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Blood Lead Levels Measured Prospectively and Risk of Spontaneous Abortion

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Studies of low to moderate level lead exposures have reported mixed findings regarding the risk of spontaneous abortion, despite lead's abortifacient properties at very high doses. To evaluate the risk of spontaneous abortion from low or moderate lead exposures, a nested case-control study was conducted within a cohort of pregnant women in Mexico City, 1994–1996. During their first trimester, 668 women enrolled, were interviewed, and contributed blood specimens. Pregnancies were followed by home visits or telephone calls. Spontaneous abortions before week 21 ($n = 35$) were matched with pregnancies that survived beyond week 20 ($n = 60$) on maternal age, hospital, date of enrollment, and gestational age at enrollment. Mean blood lead levels were 12.03 μg/dL for cases and 10.09 μg/dL for controls ($p = 0.02$). Odds ratios for spontaneous abortion comparing 5–9, 10–14, and ≥15 μg/dL with the referent category of <5 μg/dL of blood lead were 2.3, 5.4, and 12.2, respectively, demonstrating a significant trend ($p = 0.03$). After multivariate adjustment, the odds ratio for spontaneous abortion was 1.8 (95% confidence interval = 1.1, 3.1) for every 5 μg/dL increase in blood lead. Low to moderate lead exposures may increase the risk for spontaneous abortion at exposures comparable to US general population levels during the 1970s and to many populations worldwide today; these are far lower than exposures encountered in some occupations. *Am J Epidemiol* 1999;150:590–7.

abortion; blood; lead; lead poisoning; pregnancy outcome

Adverse effects of lead on the nervous system at both high and low doses, and on the hematopoietic, renal, and reproductive systems at high doses, are well known (1). Neurodevelopmental effects from prenatal and early childhood exposures have been observed at relatively low levels of lead and may be the most sensitive endpoint for lead toxicity (2–5).

Although fetuses of exposed pregnant women are considered to be at particularly high risk for certain effects of lead (6), the specific actions of this metal in the prenatal period are not well understood, nor is it clear what the risks are at low levels of exposure. Some evidence suggests that, during pregnancy, stores of lead deposited in bone over the lifetime may be mobilized, particularly in women who smoke (7) or in women whose calcium intake is low (8). Lead has long been known to diffuse readily across the placenta (9, 10).

In the early part of this century, reports of pregnant women occupationally exposed to high levels of lead in England, Hungary, and elsewhere described increases in spontaneous abortions, stillbirths, premature births, and neonatal deaths, compared with mothers in non-exposed occupations (11). Studies at lower exposures have found inconsistent associations with birth weight and prematurity (12). A higher incidence of spontaneous abortion was observed among women who themselves had suffered from childhood lead poisoning (13), but only a few studies have examined spontaneous abortions in relation to lower levels of lead, e.g., those encountered in the general population in many urban areas of the world. The findings have been mixed, with some studies suggesting an association (14–15) and others showing none (16–19). Methodological problems in these studies, mainly in regard to the assessment of exposure, hamper interpretation. In particular, exposure assessment relied on questionnaires (18, 19), on measurements taken after the abortion occurred (14) or later in pregnancy for non-cases than for cases (15, 16), or on ecologic classification based on residence at a later time point (after the pregnancy in question) (17, 18). For

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Abbreviations: ANOVA, analysis of variance; CI, confidence interval; OR, odds ratio; VDT, video display terminal.

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most of these investigations, spontaneous abortion was not the primary outcome of interest, and several studies involved very small numbers of cases (13, 15, 16).

In light of the inconclusive evidence from previous reports and their methodological deficiencies, this investigation was conducted to evaluate if currently observed levels of lead increased the risk of spontaneous abortion in pregnant women of Mexico City. Environmental sources of lead exposure in Mexico City include lead-glazed ceramic cookware and leaded gasoline (20). The design of the study ensured 1) measurement of blood lead early in pregnancy and 2) prospective ascertainment of pregnancy losses after the date of blood draw.

MATERIALS AND METHODS

A nested case-control design was carried out within a cohort of 668 pregnant women seeking pregnancy diagnosis or prenatal care in 13 private and public hospitals in Mexico City. Women were recruited during the first 12 weeks of gestation at their first visit to the clinic. All of the pregnancies were confirmed with urine human chorionic gonadotropin (hCG) and/or ultrasound. Informed consent procedures were approved by the institutional review board at the Instituto Nacional de Salud Publica. After informed consent was acquired, blood specimens were obtained, and a questionnaire administered. The questions addressed sources of lead; nutritional factors that could influence absorption or toxicity of lead; sociodemographic, occupational, and life-style factors; drugs used; and reproductive and medical histories of the women. The blood specimens were used for measurement of lead and also of serum antibodies against infectious agents potentially associated with pregnancy loss.

Each woman was regularly contacted, once every 2 weeks, either by telephone (83 percent) or by means of home visits by trained study personnel (17 percent) when telephone calls were not possible, to determine the status of her pregnancy through week 20 of gestation. For two of the cases, the cooperating physicians from the private clinics also informed us of spontaneous abortions among their patients. For each woman who had a spontaneous abortion, defined as a pregnancy loss by week 20 of gestation, two controls were randomly selected from women with normal pregnancies at the time that the case occurred, with matching on maternal age (±2 years), the calendar date and gestational age at which the first blood sample was drawn (±2 weeks), and the type of clinic (private vs. public). The monitoring of controls continued through week 20 of gestation, to ensure that they did not have an abortion. For some of the women, only one control was identified that satisfied the matching criteria.

For women recruited from private clinics, the questionnaires were self-administered, whereas for women from the public clinics, the interviews were carried out through in-person interviews, because some of these women could not read or write. This strategy ensured that the method of interview was the same within each matched set.

When blood was drawn for pregnancy diagnosis or clinical purposes, a sample was also collected for this study. Blood was drawn from the antecubital vein through a vacutainer system to prevent atmospheric contamination. For lead measurements, blood was collected in lead-free plastic tubes containing EDTA as anticoagulant. Within 2 hours, these were transported to the laboratory in cold packs, and then stored refrigerated at 5°C. A second tube was collected and centrifuged and the sera specimens were frozen and stored for later analyses among cases and controls.

Blood lead determinations were carried out in duplicate using atomic absorption spectrophotometry with a graphite furnace (21). These analyses were conducted at the Laboratorio de Neuroquimica at the Instituto Nacional de Neurología y Neurocirugía in Mexico City. This laboratory participates in the blood lead proficiency testing program of the US Centers for Disease Control and Prevention in Atlanta, Georgia. The coefficient of variation for duplicate samples was 4.8 percent. With each batch of samples, one method blank, one spiked sample, and one duplicate sample are routinely analyzed. Calibration verification was performed after each batch of samples.

For the determination of maternal infections, sera samples were transported to the Laboratorio de Referencia Sociedad Anonima (Mexico City) where assays were carried out for immunoglobulins against toxoplasma, rubeola, cytomegalovirus, herpes type 1, herpes type 2, chlamydia, and syphilis. The following kits were used: Toxotest HAI (Weiner Laboratories, Argentina) for immunoglobulin M (IgM) against toxoplasma; enzyme-linked immunoadsorbent assay (ELISA) (GULL Laboratories, Salt Lake City, Utah) for IgM against rubeola, cytomegalovirus, and herpes types 1 and 2; enzyme immunoassay (EIA) (GULL Laboratories) for immunoglobulin G against chlamydia; and venereal disease research laboratory (VDRL) test (Wiener Laboratories, Argentina) to detect antibodies against *Treponema pallidum*. The sera specimens for these assays were kept frozen up to 6 months until analyzed.

The information from the questionnaires and samples was captured electronically using double entry, checked for range and consistency, and corrected. Descriptive analyses were conducted on all variables. Crude (unadjusted) analyses included both a compari-

son of mean blood lead level in cases to that in controls using two-way analysis of variance (ANOVA), and the calculation of a matched sets odds ratio using the McNemar method (22). (These methods allow for varying numbers of controls per case.) Blood lead was analyzed as a categorical variable using 5 μg/dL increments (<5, 5–9, 10–14, ≥15 μg/dL) in order to assess whether the basic assumption of logistic regression, namely that the logit (the logarithm of the odds of disease) increases linearly with exposure, was violated. As the data supported this assumption, further analyses used a continuous variable for blood lead.

To control for confounding, conditional logistic regression models were fit, in which each stratum consisted of a spontaneous abortion case and its matched control(s). Model-building proceeded stepwise by forward selection. Potential confounders were: medical conditions (toxoplasmosis, diabetes, thyroid disorder and hypertension); reproductive characteristics (gravidity, previous spontaneous abortion, menstrual irregularity, age at first sexual contact, previous C-section and spermicide use as last method of contraception); sociodemographic variables (age, education); and lifestyle factors (active and passive smoking, coffee consumption, alcohol consumption, calcium supplementation during pregnancy, use of hair dye, video display terminal (VDT) exposure, and unusual physical exertion). These were evaluated for inclusion in the model by checking changes in the estimated odds ratio for lead and spontaneous abortion (23). We also retained variables that were predictive of spontaneous abortion ($p < 0.10$), or that are established risk factors on which we did not match.

RESULTS

The cohort included 668 women recruited between January 1994 and June 1996, 202 from private hospitals and 466 from public hospitals (table 1). Their age ranged from 14 to 43 years, with a mean of 27 years. On average, these women were recruited in gestational week 9 (dated from the first day of their last menstrual period). The women had an average blood lead level at enrollment of 11.03 μg/dL, almost identical to the initial findings from a subset of the cohort (20). Loss to follow-up (moved and could not be located or never returned to the clinic or gynecologist) by week 20 was 15.8 percent, and was similar for private versus public clinic patients.

Of the 562 women who were successfully followed to week 20, a total of 36 women experienced a spontaneous abortion, for a crude risk of 6.4 percent. One of these cases experienced an accident and was excluded from further analyses. For the remaining 35 cases, a total of 60 controls were identified, that is, two controls for each of 25 cases, and one control for each of 10 cases. Most of the abortions occurred before week 12.

TABLE 1. General characteristics of the cohort of pregnant women: case-control study of blood lead levels and spontaneous abortion, Mexico City, 1994–1996

Variable	No.	%
Clinic type (n = 668)		
Private	202	30.2
Public	466	69.8
Pregnancies (n = 668)		
1st pregnancy	301	45.1
≥2nd pregnancy	367	54.9
Gestational age at entry (weeks) (n = 668)		
4–6	116	17.4
7–9	311	46.5
10–12	241	36.1
Gestational age at pregnancy losses (weeks) (n = 35)		
7–9	13	37.1
10–12	8	22.9
13–15	7	20.0
16–18	5	14.3
19–20	0	0.0
Unknown	2	5.7

Table 2 compares cases and controls with respect to continuous variables, including sociodemographic and other factors. No differences were seen for age, self-reported education, per capita income, or age at first sexual contact. However, compared with the controls, the cases reported spending time near a greater number of smokers at their homes and workplaces. Table 3 compares cases and controls for dichomotous factors. Cases were more likely to report menstrual irregularity, a previous cesarean section, a previous spontaneous abortion, spermicide use as the last method to avoid pregnancy, working with VDTs, and alcohol

TABLE 2. Comparison of cases and controls on selected variables: case-control study of blood lead levels and spontaneous abortion, Mexico City, 1994–1996

Variable	Cases (n = 35)	Controls (n = 60)	p value*
Maternal age (years)	28 (16–40)†	28 (16–40)	0.85
Education (no. of completed years)	12 (6–17)	10 (3–17)	0.78
Gestational age at entry (weeks)	8 (4–10)	8 (4–12)	0.72
Age (years) at first sexual contact	22 (13–34)	19 (13–30)	0.11
No. of cigarettes smoked during pregnancy (for smokers only)	1 (1–10)	3 (2–5)	0.12
No. of persons who smoke nearby	1 (0–20)	1 (0–5)	0.10

* p value by Kolmogorov-Smirnov test. However, all variables were examined for confounding in the multivariate model, using the change-in-estimate criterion.

† Median value (range) throughout table.

TABLE 3. Paired odds ratios of binary exposures for spontaneous abortion: case-control study of blood lead levels and spontaneous abortion, Mexico City, 1994–1996

Variable	Cases (n = 35)		Controls (n = 60)		Odds ratio*	95% CI†
	No.	%	No.	%		
Reproductive factors						
Menstrual irregularity	12	34	13	22	2.1	0.65, 6.7
Primigravida	21	60	28	47	2.8	0.85, 9.0
Previous spontaneous abortion	5	14	3	5	2.2	0.51, 9.3
Previous cesarean section	8	23	3	5	4.0	1.0, 15.3
Spermicide use‡	3	9	2	3	3.0	0.50, 18.0
Life-style/occupational						
Smoker	4	11	10	17	0.62	0.19, 2.1
Coffee consumption	10	29	15	25	1.2	0.42, 3.5
Alcohol consumption§	3	9	1	2	5.6	0.62, 57.7
Calcium supplementation during pregnancy	6	17	27	45	1.6	0.41, 6.3
Dyed hair	6	17	9	15	1.1	0.34, 3.9
Video display terminal exposure	6	17	2	3	5.2	1.0, 25.9
Unusual physical exertion	12	34	18	30	1.2	0.46, 3.0
Medical factors						
Chronic conditions¶	9	26	14	23	1.1	0.42, 2.7
Serum positive for toxoplasmosis	2	6	1	2	3.6	0.36, 44.1

* The matched set odds ratio is calculated using discordant sets and cannot be directly obtained from the first two columns of the table.
† CI, confidence interval.
‡ As the last method of birth control used.
§ More than one glass a week of wine, beer, or liquor.
¶ Includes diabetes mellitus, hypertension, and thyroid disorder.

consumption more than once a week, although for all of these risk factors, the numbers of exposed subjects were small. Confidence intervals included the null value, except for previous cesarean section and VDT exposure. Cases were more frequent in primigravidas. None of the cases or controls were positive for current infection of rubeola, cytomegalovirus, herpes type 1, herpes type 2, chlamydia, or syphilis. Two cases and one control were positive for toxoplasmosis.

The mean blood lead level of cases was 12.0 μg/dL (range 3.1–29 μg/dL) and of controls, 10.1 μg/dL (range 1.3–26 μg/dL). The two-way ANOVA test to take into account multiple controls per case yielded an F statistic of 5.61 ($p = 0.021$). The risk for spontaneous abortion showed a monotonic rise with increases in blood lead. Compared with the reference category of <5 μg/dL of blood lead, women whose blood lead levels were 5–9, 10–14, and ≥15 μg/dL had increasingly greater risks for spontaneous abortion: odds ratios (based on matched sets) were 2.3, 5.4, and 12.2, respectively (test for trend, $p = 0.03$). Graphical inspection of logits, or equivalently, odds ratios plotted on a logarithmic scale (figure 1), indicates that the assumption of linearity was met; hence further analyses used blood lead as a continuous variable.

In a multiple conditional logistic regression model predicting a spontaneous pregnancy loss by week 20, the only retained variables were a previous spontaneous abortion (an established risk factor) and blood lead level. Matching factors were included in the initial models but the matching was apparently quite effective, as none of these factors was predictive of the outcome nor did any factor confound the association between lead and spontaneous abortion. Similarly, age, education, life-style, and medical conditions also were not confounders, i.e., adjustment for them did not alter the estimated odds ratio for the association of lead and spontaneous abortion. Thus, the final model is shown in table 4.

The risk of spontaneously aborting the current pregnancy increased 2.5-fold (95 percent confidence interval (CI) 0.53, 11.7) for women with a history of a spontaneous abortion. For each 1 μg/dL increase in blood lead, the risk increased 1.13-fold; this magnitude of association represents close to a doubling of spontaneous abortion risk for every 5 μg/dL increase in blood lead (odds ratio (OR) = 1.8, 95 percent CI 1.1, 3.1).

DISCUSSION

This study provides evidence that blood lead levels once considered moderate may be associated with an increased risk of spontaneous abortion. Many decades ago, elevated rates of fetal loss of fivefold and higher

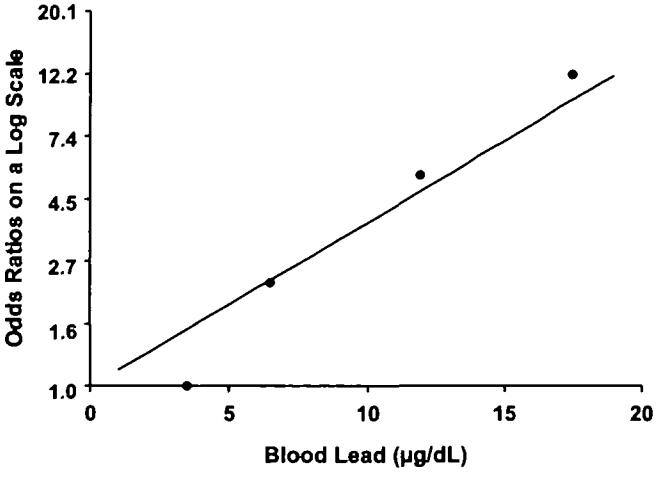

FIGURE 1. Spontaneous abortions versus blood lead level in Mexico City, 1994–1996. Odds ratios are plotted on a logarithmic scale in relation to blood lead, measured both continuously and categorically. The points are calculated from a conditional logistic regression model with three indicator variables, comparing blood lead in the ranges of 5 to <10, 10 to <15, and ≥15 µg/dL with blood lead <5 µg/dL; they are plotted at the median blood lead level in each category. The plotted line is based on the model with blood lead as a continuous variable (fitted model shown in table 4), which assumes that an odds ratio of 1.0 corresponds to a blood lead concentration of zero. The graph allows visual inspection to assess the assumption of linear logits with increasing blood lead. Because this assumption is reasonably well met by the data, the use of a model with the continuous variable for blood lead is supported.

TABLE 4. Final model—multivariate adjusted* odds ratios and 95% confidence intervals (CI) for spontaneous abortion: case-control study of blood lead levels and spontaneous abortion, Mexico City, 1994–1996

Variable	Coefficient	Odds ratio	95% CI	*p* value
Blood lead (per 1 µg/dL)	0.12	1.13	1.01, 1.3	0.03
Previous spontaneous abortion (yes:no)	0.92	2.5	0.53, 11.7	0.25

* Based on a conditional logistic regression model.

were observed in occupationally exposed women at high doses (11, 24). The levels of lead in blood in the women in this study are all below the acceptable standard for occupational exposures. Although the number of cases is relatively small, the associations are statistically significant and demonstrate a clear monotonic dose-response across four levels of exposure. We consider the biologic plausibility of these findings and the strengths and limitations of the study.

There is a growing literature on the endocrine disruptive properties of lead in males and females which can explain failures to conceive (25–28). However, the mechanisms for losses after implantation, as observed in this study, of recognized and confirmed pregnancies, are not totally clear. Possible mechanisms include preconceptional effects on gametogenesis in both males and females, impairment of the hormonal environment needed to maintain pregnancy, and direct teratogenic effects on the fetus.

Paternal exposure to lead may be related to spontaneous abortions by three pathways: 1) lead in the father is passed through semen to the mother; 2) lead in the father's work clothes, equipment, hands, etc., is a source of exposure for the mother; 3) lead burden in the father alters his sperm. The first scenario would not necessarily result in elevated maternal blood lead, while the second would likely have such an effect and could have been operating in our study subjects. As for sperm alterations, studies of exposed workers in Romania (29) and Southern Italy (30) showed alterations in sperm cytology without perturbation of the hypothalamic-pituitary system, suggesting a direct toxic effect on sperm production and transport. Other work suggests the potential impact of pre- or periconception paternal exposures on later events in pregnancy (31). In the current study, a direct effect of paternal exposure cannot be ruled out, because such exposure was assessed only indirectly (by maternal questionnaire) and neither blood lead levels nor sperm or semen parameters were measured. However, only nine participants (three cases and six controls) reported that their partner was occupationally exposed.

Experimental evidence supports effects of lead on female reproductive function both at high and moderate levels. In pregnant rodents administered lead at moderate doses (achieving 10–40 µg/dL in blood), serum progesterone levels were reduced in dams, and hypothalamic levels of gonadotropin-releasing hormone (GnRH) and somatostatin were suppressed in both dams and fetuses (32). In female monkeys, lead intoxication at high doses causes degeneration of ovarian follicles (33). Lead is also a demonstrated teratogen in rats, causing congenital malformations (34). Human cytogenetic studies in both males and females with occupational exposure suggest that lead increases the rate of chromosomal aberrations in cultured lymphocytes (35, 36).

Our study has several strengths not found in previous investigations of reproductive effects in populations exposed environmentally to lead. Blood lead levels were measured early in pregnancy and prior to the spontaneous abortion; information on spontaneous abortions was collected prospectively; and important potential confounders were efficiently controlled through matching and the corresponding matched analysis. Each of these features added to the validity of our findings.

Olsen and Skov (38) recommend that in a case-control study, the controls should be pregnant women

sampled from the same population at risk and matched for gestational age at enrollment so that the time window during which any exposure can occur is the same in both groups. Our design followed this recommendation. Because blood lead levels (6) and the risk of spontaneous abortion (37) both change as pregnancy progresses, an inappropriate timing of lead measurement in terms of gestational age could either mask an association or create an artifactual one. The measurement of blood lead levels prior to the event of interest is important to assure a nonspurious association. None of the previous studies were designed to address these issues.

A further strength of our study was the substantial range of exposures, from 1.4 to 29 μg/dL. Prior studies with a smaller range would have had lower statistical power (39).

In this study, we matched on gestational age at entry measured since the last menstrual period. However, if lead causes menstrual irregularities at the higher doses observed in this study, bias could be present. The gestational age at entry could be an overestimate of true gestational age for these women, because their interval between last menses and the conceptive ovulation could have been longer. This scenario would imply a shorter time-since-conception when they entered the study, and hence a higher cumulative probability of spontaneously aborting between entry into the study and week 20; thus, the women who are more highly exposed would be overrepresented among cases, leading to an overestimate of the association, if any, with spontaneous abortion.

Another potential source of upward bias would be present if problem pregnancies are characterized by a smaller or delayed increase in fluid volume. A lack of the normal increase in blood volume leading to a less viable pregnancy would be associated with the appearance of increased blood lead concentrations. However, fluid volume does not begin to increase until the tenth week of pregnancy (40), whereas blood lead was measured before week 10 for the majority of cases and controls (both means were approximately week 8, as shown in table 2).

If a long-term exposure affected women's capacity to carry to term, then use of whole blood lead rather than bone lead (which represents cumulative maternal exposure over decades) could have diluted the associations (41, 42). On the other hand, if the viability of a given pregnancy is more closely related to currently bioavailable lead, then blood lead would be preferable to bone lead. (Pregnancy-induced mobilization of bone stores would not have begun by the time the spontaneous abortions occurred (6).) In this case, plasma lead may be even more appropriate than whole blood lead (42, 43), but technical feasibility and cost were prohibitive for this study.

A potential source of confounding was the temporal variation in blood lead levels during the course of the study period (20). This problem was avoided by matching controls to cases on calendar time at enrollment. Neither life-style factors nor infectious diseases confounded the associations due to their low correlations with lead exposure and/or their low prevalence.

The use of self-report of spontaneous abortions could be a limitation in this study; however, given that these reports were made within a short time of the reported event and that the pregnancies had all been medically confirmed prior to the event, errors of recall seem unlikely. Overall, bias in the estimated associations due to under-ascertainment of recognized spontaneous abortions does not seem probable. Similarly, the possibility of false positives is unlikely, because we had laboratory confirmation of pregnancy for all women.

Although the quality of data may have differed between the private and public clinic patients as a result of differences in educational level and in the mode of administration of the questionnaires, these differences could not have introduced any bias, since cases and controls were matched on type of clinic and we conducted matched analyses. Because the women for this analysis were restricted to those who entered for prenatal care early in pregnancy, these women may have had better nutritional status than the general population of Mexico City. The shape and magnitude of the dose-response curve could therefore have been altered.

The possibility of selection bias due to differential loss to follow-up cannot be totally excluded. However, the mean blood lead level of women lost to follow-up was similar to that of the whole cohort and it fell between the mean of the cases and that of the controls. Furthermore, loss to follow-up was nondifferential with respect to clinic type, suggesting that differences between the 85 percent successfully followed and those lost to follow-up would have had a negligible effect on the findings. An additional potential source of selection bias is unrecognized early losses, not detectable unless pregnancy is diagnosed using close hormonal surveillance (44). The only scenario which could lead to artifactually higher lead in women with recognized spontaneous abortions would be if early unrecognized losses were *inversely* related to lead exposure. In other words, their blood lead levels would need to have been lower than the levels in surviving pregnancies (viz., a protective effect), on average. We have no data on unrecognized losses, but we know of no evidence supporting biologic plausibility of this scenario. On the contrary, animal studies suggest that lead can interfere with implantation or with sex steroid

production immediately following implantation (45–47), which would imply a possibly higher lead level in women who experienced early pregnancy losses. Thus, any association between lead and total pregnancy losses by week 20 might be stronger, not weaker, than the association we observed among the clinically recognized losses.

By a similar argument, if previous spontaneous abortions were associated with elevated blood lead levels in those earlier pregnancies, our analysis, which adjusted for previous loss, theoretically could have resulted in an underestimate of the true association with lead (48). However, removal of previous spontaneous abortions from the model had no impact on the coefficient or standard error for blood lead level.

Using a study design that avoids the pitfalls of many recent reports on this topic, we observed that increased blood lead level was associated with an elevated risk of spontaneous abortion among women in Mexico City. The risk rose in a dose-response manner, nearly doubling for each 5 μg/dL increase in blood lead. The mixed findings in recent studies of humans exposed environmentally (13–19) may have been a result of inadequate control for confounders in some instances, non-comparable timing for measurement of exposure among cases as compared with survivors, or differences in susceptibility among the various populations studied (e.g., nutritional status and other environmental exposures may modify the effect of lead (49, 50)).

The findings from this study provide evidence that lead may increase the risk of spontaneous abortion at currently encountered exposure levels, but further studies are needed to confirm these results. Such studies should also address the possibility of an artifactual association resulting from menstrual irregularity among women with higher lead levels.

The range of lead exposures in this study was 1.4 to 29 μg/dL, with a mean among controls of 10 μg/dL; these levels of exposure, although common in the US general population during the 1970s, are rare in the US general population today. They are, however, still common in many parts of the world, and are far lower than occupational exposures or the acceptable standards for these exposures in either Mexico or the United States. If our findings are confirmed, lead may be an important contributor to pregnancy loss in populations with similar or higher exposures.

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