Changes in Serial Blood Lead Levels During Pregnancy

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The first step in modeling lead kinetics during pregnancy includes a description of sequential maternal blood lead (PbB) during pregnancy and the factors controlling it. We analyzed PbB of 105 women living in the Valley of Mexico from week 12 to week 36 of pregnancy and again at parturition. We also used data from all women contributing blood at any stage of pregnancy to determine antecedents of PbB. Pregnancies were uneventful, and offspring were normal. Although geometric mean PbB level averaged around 7.0 µg/dl (0.34 µmol/l), with a range of 1.0–35.5 µg/dl throughout pregnancy, analysis of variance revealed a significant decrease in mean PbB from week 12 to week 20 (1.1 µg/dl) and various significant increases in mean PbB from week 20 to parturition (1.6 µg/dl). Regression analyses confirmed the positive linear PbB trend from 20 weeks to parturition and additional contributions of dietary calcium, reproductive history, lifetime residence in Mexico City, coffee drinking, and use of indigenous lead-glazed pottery. Although decreasing hematocrit has been suggested to explain first-half pregnancy PbB decrease, the time course of hematocrit decrease in the present study did not match the sequential changes in PbB. While hemodilution and organ growth in the first half of pregnancy may account for much of the PbB decrease seen between 12 and 20 weeks, the remaining hemodilution and accelerated organ growth of the last half of pregnancy do not predict the trend toward increasing maternal PbB concentration from 20 weeks to delivery. Mobilization of bone lead, increased gut absorption, and increased retention of lead may explain part of the upward PbB trend in the second half of pregnancy. Reduction of lifetime lead exposure may be required to decrease risk of fetal exposure. *Key words:* blood lead, bone lead, caffeine, calcium, pregnancy. *Environ Health Perspect* 102:876–880 (1994)

The period of fetal growth is often the stage of development at which the organism is most sensitive to toxic agents. However, we cannot directly measure fetal exposure during pregnancy in human research studies. Maternal measurements are the only exposure indices ethically available. To infer fetal lead exposure from maternal measurements of blood lead (PbB), we need a detailed understanding of both the factors influencing and the kinetics of maternal–fetal lead transfer. Given the strong interest in the effects of low-level lead on child development, we know surprisingly little of even the time course of maternal PbB levels during pregnancy.

Cross-sectional studies of groups of women at different stages of pregnancy present conflicting results (*1-3*), and the design is inadequate to study serial changes of lead during pregnancy. Case studies with serial measurements of PbB in pregnant women are interesting (*4–6*), but these are usually of women suffering frank lead intoxication.

The only detailed work prospectively studying PbB in pregnant women is that of Barltrop (*7*), published over 25 years ago. He examined serial PbB levels in 12 women from as early as the first trimester of pregnancy to delivery and could discern no recognizable pattern.

We present here serial PbB measurements from week 12 to delivery from 105 women with uneventful pregnancies and deliveries from the Mexico City Prospective Lead Study. Our aim is to characterize PbB changes during normal pregnancy and to investigate some of the many factors, both environmental and physiological, that influence alterations in PbB as a necessary first step in understanding the dynamics of lead metabolism during pregnancy.

Methods

Subjects. Outpatient staff screened women arriving at the outpatient service of the National Institute of Perinatology around or before week 12 of pregnancy as calculated from the date of last menses. As the institute is a service, training, and research center for treating reproductive problems, including high-risk pregnancies, pregnant women not presenting a risk factor are normally referred to other treatment facilities. Between March 1987 and June 1992, however, pregnant women not meeting the institute's admission requirements were referred to the lead study's physician for further screening.

A priori exclusion criteria for the study were: 1) younger than 15, older than 42; 2) active diabetes, German measles, hepatitis, or toxoplasmosis, as determined by laboratory test, 3) habitual use of alcohol or drugs, 4) use of prescription medications, 5) hypertension controlled with medication, 6) active psychosis. Women not excluded by these criteria were informed of the purpose of the study and the procedures involved. They read, or were read, a statement of informed consent approved by the institutional review board, and signed it.

A total of 532 women passed the exclusion criteria and were enrolled in the study. Of this total, 30 never arrived at the project office for their first or following appointments. One case developed hypoglycemia and 27 developed conditions described by the above exclusion criteria during their pregnancy; 22 spontaneously aborted, and 16 were stillbirths. We will report these data elsewhere. The exclusion of these subjects left 436 participants.

Some of the remaining women gave birth to babies meeting the following *a priori* exclusion criteria, and these 22 pregnancies were also removed from the present data set: 1) birth weight under 2000 g, 2) gestation age under 36 weeks, 3) 5-min Apgar score under 6, 4) multiple birth, and 5) major congenital anomaly. An additional 41 babies suffered from hyperbilirubinemia, high lead level [one baby was born with a cord level of 69 µg/dl (3.33 µmol/l); see Rothenberg et al. (*6*) for description of this case], minor congenital anomaly, severe infection, birth trauma, asphyxia, respiratory difficulty, or early infant death, and these cases were also excluded from the data set.

Table 1 summarizes data on 159 patients who were excluded or who dropped out of the study and compares them to 373 patients retained in the study. Excluded patients were significantly older, had more pregnancies and abortions, and gave birth to lower birth-weight and lower

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Table 1. Comparison of excluded and drop-out cases with retained sample.

Parameter[a]	Excluded (N = 159)	Retained (N = 373)
Age of mother (years)	29.8†	27.5
Pregnancies	2.75*	2.51
Abortions	0.84**	0.63
Birth weight (g)	2697†	3186
Gestation age (weeks)	37.6†	39.9
Socioeconomic status (1–9)	3.8	3.7
Lead level, 12 weeks (μg/dl)[b]	7.7	7.7
Lead level, 20 weeks (μg/dl)	6.3	6.8
Lead level, delivery (μg/dl)	8.3	8.3

[a]Significance measured by *t*-test except for socioeconomic status, for which Mann-Whitney *U* was used. *$p<0.10$. **$p<0.05$. †$p<0.001$. [b]Conversion factor for blood lead, 10.0 μg/dl = 0.48 μmol/l.

gestation-age babies than included mothers. The latter two differences were not unexpected, as low birth weight and gestation age were part of the exclusion criteria. The two groups did not differ according to marital status, socioeconomic level, or, where available, PbB.

The exclusion criteria ensured basically healthy pregnancies and deliveries in the sample. The sample was predominantly urban or suburban, all living within the Valley of Mexico during their pregnancies, of lower socioeconomic status, small families, mostly married, and with low alcohol and cigarette use. Socioeconomic status was calculated as the unweighted mean of three ordinal scales measuring head of family's education and occupation and total income, the latter determined by multiples of minimum wage current at time of measurement. The 1980 national census indicated that just under 8% of the national population was of pure indigenous ancestry but gave no other ethnic or racial breakdown. We made no attempt at racial or ethnic classification of the sample.

Only 105 subjects in the sample contributed 5 analyzable blood samples, one at each period of the pregnancy and one at delivery. There were no significant differences between the group with complete PbB data and the remainder of the sample on the demographic, socioeconomic, and reproductive history variables mentioned above.

Blood Sampling. Blood samples were drawn by venipuncture at 8-week intervals (± 2 weeks) from week 12 to week 36 of pregnancy and again from the mother within 15 min of delivery. An umbilical cord blood sample was also drawn (data reported elsewhere). In all cases venipuncture sites were thoroughly cleaned with antiseptic soap, finishing with unidirectional wipes with prepared alcohol-saturated pads. At least 2 ml of blood was drawn for the PbB samples and stored in purple-top Vacutainers (Becton-Dickinson) with EDTA. At the 12 to 36 week appointments, blood was also drawn for clinical blood workup. Vacutainers were stored at 4°C until shipping.

Blood Lead Analysis. The Vacutainers were shipped to Environmental Sciences Associates (ESA) Laboratories, Inc. (Bedford, Massachusetts) for analysis. ESA Laboratories is one of the reference laboratories for the Centers for Disease Control Blood Lead Proficiency Testing Program and is a participant in the New York State Department of Control Program.

All samples were analyzed in duplicate by the method of anodic stripping voltammetry. Samples with mean duplicate values below 5 μg/dl (0.24 μmol/l) were reanalyzed in duplicate by atomic absorption spectrometry with graphite furnace, and the previously analyzed values were discarded. Mean values of the duplicate analyses were used as data. In cases where mean values were below 1 μg/dl (0.05 μmol/l), values were rounded up to 1 μg/dl (0.05 μmol/l).

Comparison of ESA Laboratories performance with the other five CDC reference labs over the study period showed that ESA Laboratories reported an average lead value 0.7 μg/dl (0.03 μmol/l) lower for the low and mid-range samples (usually covering the lead range found in our sample). This included 3 different months when ESA Laboratories results exceeded the control limit (Hotelling T-square, α = 0.05) based on the other five laboratories on one or more of the three CDC samples. None of our samples was analyzed in those 3 months. Mean difference of the duplicate values of all maternal samples from the study (N = 1913) was 1.2 μg/dl (0.06 μmol/l) with only 4.0% of the samples exceeding a difference of 3.0 μg/dl (0.14 μmol/l). For samples with mean lead level less than 5.0 μg/dl (0.24 μmol/l), i.e., those analyzed with atomic absorption spectrometry, the comparable values were 0.9 μg/dl (0.04 μmol/l) and 3.3%. Use of mean duplicate values in the statistical analyses reduced reliability error.

Statistical Analysis. Statistical analysis was performed separately on the 105 subjects with complete PbB data through the pregnancy and on the entire data set. The goal of the analysis was to determine significant changes and significant trends in lead during the pregnancy and to account for intrinsic and extrinsic variables associated with lead at each stage of pregnancy.

All PbB measurements were converted to their natural logarithmic values in an effort to normalize the positively skewed lead distributions. Nevertheless, transformed distributions were slightly tail heavy on the low side of the distribution, likely due to adopting the strategy of rounding all measured lead levels below 1 μg/dl up to 1.

A repeated-measures fixed-effects model ANOVA was used to assess significant changes in maternal lead during pregnancy on the group with complete data, with post-hoc comparisons performed using least significant differences. We used linear and multiple linear regression models to calculate trends in maternal lead during the pregnancy.

To assess the variables that were significantly associated with lead at each time period during pregnancy, we performed a series of univariate and bivariate statistical tests of control and confounding variables against natural log-transformed lead using the entire available data set. Variables significantly associated with maternal lead ($p<0.10$) at each period in pregnancy were retained for possible entry in a forward, stepwise multiple regression with backward elimination (entry and elimination criteria were $p<0.10$ and $p>0.10$, respectively). This technique assured that multicollinearity was minimized and that the statistical effect of each variable retained in the model against lead was independent of the other variables. Final multiple regression models maximized variance of lead accounted for at each period in the pregnancy. Statgraphics Plus (Manugistics, Rockville, Maryland) and SPSS (Chicago) were used for data analysis.

Results

Figure 1 shows geometric mean PbB at each measurement period in the pregnancy for the group with complete lead data and the group with one or more missing data points. Although there was a tendency for the incomplete group to have higher lead levels than the complete group, *t*-tests for

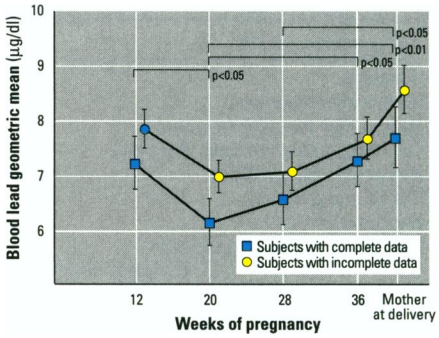

Figure 1. Plot of time course of maternal blood lead (geometric mean and SEM) during pregnancy for subjects with complete and incomplete data. Incomplete data are offset on the X-axis for clarity. Upward trend of complete subjects from 20 weeks to term is significant. Ranges of horizontal lines above the data indicate significant comparisons using least significant differences post-hoc test, with indicated probabilities. Conversion factor for blood lead is 10.0 μg/dl = 0.48 μmol/l.

Table 2. Multiple regression model fitting results for blood lead (PbB) levels at different times[a]

Independent variable	Coefficient	SE	p
PbB, 12 weeks			
Constant	2.749	0.275	
Canned fruit, frequency of consumption	0.136	0.064	≤0.05
Home remedies, last 3 months	0.205	0.089	≤0.05
Birthplace, (Mexico City)	0.236	0.100	≤0.05
Low-temperature ceramic ware use	0.160	0.080	≤0.05
R^2 (adjusted) = 0.056	SE = 0.630	MAE = 0.472 N = 261	
PbB, 20 weeks			
Constant	2.532	0.187	
Coffee	0.174	0.091	≤0.10
Low-temperature ceramic ware use	0.368	0.081	≤0.001
Date of PbB sampling (months)	0.005	0.002	≤0.01
R^2 (adjusted) = 0.094	SE = 0.674	MAE = 0.494 N = 296	
PbB, 28 weeks			
Constant	3.204	0.334	
Pregnancies (number)	-0.097	0.034	≤0.01
Soft drinks, frequency of consumption	0.060	0.031	≤0.10
Canned milk, frequency of consumption	0.117	0.033	≤0.001
Coffee drinking	0.296	0.097	≤0.01
Birthplace (Mexico City)	0.399	0.105	≤0.001
Low-temperature ceramic ware use	0.280	0.081	≤0.001
Complications in previous pregnancies	0.201	0.093	≤0.05
Date of PbB sampling (months)	0.006	0.002	≤0.01
R^2 (adjusted) = 0.209	SE = 0.674	MAE = 0.514 N = 288	
PbB, 36 weeks			
Constant	2.902	0.294	
Abortions (number)	-0.188	0.045	≤0.001
Alcohol (quantity)	0.138	0.071	≤0.10
Milk, frequency of consumption	-0.108	0.043	≤0.05
Soft drinks, frequency of consumption	0.057	0.031	≤0.10
Complications in previous pregnancies	0.166	0.084	≤0.05
Low-temperature ceramic ware use	0.435	0.083	≤0.001
Date of PbB sampling (months)	0.007	0.002	≤0.001
R^2 (adjusted) = 0.212	SE = 0.635	MAE = 0.489 N = 253	
PbB at delivery			
Constant	2.896	0.231	
Abortions (number)	-0.100	0.044	≤0.05
Family members (number)	-0.182	0.076	≤0.05
Low-temperature ceramic ware use	0.293	0.085	≤0.001
Birthplace (Mexico City)	0.214	0.109	≤0.05
Date of PbB sampling (months)	0.007	0.002	≤0.001
R^2 (adjusted) = 0.121	SE = 0.687	MAE = 0.515 N = 281	

MAE, mean absolute error.
[a]Conversion factor for blood lead, 10.0 µg/dl = 0.48 µmol/l. Coefficients are in units of natural logarithm PbB (µg/dl).

Table 3. Multiple regression model: natural logarithm of maternal lead (µg/dl), 20 weeks to term[a]

Independent variable	Coefficient	SE	p
Constant	2.558	0.290	
Weeks of pregnancy	0.012	0.004	≤0.01
Date of PbB sampling (months)	0.005	0.002	≤0.01
Low-temperature ceramic ware use	0.203	0.074	≤0.01
Birthplace (Mexico City)	0.174	0.089	≤0.05
Coffee consumption	0.237	0.074	≤0.01
Abortions (number)	-0.083	0.032	≤0.01
Milk, frequency of consumption	-0.058	0.034	≤0.10
R^2 (adjusted) = 0.114	SE = 0.665	MAE = 0.513 N = 420	

MAE, mean absolute error.
[a]Conversion factor for blood lead, 10.0 µg/dl = 0.48 µmol/l.

independent samples yielded an insignificant difference (using natural log-transformed data) between groups (p>0.10) for each time point during pregnancy.

A repeated-measures ANOVA on data from the complete group using the log-transformed PbB values produced a significant weeks-of-pregnancy effect [F(4,524) = 2.69, p = 0.03]. A least significant difference post-hoc analysis (see ranges in Fig. 1) showed a significant drop in PbB from week 12 to week 20 and various significant increases in PbB from week 20 through delivery. Using data from week 20 through delivery, an analysis for linear trend confirmed the significant PbB rise through this period of pregnancy [F(1,419) = 6.44, p = 0.01].

Multiple regression models of maternal lead at each 8-week period of pregnancy and at delivery were constructed using data from all subjects (Table 2). Dietary factors such as use of canned foods, soft drinks, coffee, and alcohol were associated with increased maternal lead during various periods of pregnancy, while use of lead-glazed ceramic ware was associated with increased maternal lead throughout all the pregnancy. Increased milk consumption was associated with decreased maternal lead late in the third trimester. Birthplace was a significant predictor of maternal lead at various times during pregnancy; mothers born in the Valley of Mexico had higher lead than those born outside the valley. Reproductive history, especially history of abortions or gravidity, which were associated with decreased maternal lead, were prominent in the last trimester. Later date of blood sampling during the study period was significantly associated with increased PbB in the last half of pregnancy.

Table 3 shows the trend from 20 weeks of pregnancy through delivery for the group with complete data corrected for significant predictors of maternal PbB at two or more time points in pregnancy discovered through the multiple regression modeling. Despite correcting blood lead values by these important determinants of blood lead during pregnancy in the multiple regression analysis, weeks of pregnancy in the last half of pregnancy was still significantly associated with increased maternal PbB.

Figure 2 shows maternal hematocrit from weeks 12 to 36 of pregnancy. Maternal hematocrit decreased from weeks 12 to 28 and remained unchanged at 36 weeks. Maternal PbB and hematocrit did not follow the same time course from week 12 to week 36 of pregnancy.

Discussion

Dietary sources of lead, especially prominent in the study population, were associated with increased PbB during pregnancy. Mexico has a nearly 500-year history of using lead-glazed pottery for cooking, serving, and storing food and drink. Although lead in domestic articles was recognized in Mexico as a source of lead poisoning in children nearly two centuries ago (*8*), and despite repeated notice to public health authorities regarding lead in ceramic ware (*9–11*), little has been done to remedy the problem until recently. As a result, the more than 40% of our sample reporting use of lead-glazed pottery showed elevated PbB during the last 28 weeks of pregnancy.

Canned foods using lead-soldered seams were common in the Mexican mar-

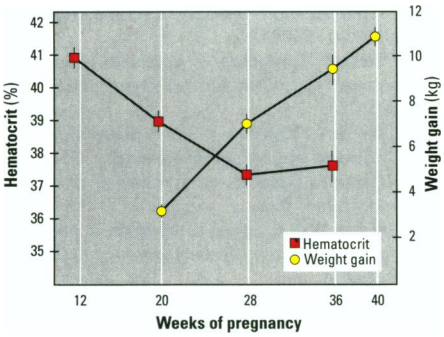

Figure 2. Time course of mean maternal hematocrit and mean maternal weight gain during pregnancy. Error bars are standard error of the mean. Weight gain was not measured at 12 weeks, and hematocrit was not measured at delivery.

ketplace until 1993, when seamless or welded-seam cans replaced all but a small fraction, represented by imported foods. Canned foods, associated with increased maternal PbB, were also related to higher lead in children born to mothers participating in this study in a preliminary report (*12*). As existing stocks of lead–soldered cans are reduced, we expect the contribution of this source to the national lead load to disappear.

All mothers entering the study were given basic information on the major sources of lead and on the effects of lead on the fetus and young child and were urged to discontinue habits leading to increased lead intake. As we only assessed food preparation habits and food use at the beginning of the study period, we were unable to determine the extent that these patterns changed during the pregnancy and thus may have contributed to the alterations of PbB measured. However, to the extent that the educational efforts were successful in reducing lead intake during pregnancy, the reported increases in lead in the last 20 weeks of pregnancy would be underestimated.

Investigators using a cross-sectional design have reported a drop in maternal PbB during periods roughly corresponding to our 12- to 20-week interval (*3*). The decrease observed during this period has usually been attributed to increased fluid volume, measured by hematocrit, during the first half of pregnancy. The increase in plasma volume during pregnancy is well documented and amounts to an average of 1200 ml in the first 34 weeks of pregnancy (*13*). The expansion of blood volume is greatest in the second trimester, but the increased erythrocyte production during pregnancy does not keep pace with increased fluid volume, resulting in decreased hematocrit.

We observed the expected decrease in hematocrit in the first half of pregnancy as well. However, hematocrit decreased every 8 weeks from week 12 to week 28 and then remained unchanged at 36 weeks in our study. The time course of the hematocrit change across pregnancy did not correspond to the time course of PbB change. Furthermore, hematocrit-corrected PbB values followed the same time course throughout the pregnancy as non-hematocrit-corrected PbB, and hematocrit was not statistically associated with lead in the multivariate models. Although hematocrit changes in the first 20 weeks of pregnancy could explain some of the observed PbB decrease between 12 and 20 weeks, decreased hematocrit cannot account for the observed PbB increase thereafter.

Growth in other organs can also serve as a sink for circulating maternal PbB in the first 20 weeks of pregnancy. The fetus has attained 10% of its term weight, the placenta over 25%, the uterus 30%, the mammaries over 40%, with total weight gain in the mother around one-third that experienced at the end of pregnancy (*14*). Almost all of the increase in cardiac output and in glomerular filtration rate is achieved by 20 weeks of pregnancy (*15,16*), and though never reported, excretion of lead during the first half of pregnancy might be enhanced. Assuming unchanging lead intake, the combination of hemodilution, increased weight of organs and enhanced metabolic activity could account for much of the observed decrease in whole PbB between 12 and 20 weeks of pregnancy.

Although the time course of these factors is correlated with the decrease in PbB in the first 20 weeks of pregnancy, the majority of the change in fetal and maternal organ size occurs after 20 weeks (see Figure 2 for weight gain in our subjects). Other factors must intervene to produce the measured increase in blood lead in the last half of pregnancy despite increasing hemodilution and organ weights.

Various physiological changes during pregnancy may account for increased PbB in the last half of pregnancy. Accelerated absorption of dietary lead and decreased elimination of lead from the body, perhaps following the calcium conservation strategies of late pregnancy (*17*), and release of bone lead may all operate to yield the observed pattern of lead during pregnancy.

Although lead in blood and other soft tissues has a mean-life after single dose of 35 days (*18*), the half-times of lead in bone are 5–20 years (*19*), allowing it to accumulate over the life of an individual. Lead accumulates in bone by replacing calcium in the apatite. Its flow from blood to bone is mediated by osteoblast activity, whereas the principal return from bone to blood is related to osteoclast activity (*20*). Saltzman (*21*) estimated that at age 20, about 78% of the total lead in the body of humans resides in bone, rising to 96% at age 80. Although normally lead in bone is nearly immobile, some processes that increase bone turnover, notably pregnancy, may increase mobilization of lead from bone (*22–26*).

Most of the accumulation of fetal calcium occurs in the last trimester, coinciding with the mineralization of the fetal skeleton. Parathyroid hormone responds to changes in plasma calcium, decreasing during the first trimester of pregnancy and increasing thereafter (*17,27*). Increased parathyroid hormone is associated with increased bone resorption, increased intestinal absorption of calcium, and kidney reabsorption of calcium, likely in response to fetal need, and it stimulates renal biosynthesis of $1,25(OH)_2D$, which mobilizes calcium from the bone (*28*). Processes that mobilize calcium from bone during pregnancy could also mobilize lead from bone.

Several of our findings suggest that the increasing PbB found in the last half of pregnancy derives in part from maternal bone lead in addition to increased gut absorption. First, the timing of the increase in the last half of pregnancy coincides with increased fetal need for and increased maternal provision of calcium (*29*). If some of the additional fetal calcium requirement is supplied from maternal bone, mothers with high bone loads of lead may transfer more lead to the bloodstream with the calcium.

Second, mothers in our study who had low milk intake, our measure of dietary calcium, had higher PbB levels late in pregnancy. Calcium-deficient diets are associated with increased intestinal absorption of dietary lead (*28*). But lead may also be provided from the bone during times of high calcium stress in pregnant women with calcium-deficient diets (*24*).

Third, mothers born and living most of their lives in Mexico City had higher late pregnancy PbB than mothers born outside of the city. Mexico City has had historically high air lead levels, due primarily to the use of heavily leaded gasoline (*30*). These levels peaked in the early 1980s and have been dropping since then as programmed gasoline lead reductions have been implemented. Mothers born, growing up, and living in Mexico City all their lives may have higher lifetime exposures to lead than mothers born elsewhere in the country, and this would be reflected in higher bone lead.

Fourth, mothers in our study with more abortions or more prior pregnancies had lower PbB levels in the last trimester of

pregnancy. If the fetus transports substantial maternal lead from the mother's body, lowering body (bone) stores of lead in subsequent pregnancies, multigravid women should have lower PbB. Indeed, lower cord PbB has been reported before in multigravid women (*31*).

Fifth, maternal coffee consumption was associated with increased PbB. This relationship has been reported before in a study investigating cord PbB, though it was not discussed (*31*). Although drinking coffee prepared and served in lead-glazed ceramic ware is common in Mexico, the association between coffee drinking and increased lead is independent of the effect of use of lead-glazed ceramic ware on PbB, as noted in the multiple regression analyses (Table 3). Caffeine intake is associated with increased calcium excretion in women (*32,33*), likely due to its effect on renal reabsorption (*34*). There are no data reported in the literature regarding the effect of caffeine on lead excretion. As in women with reduced milk intake, the increase in PbB with coffee use might arise from compensatory increased gut absorption of lead. However, the still-disputed link between caffeine intake and bone loss in post-menopausal women (*35*) also suggests the possibility that some of the increased PbB related to coffee drinking seen in this study may derive from bone lead release in women whose calcium balance is further compromised by caffeine during pregnancy.

Since no measurements of bone, environmental, or dietary lead were made, the sources for maternal lead changes during pregnancy suggested by the models can only be considered tentative. Although the increased PbB in the last half of pregnancy is small, on the average about 1.6 µg/dl (0.07 mol/l; approximately 20%) from 20 weeks to parturition, this increase is found in the face of hemodynamic, metabolic, and organ size changes, all of which act to reduce maternal PbB concentration. Thus the measured increase indicates that, whatever the source, the amount of lead put into circulation in the last half of pregnancy may be substantial and physiologically significant.

The preceding results suggest that women with higher lifetime exposures, and thus more bone lead, and calcium-deficient women may have higher circulating lead levels during the second half of pregnancy with consequent increased exposure to the fetus. The results imply that to gain maximum public health savings through lead-reduction programs, our goal should be to reduce lead-exposure of women at the earliest age possible and maintain the reduction through their reproductive years. We might expect a time lag of a generation or more before the benefits of reduced environmental lead are fully passed on to the fetus.

Many kinetic models of lead in organisms have been developed, though none yet treats lead during pregnancy in humans. Any valid kinetic model of the maternal–fetal PbB system must not only account for the decrease in maternal PbB in the first 20 weeks of pregnancy, it must also account for the measured increase in the second 20 weeks.

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