# Lead exposure among mothers and their newborns in Toronto

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Recent studies have suggested that a fetal blood lead level of 0.48 μmol/L (much lower than 1.21 μmol/L, which is the level previously believed to be toxic to the developing brain) may impair brain development permanently. We measured the maternal and umbilical cord blood levels of lead and free erythrocyte protoporphyrin (FEP) among 95 consecutive mother-infant pairs to determine whether neonates in Toronto are in the high-risk group. There was a significant correlation between the maternal and the cord blood lead levels ($r = 0.59$, $p < 0.0001$). Most (99%) of the infants had cord blood lead levels below 0.34 μmol/L; in 11 cases the levels were below the detection limit of 0.01 μmol/L. The cord blood FEP levels were higher than the maternal levels. The US Centers for Disease Control, Atlanta, currently finds acceptable a blood FEP level of 0.62 μmol/L among children up to 10 years of age; however, this is not applicable to newborns since their higher FEP levels apparently reflect immature heme synthesis and increased erythrocyte volume rather than lead poisoning. Our data suggest that living in Toronto does not impose increased teratogenic risk from intrauterine exposure to lead; however, residents in high-risk areas should be followed up.

Des travaux récents donnent à penser qu'une plombémie foetale à 0,48 μmol/L pourrait nuire de façon permanente au développement cérébral, alors que jusque-là on fixait la limite inférieure de toxicité cérébrale à 1,21 μmol/L. Afin de savoir si les nouveau-nés torontois sont exposés à un tel risque nous dosons le plomb et la protoporphyrine érythrocytaire libre (PEL) du sang maternal et du sang du cordon chez 95 couples de mères et de nouveau-nés. La corrélation est significative entre les plombémies maternelle et infantile ($r = 0,59$, $p < 0,0001$). Celle des nouveau-nés est inférieure à 0,34 μmol/L dans 99% des cas; dans 11 cas elle est inférieure à 0,01 μmol/L. Les concentrations sanguines de PEL sont plus élevées chez les nouveau-nés que chez les mères. Si à l'heure actuelle les US Centers for Disease Control, d'Atlanta, disent tolérable une concentration de 0,62 μmol/L jusqu'à l'âge de 10 ans, cette norme ne s'applique pas au nouveau-né, chez qui de plus fortes concentrations de PEL semblent résulter de l'immaturité de la synthèse de l'hème et du fort volume érythrocytaire, plutôt que d'un saturnisme. Nos trouvailles laissent croire que vivre à Toronto ne comporte pas de risque de tératogénèse du fait du plomb. Mais il faut suivre à cet égard les habitants des régions à risque élevé.

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The detrimental effects of lead on the developing brain have long been recognized.[1,2] However, most of the data are derived from studies of exposure during infancy and early childhood; little is known about the risks of transplacental exposure to lead.

Infants and children with accumulated blood lead concentrations greater than 1.21 μmol/L are at high risk for brain damage.[3] Consequently, high levels should prompt investigation of the source of contamination and discontinuation of the exposure. Blood lead levels greater than 1.9 to 2.1 μmol/L should necessitate chelation therapy[2] to prevent or minimize permanent brain damage.

Bellinger and associates[4] have suggested that the above limits may be too liberal during pregnancy; they found that after correcting for possible confounders (e.g., socioeconomic class and maternal education) blood lead levels greater than 0.48 μmol/L at birth were associated with significantly lower Bayley Mental Development Index (MDI)[5] scores at 6, 12, 18 and 24 months of age among children of middle and upper class women in Boston. Such levels are not known to be neurotoxic postnatally; therefore, during pregnancy the developing brain may have a lower sensitivity threshold.

Toronto does not appear to be as plagued with cases of postnatal toxic effects of lead as many other large cities around the world. However, the possibility that women and their babies are exposed to lower, yet fetotoxic levels had never been explored.

The Motherisk Program in Toronto focuses on exposure to drugs, chemicals and radiation during pregnancy and lactation. In addition to counselling pregnant women and health care professionals on the teratogenic risks and following up fetal outcome, the program members conduct research into reproduction toxicology.[6,7]

We performed this study to address the magnitude of the risks of prenatal lead exposure in Toronto. Specifically, we wanted to investigate whether babies born in Toronto belong to the high-risk group, those with measured blood lead concentrations above 0.48 μmol/L.

## Patients and methods

After approval by the Research Ethics Board of Women's College Hospital, Toronto, and informed maternal consent were obtained, umbilical cord and maternal blood samples from 95 consecutive mother–infant pairs were measured for lead and free erythrocyte protoporphyrin (FEP) levels.

The medical charts were reviewed for details on maternal health, obstetric history, smoking and drinking habits and residential address. The course of delivery, Apgar scores, birth weight and special neonatal health problems were also recorded. Preterm infants were excluded from the study.

The blood samples were kept at 4°C until analysis, which was performed within a week after collection. Atomic absorption spectrophotometry was used to measure the lead level,[8] and a ZnP Model 4000 hematofluorometer (ESA Ltd., Burlington, Mass.) was used to measure the FEP level. The lower limit of detection was 0.01 μmol/L for lead and 0.02 μmol/L for FEP. The coefficient of variation was less than 5%.[8]

The correlation between the maternal and neonatal levels of lead and FEP was studied by means of least squares regression analysis; both linear and nonlinear equations were examined. Differences between the mean maternal and neonatal concentrations were compared by means of the paired Student's *t*-test. The chi-squared test was used to compare differences in the proportions of low (less than 0.14 μmol/L), medium (0.29 to 0.34 μmol/L) and high (0.48 μmol/L or greater) lead levels between the neonates in our study and those in the Boston study.[4]

## Results

The characteristics of the 95 women (all from greater Toronto) and their infants are in Table 1. There was a significant correlation between the maternal and the neonatal blood lead concentrations ($r = 0.59$, $p < 0.0001$) (Fig. 1). In 11 cases the cord

Table 1: Characteristics of 95 mothers and their newborns in Toronto in study to assess blood lead concentrations

| | |
|---|---|
| Mothers | |
| Age, yr | |
| Mean (and standard deviation [SD]) | 30.2 (4.2) |
| Extremes | 20–38 |
| Marital status (% single) | 1 |
| Reproductive history | |
| Mean gravidity (and SD) | 2.1 (1.1) |
| Mean parity (and SD) | 0.8 (0.8) |
| Miscarriage, % | 27 |
| Mean length of gestation (and SD), wk | 39.5 (1.2) |
| Vaginal delivery, % | 76 |
| Cesarean section, % | 24 |
| Cigarette smokers, % | 7 |
| Alcohol consumers, % | 24 |
| Newborns | |
| Birth weight, g | |
| Mean (and SD) | 3570 (484) |
| Extremes | 2610–4770 |
| Mean Apgar score (and SD) at 5 minutes | 9.0 (0.4) |
| Sex (% male) | 53 |
| Congenital malformations, % | |
| Minor | 5 |
| Major | 0 |

blood levels were below the detection limit. The mean maternal levels (and standard deviation) were almost invariably higher than the neonatal levels (0.14 [0.05] v. 0.08 [0.07] μmol/L) ($p < 0.0001$).

Conversely, the cord blood FEP levels were consistently higher than the maternal levels (0.86 [0.34] v. 0.53 [0.22] μmol/L) ($p < 0.0001$). (The 11 samples in which lead could not be detected were not included in the analysis.) However, there was no correlation between the maternal and the neonatal FEP levels.

Most (99%) of the babies in our study had cord blood lead levels less than 0.34 μmol/L, as compared with 34% of the infants in the Boston study (Table 2). Only 1% of the infants had a cord blood lead level between 0.29 and 0.34 μmol/L, as compared with 34% in Boston. The differences in distribution of lead levels were highly significant ($p < 0.001$).

## Discussion

Lead freely crosses the placenta. High environmental exposure to the cation has been associated with spontaneous abortion, premature rupture of the membranes and preterm delivery.[1,2] Among children, hyperactivity, minimal brain dysfunction, neuropsychologic impairment and a reduced intelligence quotient have all been linked to elevated blood lead levels.[3] In 1987 Bellinger and associates[4] reported an association between cord blood lead levels greater than 0.48 μmol/L and low Bayley MDI scores at 6, 12, 18 and 24 months. Postnatal blood lead levels were not associated with low MDI scores or with low Bayley Psychomotor Development Index (PDI) scores.[4]

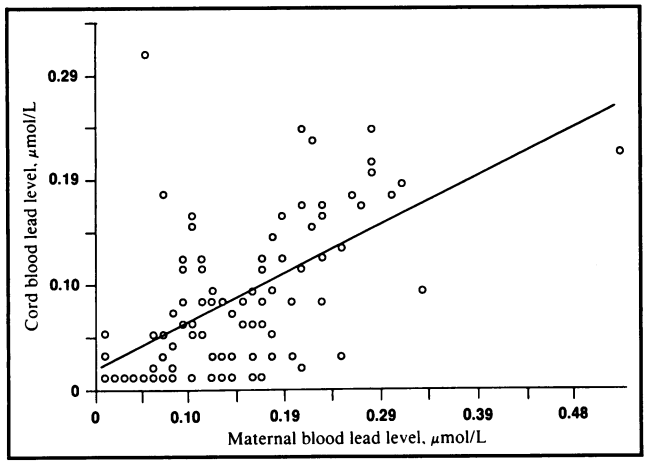


**Fig. 1: Correlation between maternal and umbilical cord blood levels of lead among 84 women and their newborns in Toronto. Eleven cases in which cord blood levels were below detection limit were excluded.**

In another study[9] Bayley MDI and PDI scores were obtained for 592 children at 24 months of age in Port Pirie, a lead smelter town in South Australia. The maternal and cord blood levels were significantly higher in Port Pirie (mean 0.48 μmol/L) than in the adjacent towns and countryside, and the mean postnatal lead levels rose sharply between 6 and 15 months of age (from 0.67 to 1.01 μmol/L). As in the Boston study there was a significant association between increased lead levels and poor MDI scores. However, unlike the data from a highly polluted town like Port Pirie, the results from the Boston study are alarming since they suggest a teratogenic risk among women at low risk for other reproductive hazards who are not exposed to what were believed to be toxic lead levels, even if the cord blood levels are well below 1.21 μmol/L.

Our study showed a significant correlation between maternal and neonatal lead levels. The maternal levels were consistently higher and indicated that the maternal burden contributed 35% to the variability in the fetal lead levels. Other sources of variability might have been differences in the rates of placental transport and in fetal distribution of lead.

Measurement of FEP is widely used as a sensitive screening test for detecting both lead poisoning and iron deficiency anemia.[3] Lead inhibits several enzymes in the heme biosynthetic pathway, including heme synthetase, which is responsible for the incorporation of iron into the protoporphyrin ring. In the presence of lead, protoporphyrin IX, the immediate precursor of hemoglobin, is found in increased concentrations. Because of its high sensitivity most authorities feel that screening for FEP levels should be included in the assessment of

Table 2: Comparison of cord blood lead levels between present study and Boston study[4]

| | Lead level, μmol/L; no. (and %) of infants | | | |
|---|---|---|---|---|
| City* | Low (< 0.14) | Medium (0.29–0.34) | High (≥ 0.48) | Total |
| Toronto | 94 (99) | 1 (1) | 0 (0) | 95 |
| Boston | 85 (34) | 88 (35) | 76 (30) | 249 |

*Differences in the distribution of lead levels between the two cities were highly significant (chi-squared test; $p < 0.001$).

suspected cases of lead poisoning.[10] However, elevated cord blood levels of FEP are caused by immature heme synthesis and a high erythrocyte volume. In our study the FEP levels were consistently higher among the infants, despite low blood lead levels, than among the mothers.

The results of our study suggest a substantially lower risk of lead exposure in Toronto than in Boston, and even more so when compared with results from a high-risk city such as Port Pirie. None of the randomly examined babies in Toronto had cord blood lead levels of 0.48 μmol/L or greater; only 1 (1%) had a level between 0.29 and 0.34 μmol/L. In Toronto lead exposure from paint is not a problem in the residential areas since the city is relatively new. With the planned removal of leaded gasoline from the market a further decrease in the burden of risk from lead exposure may be expected.

This study was the first of its kind in Toronto, a highly industrialized city in Canada. The findings may help in future comparisons to identify the trends of lead exposure during pregnancy. Equally important, they may provide baseline levels with which to compare the effects of potential lead exposure among women in occupational settings (e.g., glass painting plants and gas stations).

Although the results are reassuring, our study was not designed to identify a higher risk of lead exposure among babies of women residing or working in lead-polluted industrial areas of Toronto than among infants in other areas.

Our results suggest that the current standard of the US Centers for Disease Control, Atlanta, for an acceptable blood FEP level (0.62 μmol/L) among children up to 10 years of age[10] is not applicable to newborns; an elevated FEP level in newborns apparently reflects immature heme synthesis and a high erythrocyte volume rather than lead poisoning. Because of the new evidence supporting the adverse intrauterine effect of relatively low lead levels new standards for newborn FEP levels should be defined.

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**On the subject of reading**

*One point I should like to mention . . . is the speed of reading. I know that American schools try to teach their students to read as quickly as possible. . . . If the physician can devote only two hours a day to reading, it is obviously important for him to be able to read much in a short time. I am a hopelessly slow reader and therefore probably prejudiced in the matter. When I read a book and a paragraph strikes me as particularly good I may read it several times and make notes about it. I wonder if studies have been made with quick readers to find out how much they remembered of what had particularly impressed them in a book, after 5, 10 or 15 years. Some books we wish to forget as soon as possible as they are not worth being remembered, but others we want to assimilate, want them to become part of ourselves, and this takes a certain time.*

*Henry E. Sigerist (1891-1957)*



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