Relationship of Blood and Bone Lead to Menopause and Bone Mineral Density among Middle-Age Women in Mexico City

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To describe the relationship of blood lead levels to menopause and bone lead levels, we conducted a cross-sectional study on 232 pre- or perimenopausal (PreM) and postmenopausal (PosM) women who participated in an osteoporosis-screening program in Mexico City during the first quarter of 1995. Information regarding reproductive characteristics and known risk factors for blood lead was obtained using a standard questionnaire by direct interview. The mean age of the population was 54.7 years (SD = 9.8), with a mean blood lead level of 9.2 µg/dL (SD = 4.7/µg/dL) and a range from 2.1 to 32.1µg/dL. After adjusting for age and bone lead levels, the mean blood lead level was 1.98 µg/dL higher in PosM women than in PreM women (p = 0.024). The increase in mean blood lead levels peaked during the second year of amenorrhea with a level (10.35 µg/dL) that was 3.51 µg/dL higher than that of PreM women. Other important predictors of blood lead levels were use of lead-glazed ceramics, schooling, trabecular bone lead, body mass index, time of living in Mexico City, and use of hormone replacement therapy. Bone density was not associated with blood lead levels. These results support the hypothesis that release of bone lead stores increases during menopause and constitutes an internal source of exposure possibly associated with health effects in women in menopause transition. Key words: blood lead, bone lead, bone mineral density, menopause. Environmental Health Perspectives 111:631–636 (2003). doi:10.1289/ehp.5149 available via http://dx.doi.org/ [Online 16 December 2002]

For decades the population of Mexico City was exposed to high environmental lead levels because of the combustion of leaded gasoline and poor environmental control of industrial activities. However, this situation changed in 1986 with regulatory actions that reduced the lead emissions and lead content of gasoline, culminating in its elimination in 1997 (Hernández-Avila et al. 2000). Similar regulatory actions were established for other sources of lead exposure such as paints, solders in canned food, and cosmetics. In addition, in 1995 the Mexican government initiated the search for alternative substitute for lead used in low-temperature hand-made ceramics, but at present this type of ceramic remains the main non-occupational source of lead exposure in Mexico (Hernández-Avila and Romieu 1991; Romieu et al. 1994).

Lead from environmental and occupational sources enters the body through inhalation of particles or intake of lead-contaminated food (Lockitch 1993). It is transported by blood to soft tissues, where it remains for short periods and is finally deposited in bone tissue (Barry and Moshmann 1970). More than 90% of the lead present in the body is stored in bones throughout life, where it may remain for decades (Barry and Moshmann 1970). Nevertheless, bone tissue does not represent a site of permanent sequestration of lead but rather a source of continuous internal exposure that may increase as a result of the changes in bone turnover observed at different life stages (Gulson et al. 1995; Pounds et al. 1991). This may be the case with menopause, where bone mass loss is a frequent phenomenon that typically starts in the perimenopausal years and continues with an accelerated loss in the early postmenopausal years (Cummings et al. 1985; Elders et al. 1988; Nilas and Christiansen 1988; Riggs and Melton 1986; Ruesegger et al. 1984; Silbergeld et al. 1993).

Although previous studies demonstrated the blood lead increase during this stage of life (Muldoon et al. 1994; Silbergeld et al. 1988; Symansky and Hertz-Picciotto 1995; Weyerman and Brenner 1998), only one study recently published simultaneously measured lead levels in blood and bone among perimenopausal women (Korrick et al. 2002).

The objective of this study was to examine the relationship between blood and bone lead during menopause under the hypothesis that postmenopausal (PosM) women have higher blood lead levels in comparison with premenopausal women after controlling for bone lead content, age, and exposure to environmental sources. A second hypothesis is that higher bone remodeling rates among PosM women—using bone mineral density (BMD) as an indicator—is associated with higher blood lead levels after controlling for age and bone lead among other variables.

Materials and Methods

The study population was recruited from women attending an osteoporosis-screening program carried out by the Mexican Committee for Osteoporosis Research in Mexico City. Women were recruited through conferences given live during a radio program aimed at women. During the program, one of us (J.T.O.), an expert in osteoporosis, explained to the audience a set of actions to prevent osteoporosis and provided information regarding its diagnosis and treatment and the screening program. The radio programs were broadcast during the first quarter of 1995, and a total of 961 women were recruited. Once the clinical procedures necessary for osteoporosis dating were carried out, all participants were invited for complimentary measurements of blood and bone lead levels. A total of 653 women consented to the blood lead test, and 35% of these (n = 232) completed measurements of both blood and bone lead. The primary reason for not completing the bone lead measurement was the inconvenience of participants visiting a different clinic far from the initial enrollment and screening center. For the analyses, the final sample was made up of these 232 women, of whom 36 were pre- or peri-menopausal (PreM) and 196 were PosM.

The research protocol was approved by the Human Subjects Committee of the National Institute of Public Health of Mexico. All participants gave their informed consent and received a detailed explanation of the study and procedures used, as well as counseling on how to reduce lead exposure.

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We used a structured questionnaire that collected information on sociodemographics, life styles, reproductive history, and sources of environmental exposure to lead. The education level of the subjects was grouped in the following three categories: less than primary school, primary and secondary school, and high school or more. We also asked about tobacco consumption, alcohol consumption, and physical exercise. With regard to tobacco, the subjects were classified according to current smoking habits. Alcohol consumption was analyzed according to frequency (abstainers, less than once a month, once a month but at least once a year, from two to three times a month, and one or more times a week) and the number of drinks consumed per occasion. Regarding physical activity, participants were asked whether they currently exercised on a regular basis. In the section of reproductive characteristics, we collected information on the use of exogenous hormones and the time of their use, either for family planning purposes or to treat symptoms due to pregnancy, lactation, or any disease or surgical procedure. Finally, menopause was classified as natural or surgical. Years since menopause was calculated as the time since the last menstrual period or time since hysterectomy. The questionnaire also included a section to identify sources of environmental and indoor exposure to lead. Among them, the following were identified: type of vehicular traffic next to the place of residence (intense, intermediate, or low), residence time (0–5 years, 6–9 years, and ≥ 10 years), and overall time spent in preparing and storing food in lead-glazed ceramics. These characteristics represent the most important sources of lead exposure previously identified in our population (Hernández-Avila and Romieu 1991; Romieu et al. 1994).

**Table 2. Study population according to selected variables.**

| Variables                          | n   | Percentages or means and SD values | Range     |
|------------------------------------|-----|------------------------------------|-----------|
| Age (years)                        | 232 | 54.1 ± 9.8                         | 28–88     |
| Postmenopausal                     | 196 | 82.2                               |           |
| Premenopausal or perimenopausal    | 36  | 17.8                               |           |
| Smoking (%)                        | 183 | 78.8                               |           |
| No smoking                         | 104 | 44.8                               |           |
| Smoking occasional                 | 68  | 30.3                               |           |
| Smoking daily                      | 42  | 18.1                               |           |
| History of breast-feeding (%)      | 187 | 80.6                               |           |
| No                                 | 26  | 11.2                               |           |
| Nulliparous                        | 19  | 8.2                                |           |
| Premenopausal or perimenopausal    | 36  | 15.5                               |           |
| Postmenopausal                     | 36  | 15.5                               |           |
| Surgical                           | 76  | 32.8                               |           |
| Natural                            | 120 | 51.7                               |           |
| Age at menopause                   | 196 | 45.3 ± 7.0                         | 24–60     |
| Years since menopause              | 191 | 11.3 ± 6.7                         | 1–42      |
| BMD lumbar spine (g/cm²)           | 221 | 1.022 ± 0.18                       | 0.47–1.62 |
| BMD femoral neck (g/cm²)           | 220 | 0.873 ± 0.14                       | 0.54–1.31 |

*Some variables have missing values.*
was calibrated by standardized mineral density (GE Lunar Corp., Madison, WI). On initiat- 
energy x-ray absorptiometry) densitometer and 6.9 (3.1), respectively.

of overlying tissue, which resulted in estimates either because the movement of the 
limb being measured was out of the measure-
ment field or because of the extreme thickness
of underlying tissue, which arises predominantly from the calcium and phos-
phor present in bone mineral. For the present
study, 30-min measurements were taken at the midshaft of the left tibia (cortical bone) and at the left patella (trabecular bone) after each region had been washed with a 50%
solution of isopropyl alcohol. The instrument
provides an estimate of the uncertainty
associated with each measurement; for purposes of
quality control of bone lead measurements,
we excluded 14 individuals with questionable
values either because the movement of the
limb being measured was out of the measure-
ment field or because of the extreme thickness
of underlying tissue, which resulted in estimates
of uncertainty greater than 10 µg Pb/g bone
mineral for the tibia or 15 µg Pb/g for the
patella. The mean uncertainty (and SD) for
patella and tibia in our study were 8.4 (2.8) and 6.9 (3.1), respectively.

BMD was measured at the lumbar spine and femur neck with a LUNAR DEXA (dual energy x-ray absorptiometry) densitometer (GE Lunar Corp., Madison, WI). On initiat-
ing each measuring session, the equipment
was calibrated by standardized mineral density
device (photons) whose coefficients of varia-
tion were lower than 4%. The results
are expressed in grams per square centimeter. We
used the criteria established by the World
Health Organization (WHO 1994) for
BMD classification: a) normal, if BMD value
was greater than or equal to 1 SD in relation to
the reference group; b) osteopenia, if BMD
was between –1.0 and –1.5 SD values; and
c) osteoporosis, if BMD was lower than
–2.5 SD values in relation to the reference
group (WHO 1994).

We performed an exploratory analysis of
each variable included in the study by univari-
ate statistics and distribution plots. The bivari-
ate analysis included test (two groups) and
analysis of variance (three or more groups);
linear regression models were used to examine
the relationship between blood lead levels and
variables of interest. The age effect was mod-
eling using linear and quadratic terms to
account for nonlinear relationships observed
between age and blood lead (Hernández-Avila
et al. 2000; Silbergeld et al. 1988).

First, the relationship between each
variable and log-e (natural log) transformation
of blood lead levels was examined. Then, we
analyzed the relationship between blood lead
and all those variables that in bivariate analysis
would have achieved 0.15 significance level.
We defined the best model by dropping
covariates one by one from a saturated model
that included all variables with a p-value below
0.15. Our final multivariate model included
all-important predictors with a statistically sig-
ificant association defined at p < 0.10.

When bone lead concentrations are very
low (< 5 µg/g bone mineral), the K-XRF
measurements may provide negative values
because of the algorithm used by equipment
software (Hu et al. 1995). To test the robust-
ness of our findings in relation to negative val-
ues, these were randomly distributed within
an interval between 0 and 5 µg Pb/g of bone
mineral. Reanalysis using these values did not
change the estimates of interest. All statistical
analysis procedures were carried out with a
Stata package (Stata Statistical Software,
release 7.0, Stata Corp., College Station, TX).

Results
The study group (n = 232) showed no
 differences in relation to nonparticipants
regarding most characteristics of interest (Table 1). Women who participated showed a
lower mean blood lead concentration and a
higher body weight.

The group of PreM women constituted
15.5% of the total population. The age of the
population ranged from 28 to 88 years, with a
mean of 54.7 years (SD = 9.8). Most of these
women (66.4%) had an intermediate level of
schooling (6–9 years). Regarding reproductive
characteristics, 92% had a history of one or
more pregnancies (mean 4.3, SD = 2.6), and
81% had breast-fed their infant. The mean
age of natural menopause was 47.6 years
(SD = 5.8) and of surgical menopause was
42.2 years (SD = 6.7). About 46% of the
participants with menopause reported the use of
hormone replacement therapy (HRT).

Life-style characteristics were as follows:
18% of the participants were classified as
current smokers; 55% exercised on a regular
basis; 22% consumed three or more alcoholic
drinks per occasion, and 23% prepared meals
in lead-glazed ceramic cookware during the
last week. Blood lead levels were distributed
between a minimum value of 2.1 µg/dL and a
maximum of 32.1 µg/dL, with a mean of 9.2
µg/dL (SD = 4.71) and a 95% confidence
interval of 8.5–9.8 µg/dL. Lead values in tra-
becular and cortical bone were distributed
with means of 22.7 µg Pb/g of bone mineral
(SD = 14.9) and 14.9 µg Pb/g (SD = 10.09),
respectively (Table 2). Lead levels in trabecu-
lar bone (patella) explained an important per-
centage of blood lead variation (r² = 18%).
For each 1 µg Pb/g of bone mineral, blood
lead levels increased by 1.1% (regression co-
efficient 0.011; p = 0.001). However, this
association varied significantly (p < 0.01)
when we stratified according to type of
menopause (Figure 1). Blood lead increased
by 0.3 and 1.1% per µg Pb/g of bone
mineral, for PreM and PosM women, respec-
tively. According to this model, a change of
10 µg Pb/g of bone mineral in PosM will be
associated with an increase in blood lead of
1.4 µg/dL, whereas a similar change among
PreM women will be associated with an
increase of 0.8 µg/dL.

Figure 1. Regression analysis between blood lead levels (micrograms per deciliter, log-e transformed) and patella bone lead levels (µg Pb/g bone mineral) for all participants and subgroups divided according to menopausal status.
Table 3. Blood lead levels (microgram/deciliter) according to sociodemographic, life style, and reproductive characteristics.

| Variables                              | n  | Mean | SD | p-Value<sup>a</sup> |
|----------------------------------------|----|------|----|---------------------|
| Age groups (years)                     |    |      |    |                     |
| < 40                                   | 12 | 10.5 | 5.5 | 0.23                |
| 40–44                                  | 23 | 9.4  | 4.1 | 9.1                 |
| 45–49                                  | 41 | 10.6 | 6.0 | 10.4                |
| 50–54                                  | 40 | 9.1  | 3.9 | 9.2                 |
| 55–59                                  | 49 | 8.5  | 3.0 | 9.1                 |
| 60–64                                  | 30 | 8.9  | 5.5 | 8.8                 |
| 65–69                                  | 19 | 8.3  | 6.4 | 8.4                 |
| ≥ 70                                   | 18 | 7.7  | 3.2 | 7.5                 |
| Literacy (years of school)             |    |      |    |                     |
| 0–5                                    | 27 | 10.2 | 5.7 | 0.06                |
| 6–9                                    | 154| 9.3  | 4.7 | 9.2                 |
| ≥ 10                                   | 51 | 8.1  | 4.1 | 8.1                 |
| No. of pregnancies                     |    |      |    |                     |
| None                                   | 19 | 9.7  | 5.7 | 0.42                |
| 1–3                                    | 82 | 8.5  | 3.2 | 8.4                 |
| 4–6                                    | 87 | 9.0  | 4.4 | 9.1                 |
| ≥ 7                                    | 44 | 10.4 | 6.7 | 10.4                |
| Breast-feeding                         |    |      |    |                     |
| No                                     | 26 | 8.2  | 3.2 | 0.43                |
| Yes                                    | 187| 9.2  | 4.8 | 9.21                |
| Menopause                              |    |      |    |                     |
| No (PreM)                              | 36 | 9.4  | 4.9 | 0.69                |
| Yes (PosM)                             | 196| 9.1  | 4.7 | 9.5                 |
| Type of menopause                      |    |      |    |                     |
| PreM                                   | 36 | 9.4  | 4.9 | 0.50                |
| Surgical                               | 76 | 9.3  | 3.8 | 9.4                 |
| Natural                                | 120| 9.0  | 5.2 | 9.5                 |
| Time since menopause (surgical, months)|    |      |    |                     |
| PreM                                   | 36 | 9.4  | 4.9 | 0.32                |
| 12                                     | 9  | 11.2 | 4.5 | 11.2                |
| 13–24                                  | 6  | 11.1 | 3.9 | 9.9                 |
| 25–36                                  | 10 | 7.5  | 2.7 | 8.2                 |
| 37–48                                  | 9  | 8.9  | 3.6 | 9.3                 |
| ≥ 49 years                             | 42 | 9.1  | 3.7 | 10.1                |
| Time since menopause (natural, months) |    |      |    |                     |
| PreM                                   | 36 | 9.4  | 4.9 | 0.23                |
| 12                                     | 15 | 9.3  | 4.3 | 7.9                 |
| 13–24                                  | 18 | 9.7  | 4.5 | 10.4                |
| 25–36                                  | 12 | 8.8  | 2.5 | 7.2                 |
| 37–48                                  | 12 | 11.2 | 7.2 | 11.4                |
| ≥ 49 years                             | 58 | 8.9  | 5.6 | 10.3                |
| HRT                                    |    |      |    |                     |
| Yes                                    | 91 | 8.5  | 3.5 | 0.20                |
| No                                     | 105| 9.7  | 5.5 | 10.1                |
| HRT (natural menopause)                |    |      |    |                     |
| Yes                                    | 53 | 7.5  | 3.1 | <0.01               |
| No                                     | 67 | 10.2 | 6.1 | 10.5                |
| HRT (surgical menopause)               |    |      |    |                     |
| Yes                                    | 38 | 9.8  | 3.7 | 0.14                |
| No                                     | 38 | 8.7  | 3.1 | 9.1                 |
| Smoking                                |    |      |    |                     |
| Yes (current)                          | 42 | 9.1  | 4.9 | 0.74                |
| Yes (past)                             | 45 | 8.0  | 4.8 | 8.4                 |
| Never                                  | 145| 9.5  | 4.6 | 9.4                 |
| Physical activity                      |    |      |    |                     |
| Yes                                    | 128| 9.6  | 5.2 | 0.09                |
| No                                     | 104| 8.6  | 3.9 | 8.6                 |
| No. of drinks                          |    |      |    |                     |
| One or less                            | 127| 8.7  | 4.7 | 0.112               |
| Two                                    | 59 | 9.5  | 5.6 | 9.9                 |
| Three +                                | 50 | 9.4  | 3.6 | 8.9                 |
| Use of lead-glazed ceramics            |    |      |    |                     |
| Yes                                    | 49 | 10.7 | 6.7 | <0.01               |
| No                                     | 183| 8.6  | 3.6 | 9.2                 |

<sup>a</sup>P-Value from ANOVA using log-e transformed blood lead as the dependent variable.

BMDs of lumbar spine and femur neck were distributed with means of 1.022 µg/cm² (SD = 0.177) and 0.873 µg/cm² (SD = 0.135), respectively. We did not find any relationship between blood lead values and BMDs of lumbar spine and femur neck. Regression coefficient for BMD of lumbar spine was 0.0048 (p = 0.962), and for femur neck was 0.1561 (p = 0.217). These coefficients were not modified after adjusting for age and bone lead.

No linear relationship was observed between blood lead levels and age (p = 0.23). The highest mean blood lead was observed for the 45- to 49-year-old group, corresponding to the mean age of natural menopause, when it reached a mean concentration of 10.6 µg/dL and progressively decreased to values smaller than those found in PreM women.

In the baseline multivariate model that adjusted for age and bone lead (Table 3), PosM women showed blood lead levels 1.98 µg/dL higher than those found in PreM women (p = 0.024). This increase was apparent for women with surgical menopause (1.91 µg/dL) and women with natural menopause (2.1 µg/dL) compared with those for PreM women. In relation to the years since menopause, the distribution of blood lead values showed two points of inflection that, in the case of women with surgical menopause, corresponded to the first and fifth year after menopause (11.17 and 10.07 µg/dL), which corresponded to a difference of 3.35 and 1.92 µg/dL compared with those in the PreM group (p = 0.158); for women with natural menopause, the two points of inflection corresponded to the second and fourth year after menopause (10.35 and 11.43 µg/dL), differences of 2.2 and 3.28 µg/dL, respectively (p = 0.063).

PosM women who used HRT (adjusting for age and bone lead) had lower blood lead levels than PosM women who did not use the therapy, with an estimated mean blood lead difference of –1.25 µg/dL (p = 0.09). When the analysis was restricted to the group of participants with natural menopause, the mean blood lead concentration was 2.64 µg/dL higher in the group of PosM women who were nonusers of replacement estrogens (p = 0.005).

The use of lead-glazed ceramics was an important predictor of blood lead levels. The women who prepared and stored food in lead-glazed ceramic cookware during the previous week showed higher blood lead levels than those who did not use it, with differences of 2.48 and 2.01 µg/dL, respectively (p < 0.05).

Finally, the most parsimonious multivariate model that explained 38.7% of the variation in blood lead levels included the following variables: age (linear and quadratic terms), time of...
postmenopause, body mass index, patella lead, use of lead-glazed ceramic cookware, schooling level greater than 6 years, and time of living in Mexico City (Table 4).

**Discussion**

Our results showed that blood lead increases significantly in the PosM period and a particularly in the first 3 years of this period. Our data suggest that once these maximum levels are achieved, the blood lead decreases in the third year and afterward starts increasing again. This finding is consistent with a particular bone remodeling pattern during the first year of postmenopause that mainly depends on higher bone turnover of trabecular bone. As is well known, the trabecular bone loss increases in the perimenopausal period, which is followed by an accelerated loss in the first year of postmenopause, and then bone resorption decreases and becomes constant (Cummings et al. 1985; Elders et al. 1988; Nilas and Christiansen 1988; Riggs and Melton 1986; Ruesegger et al. 1984).

As reported by Muldoon et al. (1994), our study did not find high blood lead levels in women with low mineral density. Measurements of BMD in cross-sectional studies provide a snapshot of the balance between bone deposition and bone resorption over preceding years, whereas blood lead levels would be expected to depend more specifically on absolute rates of ongoing bone resorption. Because of this limitation Hu et al. (1998) proposed the use of bone markers that are specific for ongoing rates of bone resorption such as the N-telopeptide of type I collagen (urinary NTX). Recent research in elderly men suggests that urinary NTX is a significant modifier of the bone lead–blood lead relationship.

The age-adjusted difference in trabecular bone lead concentrations observed between PosM and premenopausal women (difference of ~5.8 µg of lead per gram of bone mineral; $p = 0.02$) supports the hypothesis that the lead is mobilized from the bone compartments toward the circulation and contributes to the increase of blood lead levels in this stage of life. The hypothesis is also supported by our observation that the use of replacement estrogens was also associated with lower blood lead levels among PosM women. Furthermore, patella lead explained the greatest part of variations in blood lead levels, and its independent effect remained the same after controlling other important predictors of blood lead. A different pattern was found in the association between tibia lead and blood lead. These levels were marginally different between PreM and PosM women ($p = 0.06$). This difference suggests the existence of lead pools in the mineral tissue (trabecular represented by patella and cortical by tibia) that follow different turnovers. In cortical bone, it is known that its turnover is much slower than that occurring in trabecular bone, so its contribution to blood lead levels is expected to be smaller. It should be noted, however, that cortical bone composes the majority of skeletal mass (~80%), making even modest resorption of cortical bone a potentially major influence on blood lead levels. Similar results were reported by Kosnett et al. (1994) in women older than 55 years. Silbergeld et al. (1988) and Symansky and Hertz-Picciotto (1995) observed an increase of blood lead in nulliparous PosM women after comparing them with multiparous women. This finding suggests that pregnancy, and probably breastfeeding as well, may mobilize the lead deposited in bone simultaneously with calcium, to meet the calcium requirements observed in pregnancy and lactation, leaving smaller amounts of lead to be mobilized during the menopause transition. These results have not been confirmed by other investigators (Brown et al. 2000; Muldoon et al. 1994; Weyerman and Brenner 1998). In our study PosM women who breast-fed had higher bone lead levels (21.2 and 18.1 µg of lead per gram of bone mineral; $p = 0.23$). These results are similar to those reported by Brown et al. (2000) and probably reflect the fact that this cohort of women breast-fed during the years of high lead concentrations in the Mexico City air and thus incorporated additional lead during the bone gain phase that is known to follow pregnancy and lactation (Kalkwarf et al. 1997).

HRT, alone or combined, prevents bone resorption and increases the BMD in trabecular and cortical bones of women with and without metabolic bone disease (Berlin et al. 1995; Gruber et al. 1997; Webber et al. 1995). This effect may lead to a decrease of lead mobilization from bone together with a reduction in blood lead levels. Webber et al. (1995) reported that women with HRT showed greater bone lead concentrations, especially in cortical bone, without having a simultaneous decrease in blood lead. In our study, 46.4% of the PosM women used HRT, and the blood lead levels observed among them were lower than those in nonusers (difference of 2.1 µg/dL; $p < 0.05$). In addition, we found that trabecular and cortical bone lead levels were higher in women who used HRT (1.19 and 0.43 µg Pb/g of bone mineral for patella and tibia, respectively). This observation supports the hypothesis that HRT reduces bone resorption, and by preventing lead mobilization from bone and diminishing blood lead levels, HRT may be considered a preventive measure in PosM women with high bone lead levels.

Compared with women of child-bearing age living in Mexico City (Brown et al. 2000) as well as perimenopausal women living in the United States (Korrick et al. 2002), the mean bone lead levels seen in these women were significantly higher. This finding reflects the fact that women participating in our study were living in Mexico City during the time that gasoline had a higher lead content and thus were subject to higher environmental lead exposures in the recent past. The adjusted regression coefficient of patella bone lead on blood lead predicted an increase of 0.80 µg blood lead/µg bone lead for women of child-bearing age and of 0.05 µg blood lead/µg bone lead for perimenopausal women, which were lower than estimated in this study (blood lead 0.135 µg/µg of bone lead).

Our study has potential limitations that may affect the inferences derived from these data. The participants were primarily low- and middle-class women who voluntarily attended an osteoporosis program and were not a random sample of the general population. Thus, our results cannot be generalized to all women living in Mexico City. Of note, we found differences, in terms of both blood lead levels and height, between women attending the screening program and women taking part in bone lead measurements. However, the differences observed in blood lead levels decreased once we adjusted for other variables such as age, education, and menopausal status; therefore, it is unlikely that selection bias could explain our findings. We used simple questionnaire data to characterize environmental exposure to lead-glazed ceramic ware and thus may have underestimated the contribution to blood levels.

### Table 4. Results from multivariate linear regression of blood lead levels (log-e, microgram per deciliter) on selected predictors of study participants

| Variable (Years) | Coefficient | p-Value | 95% CI |
|------------------|-------------|---------|-------|
| Age linear (years) | -0.063 | 0.01 | -0.113 to -0.013 |
| Age squared (years²) | 0.0005 | 0.04 | 0.0001 to 0.001 |
| Patella lead (µg Pb/g mineral bone) | 0.012 | <0.01 | 0.008 to 0.015 |
| Time postmenopausal (1–24 months) | 0.284 | <0.01 | 0.111 to 0.456 |
| Body mass index (kg/height in m²) | 0.015 | 0.03 | 0.001 to 0.029 |
| Time living in Mexico City (years) | 2.41 | <0.01 | 2.03 to 4.764 |

*Years since menopause is in reference to PreM. Educational level of 0–5 years is the reference category.
lead levels of this major known source of environmental lead exposure in Mexico. Only 16% of our study group (n = 36) were premenopausal, limiting our ability to conduct a more in-depth analysis of potential interactions such as the potential modifying effect of menopausal status on other factors that determined blood or bone lead levels. The cross-sectional nature of these data also limited our ability to do more sophisticated kinetic modeling of bone lead–blood lead interrelationships.

Suspicion exists that the accumulation of lead in bone itself represents a risk factor for osteoporosis. Individual cases such as the subjects reported by Berlin et al. (1995) who had occupational lead exposure, a bone fracture, and diagnosis of idiopathic osteoporosis provide some circumstantial evidence of such a relationship. Other evidence supporting the hypothesis that lead can directly damage bone includes observations of fetal and neonatal growth reduction and the development of osteopenia in experimental animals exposed to lead (Gruber et al. 1997). Pounds et al. (1991) reported that bone cells, both in vivo and in vitro, may be impaired by the presence of lead. However, additional studies are required to directly assess this hypothesis and to investigate indirect routes by which lead may be related to osteoporosis, such as the possibility that lead affects calcium absorption at the level of the digestive tract or that lead reduces circulating levels of 1,25-dihydroxycholecalciferol, as has been noted in experimental animals exposed to lead (Gruber et al. 1997).

The increase in blood lead concentrations that result from bone resorption after menopause may, in turn, be associated with health effects that have not been adequately studied in elderly women. Studies of subjects in other age groups show that relatively modest exposures to lead are associated with neurologic dysfunction, behavioral disorders, hypertension, renal damage, and hematologic changes (Vig and Hu 2000). It may be particularly important to study the relationship between blood and bone lead levels and cognitive impairment in perimenopausal women because of the potential modifying role played by osteoporosis in these women.

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