Increased Blood Lead and Decreased Calcium Levels during Pregnancy: A Prospective Study of Swedish Women Living near a Smelter

Birgitta Json Lagerkvist, MD, PhD, Sven Ekesrydh, MD, Vagn Englyst, MD, Gunnar F. Nordberg, MD, PhD, Hans-Åke Söderberg, MD, and Dan-Eric Wiklund, MD, PhD

ABSTRACT

Objectives. The purpose of this study was to monitor blood lead in a northern Swedish cohort of mothers and children during pregnancy and at birth.

Methods. Blood lead was analyzed during pregnancy and in the umbilical cords of 290 women living near a smelter and in 194 control subjects.

Results. During pregnancy, there were statistically significant overall increases in blood lead concentrations by 20% and 15% in the smelter and reference areas, respectively. Mean maternal blood lead concentrations at delivery were 0.15 μmol/L (3.11 μg/dL) in the smelter area and 0.13 μmol/L (2.69 μg/dL) in the control area. Umbilical cord blood lead levels were 80% to 87% of the maternal levels. Blood lead levels were influenced by place of residence, employment at the smelter, smoking, and wine consumption. Maternal serum calcium levels decreased during pregnancy and were significantly lower than those of the newborns.

Conclusions. An increase in blood lead concentrations was found during pregnancy, despite increased blood volume and unchanged or decreasing environmental lead levels. The mobilization of lead from bone during pregnancy may explain the increase. (*Am J Public Health.* 1996;86:1247–1252)

Introduction

In recent years, increasing attention has been given to possible adverse effects on the neuropsychological development of children of exposure in utero and early childhood to relatively low levels of lead.[1-3] Blood lead levels associated with poorer performance in various mental development index tests have been as low as 10 to 25 μg/dL. Adverse effects (e.g., reduced gestational age, decrease in birthweight, and miscarriage) have also been reported.[4] Lead crosses the placenta, and umbilical cord blood lead levels have been reported to be about 85% to 90% of those of the mother.[1,3,5]

The present study was part of a survey monitoring the levels of heavy and trace metals in mothers and infants living in the vicinity of Rönnskärsverken, a copper and lead smelter in northern Sweden.[6,7] The control subjects were mothers and infants from a community 120 km south of the smelter. The two areas are similar with regard to both the size of the population and social and economic background. The control area was chosen as being clearly outside any influence from the smelter's emissions.

Methods

Study Area and Study Population

Emissions of lead to the ambient air from the smelter had gradually decreased from 500 tons per year in the late 1960s to 51 tons in 1989, when this study began. In 1983 and 1990, the deposition of metals was surveyed by analyzing the levels of lead and other metals in moss (*Pleurozium schreberi*) taken from 74 locations up to 100 km from the smelter. After drying, representative samples (mean age of plants = 3 years) were analyzed with inductively-coupled plasma emission. Moss lead levels followed a gradient, decreasing with increasing distance from the smelter emissions, and these levels decreased by 50% to 90% between 1983 and 1990. In 1990, the highest value was 54 mg/kg d.w., and levels above background were found only within 30 km of the smelter. The emissions were then purified to 97%. At the most distant location, 85 to 95 km from the smelter and 25 to 35 km north of the control area, the moss lead level was 8 mg/kg d.w. (Institute of Water and Air Research, unpublished data, 1984, 1992).

The women participating in the study were recruited on their first visit to a primary health care unit for antenatal care during a 2-year period, February 1989 to February 1991. Eighty-five percent (n = 290) of the women from the smelter area and 90% (n = 194) of the women from the reference area agreed to participate in the study. Seventeen of the environmentally exposed women were

Birgitta Json Lagerkvist and Gunnar F. Nordberg are with the Department of Environmental Medicine, Umeå University, Umeå, Sweden. Sven Ekesrydh is with the Primary Health Care Unit, Holmsmund, Sweden. Vagn Englyst is with the Company Health Care Unit, Boliden Mineral AB, Skelleftehamn, Sweden. Hans-Åke Söderberg is with the Primary Health Care Unit, Skelleftehamn. Dan-Eric Wiklund is with the Department of Obstetrics and Gynaecology, University Hospital, Umeå.

Requests for reprints should be sent to Birgitta Json Lagerkvist, MD, PhD, Department of Environmental Medicine, Umeå University, S-901 87 Umeå, Sweden.

This paper was accepted April 4, 1996.

TABLE 1—Characteristics of the Women in the Smelter and Reference Area Groups at the First Visit for Antenatal Care: Northern Sweden, 1989 to 1991

	Smelter Area (n = 290), %	Reference Area (n = 190), %
Maternal age, y		
<20	2.4	3.6
20–39	96.6	94.3
≥40	1.0	2.1
Gestational age at time of study entry, wk		
6	1.7	1.1
7–16	96.2	93.2
17–20	1.8	2.9
Not specified	0.3	2.8
Previous pregnancies, No.		
0–1	72.9	68.1
2–3	25.8	26.1
4–6	1.3	5.8
Educational level		
Elementary school (9 years)	18.4	16.7
High school (12 years)	65.3	57.2
University courses	5.5	10.1*
University graduate	7.0	11.1
Not specified	3.8	5.0
Time spent at work, hours per week		
0 or <15	13.1	10.6
15–35	45.5	41.9
>35	40.7	46.9
Not specified	0.7	0.6
Smoking		
Never smoked	45.0	38.9
Former smoker	28.4	33.3
Smoker	26.3	27.8
Not specified	0.3	0
Consumption of red wine		
1–3 times per month	8.6	21.2***
Sometimes	35.5	36.9
Never	54.8	39.7**
Not specified	1.1	2.2
Milk/yogurt consumption		
Once or less per week	7.5	11.2
2–6 times per week	13.1	14.4
Once per day	30.3	31.1
2–3 times or more per day	48.6	42.8
Consumption of calcium pills		
Never	95.1	90.8

*$P < .05$; **$P < .01$; ***$P < .001$.

employed at the smelter. The ages of the participants were similar in the two groups, the mean age being 28 years (range = 17 to 43). The mean number of previous full-term pregnancies was 1.1 (range = 0 to 6), and the mean number of all pregnancies, including those resulting in abortions, was 1.4 (range = 0 to 12). Information on education, occupation, dietary and smoking habits, and other characteristics was collected by means of a questionnaire at the beginning of the pregnancy. Written informed consent was obtained from each participant. The study was approved by the Ethical Committee of Umeå University.

Sample Collection

Samples of antecubital vein blood were taken from the mothers at about weeks 10 (range = 7 to 14) and 32 of pregnancy and at delivery. Gestational age was estimated from the date of the last menstruation. Umbilical cord blood was sampled immediately after cutting of the cord. The blood was collected in heparinized metal-free Venoject glass tubes that were randomly tested for lead contamination before use, and blood was stored for 2 to 4 days at 4°C until analysis. Prior to the study, the personnel in charge of sampling were trained and given written instructions in sampling procedures.

Chemical Analyses

Lead was determined in whole blood, after acid digestion in 0.8 M nitric acid, by flameless atomic absorption spectroscopy on a Perkin Elmer 5000 Zeeman HGA-500 spectrophotometer. The method used (standard addition) was a modification adapted from Stoeppler and Brandt.[8] The equipment used (cups and small tubes) was purchased ultraclean from Labasco, Vällingby, Stockholm. The detection limit was 0.05 μmol/L (1 μg/dL). Samples with blood lead concentrations below the detection limit were assigned a value of 0.02 μmol/L in the statistical analyses. The laboratory participates in the quality control program of the Swedish National Board of Occupational Health. The results of the quality control analyses were in good agreement with the reference values. The median value was 104% of the target values (0.37 to 1.57 μmol/L). The day-to-day variation during 1 year was 7% (blood standard from Nycomed, Lidingö, Stockholm, batch number 902, 0.3 μmol lead/L). At the beginning of the study and once during it, double samples were analyzed at the Institute of Environmental Medicine in Stockholm. Agreement between the laboratories, as measured by the correlation coefficient $r(xy)$, was .93 ($P < .001$).

Calcium in serum was determined at the Department of Clinical Chemistry, Umeå University Hospital, by a colorimetric method involving cresolphtalein. The kit was purchased from Boehringer Mannheim. Normal serum calcium values in the laboratory were 2.35 (±0.25) mmol/L.

Statistical Analyses

Student's t tests for comparisons between groups and paired observations, regression analyses, and correlation tests were used to test statistical significance in the statistical package Status II (Foresco AB, Umeå). Since the blood lead levels were best fitted by a log-normal distribution, logarithmic values were used in the statistical analyses. Chi-square calculation was used to test differences in the information given in the questionnaire.

Results

Like almost all Swedish women, the participants in this study were well educated. All had completed elementary school (9 years). Sixty-five percent of the smelter area women and 57% of the control subjects had completed high school. Seven percent in the smelter area and 11% of the controls were university graduates (Table 1). Mean education levels (±SD) were 11.7 ± 1.8 and 12.0 ± 2.1 years, respectively (the difference was not significant). Almost 90% in both groups were employed. Nearly one third were smokers. Wine consumption was low. Only 9% in the smelter area and 21% of the control subjects reported a regular intake of wine (1 to 3 times per month). At the beginning of the pregnancy, 79% vs 74% had milk or yogurt at least once a day. Less than 5% of the women took calcium tablets. Total calcium intake could not be calculated. According to a recent nationwide survey, the mean daily calcium intake of women 19 to 44 years old is 1000 mg.[9] There were no great differences between the two areas. However, wine consumption was significantly higher (although still low) among the control women ($P < .001$). The higher percentage of women with more than a high school education in the control area is probably explained by the fact that the distance from this area to the university and university hospital in Umeå is only 15 km.

TABLE 2—Blood Lead (μmol/L) during Pregnancy and in Newborn Children in the Smelter and Reference Areas

	Smelter Area			Reference Area		
Sample	Mean ± SD	GM	n	Mean ± SD	GM	n
Mothers						
Week 10	0.135 ± 0.062	0.124[a]	290	0.123 ± 0.041	0.115	194
Week 32	0.127 ± 0.051	0.117[a]	257	0.110 ± 0.040	0.102	172
Delivery[b]	0.159 ± 0.047	0.150[a]	241	0.138 ± 0.039	0.133	143
Children[c]	0.138 ± 0.041	0.131[a]	222	0.112 ± 0.038	0.104	131

Note. 1 μmol/L blood lead = 20.7 μg/dL.
[a]Significantly higher blood lead levels in the smelter area ($P < .05$ at week 10, $P < .01$ at week 32, $P < .001$ at delivery, $P < .001$ in children).
[b]Significant increase in blood lead levels between week 32 and delivery in both areas ($P < .001$).
[c]Significant correlations between mother and cord blood, lead levels and significantly lower blood lead concentrations in children as compared with their mothers at delivery in both areas ($P < .001$).

TABLE 3—Regression Analysis of the Average Blood Lead Concentration during Pregnancy (Logarithmic Value) by Sample Characteristics: The Total Group of Women from the Smelter and Reference Areas (n = 367)

	Slope (*b*)	SD (*b*)	T Value	*P*
Residency	0.110	0.028	3.9	<.001
Employment at the smelter	0.256	0.075	3.4	<.001
Age, y	0.005	0.003	1.6	NS
No. previous pregnancies	−0.016	0.014	−1.1	NS
Smoking habits	0.036	0.013	2.7	<.01
Milk consumption	−0.011	0.008	−1.3	NS
Consumption of red wine	0.042	0.018	2.3	<.05

Note. Intercept = −2.25, SD (E) = 0.25. NS = not significant.

Blood Lead Concentrations

Blood lead levels were low even in the smelter area, although they were significantly higher there than in the reference area (Table 2). In both groups, there was a statistically significant increase in blood lead levels during the last 2 months of pregnancy ($P < .001$).

Not all of the women who entered the study could be followed to delivery. From week 10 to week 32 the number decreased, mainly because of abortions. The decrease from week 32 to delivery was due mainly to a failure to obtain samples in the delivery wards. The numerical values of blood lead were similar to those for the full sample, with significant correlations in blood lead levels at weeks 10 and 32 and at delivery ($P < .001$) and a significant increase in blood lead toward the end of the pregnancy ($P < .001$). In the reduced sample, there was a slight decrease in blood lead from week 10 to week 32 in both areas (mean decrease = 0.009 μmol/L, $P < .05$).

In the smelter area, the blood lead concentrations (geometric mean [GM]) were higher in 17 women who were employed at the smelter than in other residents (GM 0.19 vs 0.12 μmol/L at week 10, $P < .001$, and 0.19 vs 0.15 μmol/L at delivery, $P = .01$). The highest blood lead value in the study, 0.70 μmol (14.5 μg/dL), was found in one of these women at week 10.

Umbilical cord blood lead levels were significantly correlated with levels in the mother at weeks 10 and 32 and at delivery ($P < .001$) and were 80% to 87% of the blood lead levels in the mother at delivery (Table 2). The regression analysis showed that the cord blood lead level was dependent on the blood lead level of the mother at delivery, in accordance with the equation $y = 0.06 + 0.45x$; $r(xy) = 0.5$ ($P < .001$).

In the smelter area, the mean infant blood lead level (0.13 μmol/L, GM) was higher than that for the mother at weeks 10 and 32 ($P < .05$ and $P < .001$, respectively). Newborn infants from the smelter area had higher blood lead levels than infants from the nonsmelter area ($P < .001$). Also, mean umbilical cord blood lead levels were higher in smelter employees than in other residents of the area (GM 0.16 vs 0.13 μmol/L, $P < .05$).

The influence of place of residence, employment at the smelter, age, number of previous full-term pregnancies, smoking habits, and consumption of milk and of red wine on average blood lead concentration during pregnancy was analyzed by multiple linear regression for the study group as a whole (Table 3). Significant positive relationships were found between blood lead and place of residence ($P < .001$), employment at the smelter ($P < .001$), smoking ($P < .01$), and wine consumption ($P < .05$). There was also a tendency toward a positive correlation between blood lead and age ($P = .13$). The correlations between blood lead and previous pregnancies and be-

TABLE 4—Serum Calcium (mmol/L) during Pregnancy and in Newborn Children in the Smelter and Reference Areas

	Smelter Area		Reference Area		Total	
Sample	Mean ± SD	n	Mean ± SD	n	Mean ± SD	n
Mothers						
Week 10	2.335 ± 0.105	268	2.335 ± 0.082	189	2.335 ± 0.097	457
Week 32[a]	2.253 ± 0.092	245	2.250 ± 0.105	151	2.252 ± 0.097	396
Delivery[b]	2.287 ± 0.107	231	2.307 ± 0.109	143	2.294 ± 0.108	374
Children[c]	2.714 ± 0.194	175	2.670 ± 0.199	121	2.696 ± 0.197	296

[a]Significant decrease in serum calcium between weeks 10 and 32 of pregnancy in both areas and in total ($P < .001$).
[b]Significant increase in serum calcium between week 32 of pregnancy and delivery in both areas and in total ($P < .001$).
[c]Significantly higher serum calcium concentrations in children as compared with their mothers in both areas and in total ($P < .001$). There were no significant differences between the two areas.

TABLE 5—Maternal and Umbilical-Cord Blood Lead Levels (μg/dL) in Mothers and Children at Delivery, in Different Studies

			Blood Lead Level	
Study	No.	Population	Maternal	Cord
Lauwerys et al.[10]	474	Belgium	9.4[a]	7.7[a]
Zarembski et al.[11]	1665	Dundee, Scotland	5.9 ± 2.5[b]	4.0 ± 2.0[b]
Soong et al.[12]	147	Taiwan	6.5 ± 2.0[b] (6.3)[a]	4.1 ± 1.0[b] (3.9)[a]
Baghurst et al.[1]		Port Pirie, Australia[c]	6.2[d] 14.3[d]	4.3[d] 15.0[d]
Grandjean et al.[13]	1023	Faroe Islands	. . .	1.6[a]
Zetterlund et al.[14]	297; 541	Kiruna–Hielsingborg, Sweden	8.7[d]	7.6[d] (range = 2.0–25.0)
Present study	241	Swedish smelter area	3.2 ± 1.0[b] (3.0)[a]	2.8 ± 0.8[b] (2.6)[a]
Present study	143	Swedish reference area	2.8 ± 0.8[b] (2.6)[a]	2.2 ± 0.8[b] (2.0)[a]

[a]Median.
[b]Mean ± standard deviation.
[c]Values for lead from the Port Pirie study are from the lowest and highest quartiles (total number = 494).
[d]Mean.

tween blood lead and milk consumption were negative but not significant (Table 3).

A significant downward trend in terms of blood lead at delivery was found in both areas by regressing the individual blood lead values against the date of sampling (regression equations: $y = 0.19 - 0.00008x$ and $y = 0.16 - 00007x$, respectively; $P < .001$). This represented a decrease of 0.03 μmol/L (or 0.6 μg/dL) per year. In the smelter area, a significant decrease was also seen in the week 32 samples ($P < .001$). Cord blood lead did not change significantly with time, although there was a tendency for values to decrease during the second year of the study.

Serum Calcium Concentrations

For the group as a whole, mean serum calcium concentrations were 2.33 mmol/L at week 10, 2.25 mmol/L at week 32, and 2.29 mmol/L at delivery (Table 4). Serum calcium was higher at week 10 than later in the pregnancy ($P < .001$). Between week 10 and week 32, there was a significant decrease in serum calcium concentrations, and, during the last 2 months of pregnancy, there was a significant increase ($P < .001$). The mean cord serum calcium concentration was 2.70 mmol/L, a level significantly higher than that for all maternal samples ($P < .001$). There were no significant differences between the samples from the smelter and control areas, and there were no significant correlations between blood lead and serum calcium levels.

Discussion

This study was characterized by a high participation rate in an ethnically homogeneous population. It comprised almost all pregnancies in two areas in Sweden during a 2-year period.

Blood lead levels in pregnant women and newborn children were low, even in the smelter area. Lead concentrations in umbilical cord blood were significantly correlated with those in the mothers and were 80% to 87% of the latter; this is consistent with the findings of other studies.[1,5] Thus, it is obvious that lead freely passes the placenta even at the substantially lower levels found in this study, and cord blood lead was even higher than maternal blood lead at weeks 10 and 32 of pregnancies in the smelter area.

Blood lead levels were lower than those reported in previous studies (Table 5), except for the study from the Faroe Islands.[1,10–14] They were also lower than those reported in five longitudinal studies from the United States and Australia, reviewed by Thacker et al., in which the effect of low-level body burdens of lead on children's intelligence was assessed.[3]

Blood lead levels were influenced by several predictors, such as place of residence, employment at the smelter, smoking, and wine consumption. The correlation found between blood lead concentration and environmental exposure is consistent with the findings of many previously published studies (e.g., Landrigan et al.[15]). Smoking and wine consumption have previously been reported to be sources of lead exposure (e.g., see Elinder et al.[16]). Even the low wine consumption reported in this study contributed to increased blood lead levels. The slightly higher wine consumption in the control area may have decreased the difference in blood lead between the two areas.

In our study, there was a temporal trend, with a significant decrease in blood lead levels with time. This is consistent with the results from a number of other studies (e.g., Ducoffre et al.,[17] Hayes et al.[18]) in which the decrease in blood lead levels was attributed to decreased environmental exposures resulting mainly from a decrease in the use of leaded gasoline. This also probably explains the findings in the present study. During the study period, the amount of leaded gasoline used decreased by 50% (from 40% to 20% of the total amount sold). Also, the emissions of lead from the smelter decreased by more than 20%.

During the third trimester, blood lead levels increased significantly. Because blood volume increases by 25% to 80% during pregnancy, we had expected a fall in the blood lead concentration during the course of pregnancy.[19,20] However, in recent years it has been suggested that lead might be mobilized from the skeleton during pregnancy; for example, Silbergeld et al. reported increased blood lead levels in postmenopausal women.[5,21] Lead accumulates in the skeleton, and about 95% of the body burden of lead is sequestered in bone.[22] Release of bone lead to blood has been documented in retired workers (e.g., see Nilsson et al.[23]). Experimental studies have reported mobilization of lead from body stores during pregnancy and lactation.[24,25] Human studies on blood lead levels during pregnancy have not produced consistent results.

Decreased postpartum blood lead concentrations have been reported in two case studies,[26,27] and it was suggested that the results supported the hypothesis of mobilization of bone lead during pregnancy. However, some studies have reported unchanged or decreased mean blood lead concentrations during pregnancy.[19,28–30]

Three of the studies just mentioned were cross sectional, and blood lead levels in different groups of women were analyzed at different stages of pregnancy.[19,28,30] In the study conducted by McMichael et al., blood samples were collected during weeks 14 through 20 and around week 32 of gestation and at delivery.[29] Mean blood lead values did not vary systematically with gestational stage, although there was a tendency for them to increase with the duration of pregnancy.

This study clearly indicates that blood lead levels do increase during pregnancy, whereas serum calcium concentrations decrease. This may be due to the mobilization of bone lead, together with the marked change in calcium metabolism during pregnancy (see Silbergeld[5]). The significant decrease in serum calcium and blood lead levels between weeks 10 and 32 found in our study may be a consequence of the increased blood volume and increased transfer of calcium (and possibly lead) to the fetus. The significant increase in blood lead during late pregnancy may be associated with the increased calcium requirements of the fetus during the last trimester. The concomitant increase of maternal serum calcium may be due to mobilization of bone calcium and/or an increased uptake. An increased dietary absorption of lead may also contribute to increased blood lead levels in late pregnancy. If the mother's dietary intake of calcium is insufficient, demineralization of maternal bone will occur, and bone lead may be mobilized.[5] That the fetus' need for calcium is met, whatever the maternal sources are, is supported by the fact that mean cord serum calcium is above the normal reference value of the laboratory.

In a subgroup of the study, blood lead levels in women in the smelter area had decreased 6 weeks after delivery and were not statistically different from those of the control subjects. Milk lead levels were, however, higher in the case than in the control women (0.09 vs 0.05 μg blood lead/dL). Thus, lead may be excreted in breast milk, which may consequently be a source of exposure for breast-fed infants.[31]

In conclusion, blood lead concentrations were found to be low in this group of pregnant women in Sweden. However, levels increased during pregnancy, despite the increase in blood volume and unchanged or decreasing environmental lead levels. Also, serum calcium concentrations decreased. The mobilization of lead from bone during pregnancy and lactation is thus a possibility. In view of the adverse effects reported on the intellectual and neurobehavioral development of children exposed to lead in utero and early childhood, all possible measures should be taken to reduce environmental lead exposure. Pregnant women should be encouraged to stop or at least decrease their consumption of wine and cigarettes, especially when environmental exposures are high. (Counseling of pregnant women concerning tobacco and alcohol is probably already routine in many areas because of the known adverse effects of these substances on pregnancy outcome [e.g., increased prematurity and decreased birthweight as a result of smoking and fetal alcohol syndrome as a result of heavy alcohol consumption].[32,33]) It is also crucial that maternal calcium intake is sufficient. □

Acknowledgments

This work was supported by the County Council of Västerbotten, the Work Environment Fund, and the Boliden Mineral Co Ltd, Skelleftehamn, Sweden.

Lars Jonsson and Susanne Sandberg are acknowledged for skillful technical assistance. Klas Lundbergh of the Boliden Mineral Co Ltd provided valuable information concerning the emissions from the smelter and their environmental impact. We are grateful to the participating women; to the staff at the health care centers in Skelleftehamn, Bureå, and Holmsund-Obbola; and to the obstetric clinics in Skellefteå and Umeå. Stefan Marklund and the staff of the Department of Clinical Chemistry at University Hospital are acknowledged for the serum calcium analyses.

References

1. Baghurst PA, McMichael AJ, Wigg NR, et al. Environmental exposure to lead and children's intelligence at the age of seven years. *N Engl J Med.* 1992;327:1279–1284.
2. Bellinger DC, Stiles KM, Needleman HL. Low-level lead exposure, intelligence and academic achievement: a long-term follow-up study. *Pediatrics.* 1992;90:855–861.
3. Thacker BS, Hoffman DA, Smith J, Steinberg K, Zack M. Effect of low-level body burdens of lead on the mental development of children: limitations of meta-analysis in a review of longitudinal data. *Arch Environ Health.* 1992;47:336–346.
4. Wong GP, Ng TL, Martin TR. Effects of low-level lead exposure *in utero:* review. *Obstet Gynecol Surv* 1992;47:285–289.
5. Silbergeld EK. Lead in bone. Implications for toxicology during pregnancy and lactation. *Environ Health Perspect.* 1991;91:63–70.
6. Englyst V, J:son Lagerkvist B, Lundberg K. Environmental metal exposure around a copper and lead smelter. From proceedings of the Fifth International Conference of the ISEE, Stockholm, Sweden; August 15–18, 1993:137.
7. Jakobsson Lagerkvist B, Söderberg HÅ, Nordberg GF, Ekesrydh S, Englyst V. Biological monitoring of arsenic, lead and cadmium in occupationally and environmentally exposed pregnant women. *Scand J Work Environ Health.* 1993;19(suppl 1):50–53.
8. Stoeppler M, Brandt K. Determination of lead and cadmium in whole blood by

electrothermal atomic absorption spectroscopy. In: Dors M, ed. *Diagnosis and Therapy of Porphyrias and Lead Intoxication.* Heidelberg, Germany: Springer Verlag; 1980:185–187.

9. Becker W. Food habits and nutrient intake in Sweden, 1989 [in Swedish, with summary in English]. *Natl. Food Administration.* 1989;2:349–362.
10. Lauwerys R, Buchet J, Roels H, Hubermont G. Placental transfer of lead, mercury, cadmium and carbon monoxide in women. I. Comparison of the frequency distributions of the biological indices in maternal and umbilical cord blood. *Environ Res.* 1978;15:278–289.
11. Zarembski PM, Griffiths PD, Walker J, Goodall HB. Lead in neonates and mothers. *Clin Chim Acta.* 1983;134:35–49.
12. Soong Y-K, Tseng R, Liu C. Lead, cadmium, arsenic and mercury levels in maternal and fetal cord blood. *J Formos Med Assoc.* 1991;90:59–65.
13. Grandjean P, Weihe P, Jörgensen PJ, Clarkson T, Cernichiari E, Viderö T. Impact of maternal seafood diet on fetal exposure to mercury, selenium, and lead. *Arch Environ Health.* 1992;47:185–195.
14. Zetterlund B, Winberg J, Lundgren G, Johansson G. Lead in umbilical cord blood correlated with the blood lead of the mother in areas with low, medium or high atmospheric pollution. *Acta Paediatr Scand.* 1977;66:169–175.
15. Landrigan PJ, Froines JR, Mahaffey KR. Body lead burden: summary of epidemiological data on its relation to environmental sources and toxic effects. In: Mahaffey KR, ed. *Dietary and Environmental Lead: Human Health Effects.* New York, NY: Elsevier Science Publications; 1985:421–452.
16. Elinder CG, Gerhardsson L, Oberdörster G. Biological monitoring of toxic metals—overview. In: Clarkson TW, Friberg L, Nordberg GF, Sager PR, eds. *Biological Monitoring of Toxic Metals.* New York, NY: Plenum Press; 1988:1–72.
17. Ducoffre G, Claeys F, Bruaux P. Lowering time trend of blood lead levels in Belgium since 1978. *Environ Res.* 1990;51:25–34.
18. Hayes EB, McElvaine MD, Orbach HG, Fernandez AM, Lyne S, Matte TD. Long-term trends in blood lead levels among children in Chicago: relationship to air lead levels. *Pediatrics.* 1994;93:195–200.
19. Alexander FW, Delves HT. Blood lead levels during pregnancy. *Int Arch Occup Environ Health.* 1981;48:35–39.
20. Hytten F. Blood volume changes in normal pregnancy. *Clin Haematol.* 1985;14:601–628.
21. Silbergeld EK, Schwartz J, Mahaffey K. Lead and osteoporosis: mobilization of lead from bone in postmenopausal women. *Environ Res.* 1988;47:79–94.
22. Mushak P. New directions in the toxicokinetics of human lead exposure. *Neurotoxicology.* 1993;14:29–42.
23. Nilsson U, Atewell R, Christoffersson JO, et al. Kinetics of lead in bone after end of occupational exposure. *Pharmacol Toxicol.* 1991;69:477–484.
24. Buchet JP, Lauwerys R, Roels H, Hubermont G. Mobilization of lead during pregnancy in rats. *Int Arch Occup Environ Health.* 1977;40:33–36.
25. Keller CA, Doherty RA. Bone lead mobilization in lactating mice and lead transfer to suckling offspring. *Toxicol Appl Pharmacol.* 1980;55:220–228.
26. Manton WI. Total contribution of airborne lead to blood lead. *Br J Ind Med.* 1985;42:168–172.
27. Thompson GN, Robertson EF, Fitzgerald S. Lead mobilization during pregnancy. *Med J Aust.* 1985;143:131.
28. Bonithon-Kopp C, Huel G, Grasmick C, Sarmini H, Moreau T. Effects of pregnancy on the inter-individual variations in blood levels of lead, cadmium and mercury. *Biol Res Pregnancy.* 1986;7:37–42.
29. McMichael AJ, Vimpani GV, Robertson EF, Baghurst PA, Clark PD. The Port Pirie cohort study: maternal blood lead and pregnancy outcome. *J Epidemid Community Health.* 1986;40:18–25.
30. Shukla R, Bornschein RL, Dietrich KN, et al. Fetal and infant lead exposure: effects on growth in stature. *Pediatrics.* 1989;84:604–612.
31. Palminger Hallén I, Jorhem L, Json Lagerkvist B, Oskarsson A. Lead and cadmium levels in human milk and blood. *Sci Total Environ.* 1995;166:149–155.
32. McDonald AD, Armstrong BG, Sloan M. Cigarette, alcohol and coffee consumption and prematurity. *Am J Public Health.* 1992;82:87–90.
33. Little RE, Wendt JK. The effects of maternal drinking in the reproductive period: an epidemiologic review. *J Subst Abuse.* 1991;3:187–204.