomic absorption spectrometry with graphite furnace. Our laboratory participates successfully in Centers for Disease Control (now administered by Wisconsin State Laboratory of Hygiene) and the College of American Pathologists quality assurance programs. Reliability and precision measures have been previously published (Rothenberg *et al.*, 1999).

We measured bone lead concurrently with the postpregnancy blood draw. Bone lead was measured at midtibia and calcaneus (heel) to obtain representative measures of cortical and trabecular bone lead concentration. We used a noninvasive ^{109}Cd -based K-shell X-ray fluorescence technique to measure bone lead concentrations according to methods previously published by our laboratory (Rothenberg *et al.*, 2000).

Other variables (pica, home remedy use, coffee use, age, years since immigration) were assessed by means of a previously published questionnaire (Rothenberg *et al.*, 1999) and by reference to hospital records.

We used Stata 6 (Stata Corp., East College Station, TX) for data analysis. We constructed separate multiple regression models for prenatal and postnatal blood lead level using variables previously shown to significantly predict prenatal blood lead in a larger group of women screened for inclusion in this study (Rothenberg *et al.*, 1999). We added a set of seasonal dummy variables representing each quarter of the year. We also included seasonal-bone lead interaction variables, using both tibia and calcaneus lead. In the regression model, the reference quarter for testing seasonal effects was the first quarter (January through March). All variables were entered in a block. As the regression model showed significant heterogeneity of residuals, we

used robust standard errors (Davidson and MacKinnon, 1993) for calculation of all statistical tests.

RESULTS

Figure 1 shows the effect of season on maternal blood lead level in a simple ANOVA. The decreasing linear trend with season is significant ($F_{1,413} = 7.497$, $P = 0.006$). This seasonal pattern is similar to the highly significant pattern exhibited by the larger group over nearly the same period (Rothenberg *et al.*, 1999). Blood lead level is lowest in the fourth quarter of the year and highest in the second quarter (Tukey HSD, $P = 0.03$).

Table 1 shows the multiple regression model for the natural log prenatal blood lead level with the season-bone lead interaction terms. Note that the third quarter-tibia lead interaction is the only significant season-bone lead interaction term. None of the season-calcaneus lead interaction terms was significant. Tibia lead makes the least contribution to maternal blood lead in the third quarter, compared to the first quarter ($P = 0.004$). Figure 1 also plots the coefficients of the season-tibia lead interaction.

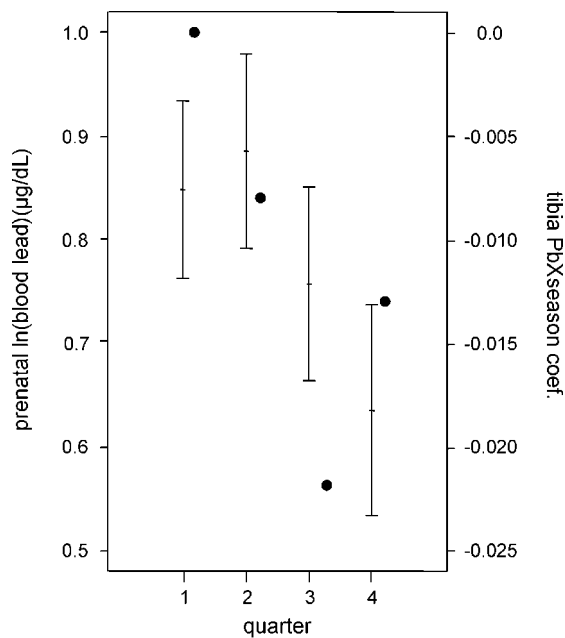


FIG. 1. Prenatal blood lead level (vertical lines are 95% confidence intervals) and tibia lead-season interaction coefficients with blood lead (filled circles) as a function of season. Seasons are quarters, starting from the January to March quarter. Data represent four complete years. As the first quarter is the reference quarter for the other seasonal interaction variables, it is assigned the value of 0.0. Note that the highest blood lead level is in the second quarter and the lowest is in the fourth quarter. Note that the maximum contribution of tibia lead to blood lead is in the first quarter and the minimum is in the third quarter.

TABLE 1
Multiple Regression Model

Regression with robust standard errors		Number of obs = 414 F(17, 396) = 5.79 Prob > F = 0.0000 R ² = 0.2255 Root MSE = .61445			
Ln(prenatal blood lead)	Coef.	Robust Std. Err.	P > t	[95% Conf. Interval]	
Ln(years after immigration)	-0.200	0.038	0.000	-0.275	-0.125
Maternal age (years)	0.008	0.005	0.090	-0.001	0.018
Drinks coffee	-0.150	0.064	0.020	-0.277	-0.023
Daily dietary calcium	-0.282	0.156	0.071	-0.589	0.024
Use folk remedies	-0.156	0.111	0.161	-0.375	0.062
Secular trend (months)	-0.009	0.003	0.001	-0.014	-0.004
Seasonal (2nd quarter)	0.060	0.105	0.568	-0.146	0.266
Seasonal (3rd quarter)	0.080	0.108	0.457	-0.132	0.292
Seasonal (4th quarter)	-0.020	0.104	0.848	-0.224	0.185
Tibia lead (µg/g)	0.017	0.006	0.003	0.006	0.028
Tibia × 2nd quarter	-0.008	0.008	0.320	-0.025	0.008
Tibia × 3rd quarter	-0.022	0.008	0.004	-0.038	-0.007
Tibia × 4th quarter	-0.013	0.009	0.132	-0.030	0.004
Calcaneus lead (µg/g)	0.005	0.004	0.298	-0.004	0.013
Calcaneus × 2nd quarter	0.009	0.006	0.154	-0.003	0.022
Calcaneus × 3rd quarter	-0.001	0.007	0.847	-0.014	0.012
Calcaneus × 4th quarter	0.005	0.008	0.522	-0.010	0.020
Constant	2.059	0.389	0.000	1.295	2.823

Note. Reference category for seasonal dummy variables is 1st quarter.

None of the season-calcaneus lead interaction terms was significant for prenatal blood lead level. None of the season-bone lead interaction terms for either tibia or calcaneus lead concentrations was significant for postnatal blood lead level (not shown).

DISCUSSION

As atmospheric concentrations of lead have fallen with increased controls on leaded gasoline and industrial emissions, explaining seasonal variation of blood lead solely by increased respiration of airborne lead emitted in summer months becomes less plausible. Although outdoor activity can increase exposure to the large reservoir of lead in soil existing in some areas, continued observation of seasonal variation in blood lead suggests the examination of alternate explanations.

There is a one-season lag (3 months) between the peak tibia lead-season interaction effect and the peak seasonal effect on blood lead. The strongest effect of tibia lead concentration on blood lead level occurs in the first quarter (Los Angeles winter), whereas the blood lead level reaches its maximum in the second quarter (Los Angeles spring). The minimum blood lead level similarly lags the minimum

tibia lead influence on blood lead by one quarter, as shown in Table 1 and Fig. 1.

It is important to note that most of the seasonal increases in blood lead concentration have been reported by others to occur between the months of June and August (mostly in children), whereas the increase reported here occurred in late spring, between April and June. This in itself points to a process other than (or in addition to) increased gastrointestinal absorption or the exposure to exterior dust previously invoked to explain the summer increase. We are struck by the coincidence of the minimum of the tibial lead contribution with the known minima of the cycle of 25-OHD in blood. We invoke the presence of some agent produced or induced by sunlight that causes cortical bone to be mobilized in late spring, as there is evidence from lead isotope ratio studies (Gulson *et al.*, 2000; Manton, 1977; Manton and Cook, 1984) that such an agent exists. As we detect seasonal interaction with bone lead only during pregnancy, and not after pregnancy, it is possibly this same agent that causes cortical bone to be preferentially mobilized in late pregnancy. We do not propose, however, that this agent is 25-OHD (because it is inactive) or any of its metabolites, whose functions are well understood

(Kovacs and Kronenberg, 1997). Given that the population sampled is for the most part immigrant women from Mexico, whose bone lead levels are higher than their U.S.-born counterparts, attributing part of the increased blood lead in the first two quarters of the year to bone lead is not unreasonable in this sample.

CONCLUSIONS

We present evidence that bone lead release is seasonally modulated and that the rise in blood lead that characterizes late pregnancy is due in part to release of lead from bone. Seasonal influences on bone mass and bone lead release and the calcium demands of pregnancy may act together to make fetuses born in the first two quarters of the year subject to the highest risk of *in utero* lead exposure.

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