ABSTRACT. This study was conducted to relate blood lead levels in infants to changes in lead emissions in Santiago, Chile, a heavily polluted setting where leaded gasoline began to be replaced with unleaded gasoline in 1993. Over an 18-mo period, 422 infants had blood lead levels, cotinine, and iron status determined at 12 mo. Blood lead levels fell at an average rate of 0.5 μg/dl every 2 mo, from 8.3 to 5.9 μg/dl, as the city experienced a net fall of 30% in the quantity of leaded gasoline sold. Time progression, car ownership, serum cotinine, and type of housing were significantly associated with a blood lead level \( < 10 \mu g/dl \). In this study, the authors demonstrated that infant blood lead levels, even if relatively low, can drop very rapidly in conjunction with decreases in environmental lead exposure.

<Key words: emissions, gasoline, infants, lead poisoning>
beginning in 1993. According to the Chilean National Energy Commission, by the end of 1997 almost 50% of the cars in Santiago used unleaded fuel. However, the number of older devaluated vehicles without converters may have increased in underprivileged areas of the city. Because the infants in our study inhabited an economically distressed area—with dwellings recently constructed and generally unpainted, surrounded by heavy traffic—the actual impact of the shift to unleaded fuel in this area is uncertain.

In other settings, the reduction of leaded gasoline use has been associated with a decrease in blood lead levels in children and adults.\textsuperscript{10–15} We focused on infants because they should be particularly sensitive to changes in environmental lead exposure, inasmuch as they play closer to the ground where lead-laden particles sediment.\textsuperscript{5} Furthermore, infants appear to be at high risk for adverse effects of lead, even at lower lead levels.\textsuperscript{16,17}

Our objective was to assess the impact of the shift from leaded to unleaded gasoline on blood lead levels in 1-yr-old infants. The fact that infant blood lead levels had been previously reported to be relatively low in Santiago\textsuperscript{18} was of particular interest, because the ill effects of low-level lead exposure are still debated. We also hoped to identify other factors associated with higher blood lead levels in this underprivileged population.

**Method**

Within a broader study of the effects of iron deficiency on infant development,\textsuperscript{19} detailed information on environmental contaminants was obtained for 504 infants enrolled between 1995 and 1997. The infants came from relatively homogeneous lower socioeconomic communities attending the Public Health Service clinics in the southeastern area of Santiago. Children were eligible if they were born weighing over 3 kg without any perinatal event or chronic illness and had a consistent literate caregiver. (As literacy is above 95% in Chile, an illiterate mother might be unusual in other respects as well.) After written informed consent was obtained from parents or guardians, children were recruited at 4 mo. From then on these children had monthly well-child health care and ad libitum access to medical assistance provided by a project physician.

As infants reached 12 mo of age, a venous blood sample was obtained, anticoagulated with EDTA, and stored as an aliquot frozen at ~20°C in polypropylene lead-free vials provided by the U.S. Centers for Disease Control and Prevention (CDC). Hemoglobin, mean cell volume, protoporphyrin, and serum ferritin were determined by standard procedures.\textsuperscript{20} Iron deficiency anemia was diagnosed if the hemoglobin level was lower than 110 gm/l and at least two other iron status measures were abnor-

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**Blood lead levels** were obtained in 83.7% (422/504) of the infants; the remainder were either lost to follow up (n = 72) or were excluded because they refused venipuncture or provided insufficient blood samples (n = 10). The missing cases had mothers with more schooling, but they did not differ in factors later identified to affect blood lead levels.

We determined blood lead levels by electrothermal atomization (graphite furnace HGA700) atomic absorption spectrophotometry (PerkinElmer 1100B [Boston, Massachusetts]).\textsuperscript{21} The CDC analyzed 120 samples, and 385 were analyzed at the Institute of Public Health of Chile, which is under CDC quality control specifications. To validate local results even further, 43 random samples were analyzed at both laboratories, with excellent correlation (r = .97; p < 0.0001) and concordance in the discrimination of levels ≥10 µg/dl (κ = 0.81; p < 0.00001).

During the period of the study, systematic airborne lead measurements were unavailable. However, we had access to accurate information on the quantity of leaded gasoline sold and the concentration of lead in leaded gasoline (provided by the Chilean Commission of Energy). The concentration of lead remained unchanged during the study. We were unable to identify new sources of lead that could have arisen or the disappearance of other existing sources in the area. Thus, it appears appropriate to consider leaded gasoline sales as a proxy for airborne lead emissions. We assembled the original monthly data on blood lead levels in bimonthly clusters in order to concentrate cases per period and to suppress a gap in data of 2 mo wherein no child had a first birthday (when venipuncture was scheduled). This approach also reduced variability (standard error ranges) from 0.694 for monthly to 0.306 for bimestral periods.

As an objective indicator of the infants’ exposure to passive smoke, serum cotinine was measured by radioimmunoassay, with the lower level of detection at 0.1 µg/ml.\textsuperscript{22}

Socioeconomic status (SES) and demographic and environmental variables were assessed with a structured interview by social workers specially trained for this task. The environmental variables included proximity to traffic and industries, the presence of indoor pollutant sources, and tobacco use in the family. The interview included the Graffar, an SES scale that is widely used in Chile for health studies.\textsuperscript{23} This scale involves 13 items...
concerning family structure, schooling, occupation, and social security of the head of the family. It also covers structural quality and health conditions of the home and the existence of home appliances and car ownership. This scale is suited to identification of strata even within relatively homogeneous lower-SES populations.

Initial analyses included comparisons of means and linear regression, with infant blood lead level as a continuous variable. We used the \( \chi^2 \) test when blood lead level was treated as a dichotomous variable with a cutoff at \( \geq 10 \, \mu g/dl \). Using the same cutoff, we constructed a multivariate logistic regression model to estimate adjusted odds ratios for continuous or dichotomous independent variables. We conducted statistical analyses with SPSS version 10.0 (SPSS, Inc. [Chicago, Illinois]).

**Results**

Most of the study infants (92%) originated from households of middle-to-low SES conditions. Mothers had an average of 9 yr of schooling and, by design, none were illiterate. Many families (56%) were living with parents or relatives in crowded households. Mother’s age averaged 26.4 yr (95% confidence interval [CI] = 25.8, 26.9) with 12.1% aged under 18 yr. Fifty-three percent of the infants were males. None of these characteristics related to blood lead levels.

Blood lead levels were skewed toward lower values. The geometric mean was 6.6 \( \mu g/dl \) (95% CI = 6.3, 6.9). Although 21.3% (95% confidence interval [CI] = 18.5–24.1) of the sample surpassed the CDC cutoff of 10 \( \mu g/dl \), most of them (55/90) classified under 12 \( \mu g/dl \). Only five infants (1%) had levels above 20 \( \mu g/dl \).

As expected, many infants were iron-deficient at 12 mo: 16.8% (95% CI = 13.2–19.6) of infants presented iron-deficiency anemia, and an additional 21.3% (95% CI = 17.9–25.1) had iron deficiency without anemia. There was no correlation between blood lead level and protoporphyrin or any other measure of iron status.

Over the course of 18 mo, a declining trend in blood lead levels was observed across the bimonthly periods. The univariate regression (\( b = 0.46; \, p < 0.0001 \)) indicated that the average blood lead levels declined almost 0.5 \( \mu g/dl \) every 2 mo between 1995 and 1997. The proportion of children with blood lead levels \( \geq 10 \, \mu g/dl \) also decreased progressively across the intervals (\( \chi^2 \) for a linear trend =17.6; \, \( p < 0.001 \)). Thirty percent of children had blood lead levels \( \geq 10 \, \mu g/dl \) in the first two bimonthly periods, compared with only 2.2% in the last two bimonthly intervals.

The fall of blood lead levels closely followed the estimated descent of environmental lead from leaded gasoline sales, from 63% at the beginning of the study period to less than 50% at the end (Fig. 1). In further support of gasoline’s contribution to infants’ blood lead levels, we found an unexpected association with the presence of a car in the household. In these poor families, cars were relatively uncommon (11%), and when

![Fig. 1. Relationship between infant blood lead levels and the amount of leaded gasoline sold. Blood lead levels are shown on the left-hand axis in bimonthly intervals ( ), and moving average quantity of leaded gasoline sold is plotted on the right-hand axis in monthly intervals ( ). The lines represent the trend estimate by linear regression for both variables. As leaded gasoline sold (continuous line) decreased from 66.3 to 46.7 m³ × 1000, infant blood lead levels (dashed line) fell from 8.3 to 5.9 \( \mu g/dl \). Respective n’s at each bimonthly time point for blood lead levels are 49, 106, 92, 68, 27, 3, 22, and 55.](image-url)
present they generally were not equipped with catalytic converters. Children living in households with cars showed an unadjusted odds ratio of 2.4 (95% CI = 1.2–4.6) for having a blood lead level ≥10 µg/dl.

Blood lead levels also showed a strong association with serum cotinine, which was measured simultaneously in 404 children. The 88 children who had blood lead levels ≥10 µg/dl had a mean cotinine of 2.58 (95% CI = 1.91, 3.25) µg/ml, a level higher than the cutoff of 2.0 µg/ml that is considered to indicate exposure to passive smoke.22 Conversely, the 316 infants with blood lead levels under 10 µg/dl had a mean cotinine of 1.73 (95% CI = 1.46, 2.00) µg/ml (F = 7.3; p = 0.007).

The relationship between blood lead levels and socioeconomic background was not as clear-cut as that described in more developed settings. Only the type of housing, which was one of the components of the SES index, was related. Children who lived in solidly constructed houses had lower blood lead levels (mean = 6.8 µg/dl; 95% CI = 6.3, 7.3 mg/dl) than children inhabiting houses built with poorer materials, often self-constructed shanties (mean = 7.6 µg/dl; 95% CI = 7.2, 8.1 µg/dl).

Children who had their first birthday in spring or summer (n = 328) had slightly but not significantly higher blood lead levels compared with their peers who had their first birthday during fall or winter (n = 94; means = 7.5 vs. 6.9 µg/dl, respectively, p = 0.17).

For the logistic regression, we entered all those variables that reached statistical significance in the univariate analyses (i.e., car ownership, cotinine, type of housing, and time interval). Although not significant, we included iron-deficiency anemia because of its theoretical role. We also included season at first birthday (the time of venipuncture), considering that children might spend more time playing outdoors in warm weather. Table 1 shows both adjusted and unadjusted estimates of risk.

When we controlled for these variables, time progression (as an indicator of decreasing use of leaded gasoline) was confirmed as having a strong protective effect (OR: 0.7; 95% CI = 0.6–0.8). For each bimonthly interval there was a 30% reduction in the risk of having a blood lead level above the CDC limit. The value of car ownership as a predictor of high blood lead levels remained high (OR: 2.9; 95% CI = 1.4–6.0). Living in poorly constructed dwellings still conferred a higher risk of blood lead levels above the CDC limit, compared with inhabiting solidly built housing (OR: 2.2; 95% CI = 1.3–3.8). Environmental tobacco smoke, estimated from serum cotinine at 12 mo, maintained its borderline significance (OR = 1.125; 95% CI = 1.028, 1.208). Season, which initially seemed to be important, lost its significance in the multiple logistic regression analysis. Iron-deficiency anemia did not emerge as a significant determinant of blood lead level.

### Discussion

Although the current CDC concern about blood lead levels has been set at ≥10 µg/dl, there is increasing discussion that even lower levels pose harm, with adverse effects on both physical and cognitive development.21,24–27 Thus, any action that contributes to the decrease in lead burden in infancy is highly desirable. In this study, we showed that the effect of decreasing quantity of leaded gasoline sold can be readily detected in infant blood lead levels. The fall in infant blood lead levels over the 18 mo of observation reflected the gradual phasing-out of leaded gasoline in the city of Santiago.

Overall, the blood lead levels of these infants were relatively low. However, a total of 21.3% (90/422) surpassed the CDC limit of concern of ≥10 µg/dl. This proportion is higher than that observed in the only prior study to measure blood lead levels in 1-yr-old infants in Santiago. It was conducted in 1992–1993—before the change to unleaded gasoline—and detected only 4.4% with levels ≥10 µg/dl and a geometric mean of 6.0 µg/dl.18 Although these findings are similar to ours at study end, the reasons for differences compared with levels earlier in our study is unclear.

We found that infants from households that owned cars had a threefold adjusted risk of having blood lead levels ≥10 µg/dl. Although car ownership is generally a sign of wealth and higher SES, houses in this setting do not have a garage. Cars are usually kept, and the engines started and warmed up, in a narrow space between the house and the fence. There is little or no yard space, so this area is also likely to be the children’s usual playground. Other studies have implicated increased hand-to-mouth activity and contact with lead-contaminated soil in the higher blood lead levels often found in infancy and early childhood.28,29 The same mechanism may explain the relationship in this study, as 1-yr-old infants are just beginning to develop independent mobility. We speculate that infants crawl and play on this narrow space where airborne

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio (95% CI)*</th>
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</thead>
<tbody>
<tr>
<td>Car ownership</td>
<td>2.3 (1.3–4.6)</td>
</tr>
<tr>
<td>Iron deficiency anemia</td>
<td>0.8 (0.4–1.4)</td>
</tr>
<tr>
<td>Serum cotinine</td>
<td>1.1 (1.0–1.2)</td>
</tr>
<tr>
<td>Season</td>
<td>1.9 (1.0–3.6)</td>
</tr>
<tr>
<td>Time interval</td>
<td>0.7 (0.6–0.8)</td>
</tr>
<tr>
<td>Type of housing</td>
<td>1.8 (1.1–3.0)</td>
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*Multivariate analyses were performed with logistic regression.
lead-laden particles have been deposited from the car's exhaust. An additional possibility is that the introduction of new catalytic vehicles caused a depreciation of cars that used leaded fuel, and the ownership of these cheaper vehicles may well have shifted toward the outlying poorer areas of Santiago, such as the one where the families of our study lived. If this is true, it would be an example of how well-intended mitigation efforts may have transient untoward effects in specific population groups, usually the underprivileged.

Declines in infant blood lead levels with changes in leaded gasoline use have been demonstrated previously. Previous studies have not examined the specific secular trend in infants in the age period of the onset of independent locomotion, nor have they shown changes in the short time span of a few months. For example, one study in Helsinki, which included some infants as part of a relatively small daycare cohort with a wide age range (1–8 yr), indicated gradual declines at three time points over a long period of time (n = 29 in 1983, n = 17 in 1988, n = 18 in 1996). Studies in Mexico City have shown secular trends over 3-yr spans for 6-mo-olds and 36-mo-olds. In those studies, declining blood lead levels were mainly attributed to decreased use of lead-glazed pottery, which was not a factor in Chile. The unique finding from the present study concerns the steady, rapid fall in blood lead levels for 1-yr-old infants over many bimonthly periods, commensurate with a drop in leaded gasoline use in Santiago over an 18-mo period. The decline in proportion of infants with blood lead levels ≥10 μg/dl at the start of the study (30.0%) versus the end (2.2%) also demonstrates the swift and dramatic impact of an environmental change.

Iron deficiency, which is a highly prevalent condition in infants of low socioeconomic status, has been associated with increased gastrointestinal lead absorption. In this study we did not observe an association between iron status and blood lead levels. Other factors noted to influence blood lead levels, such as ceramic handcrafting, automobile repair shops or other home activities requiring soldering, or proximity to industries were not factors in this study. However, exposure to environmental tobacco smoke was a contributor. Tobacco is known to contain lead, and associations between environmental tobacco smoke exposure and blood lead levels have been described. In keeping with these studies, infants exposed to passive smoke in our sample were at higher risk for a blood lead levels over the CDC limit. This relationship was detected despite the fact that both blood lead and serum cotinine levels were low.

Because infants exhibit high hand-to-mouth activity, their blood lead levels may reflect the burden of environmental airborne lead deposited on the ground. Change in blood lead levels may therefore be detected in infants much earlier than in other population groups. Evidence that infants are potentially at higher risk for adverse effects of lead exposure, even at lower levels,

References