

Biological monitoring of arsenic, lead and cadmium in occupationally and environmentally exposed pregnant women

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JAKOBSSON LAGERKVIST B, SÖDERBERG H-Å, 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;19:50—3. Lead and cadmium in blood (B-Pb and B-Cd, respectively) and arsenic in urine (U-As) were analyzed three times during pregnancy for women living around a metal smelter and women living in a reference town. The B-Pb levels were significantly higher in the smelter town. In the women of both towns, the B-Pb levels increased during pregnancy. Women who were employed at the smelter had higher B-Pb levels than women in the surrounding area. There were no significant differences in the B-Cd levels between the smelter and reference towns, except for non- and ex-smokers at the onset of pregnancy. No difference between the two areas was seen among the smokers, whose cadmium levels were twice those of non- and ex-smokers. There were no significant differences in the U-As levels, which were comparable with previously reported values in Sweden.

Key terms: metal exposure, pregnancy.

A large copper and lead smelter (the Rönnskär smelter) has been in operation in northern Sweden since the late 1920s. For many years this smelter was Sweden's largest single source of emissions of heavy metals and sulfur dioxide. As a consequence of legislative regulations, the emissions have gradually decreased during the last 25 years (table 1). Annual production of the commercially most important metals is as follows: about 100 000 t of copper, 40 000 t of lead, 270 t of silver, and 8—9 t of gold.

Adverse effects on vegetation, birds (fragile egg shells), and marine fauna have been noted in a large area around the smelter. Locally grown vegetables, fruits, and berries have contained increased levels of

lead, cadmium, and arsenic. Special recommendations have therefore been issued by the local health authorities with regard to the growth and consumption of such crops (1). A recent study (2) showed that the metal levels had decreased, and the National Food Administration considered that the acceptable (according to the Food and Agriculture Organization of the World Health Organization) weekly intake levels were unlikely to be exceeded as a result of the normal consumption of locally grown fruits and vegetables.

The objective of this study was to monitor lead and cadmium in blood (B-Pb and B-Cd, respectively) and arsenic in urine (U-As) during pregnancy in an area around the smelter and compare the results with corresponding values from a reference area. The study was approved by the ethical committee of the Umeå University.

Table 1. Emissions of metals to ambient air from the Rönnskär smelter (t/year).

Year	Arsenic	Lead	Copper	Cadmium
1967—1976	115	485	207	12
1985	40	101	41	2.7
1990	4.7	52	18	1.3

Subjects

In Sweden, all pregnant women are registered with the Public Maternity Care, and all of the women who became pregnant during a two-year period (February 1989—February 1991) were invited to join the study. This study is a report on the pregnancies during the first one and a half years. The women in the smelter area were living within a distance of 0.3—1.5 km from the smelter (Skelleftehamn, N = 147) or 10—15 km from it (Bureå, N = 62). Only 11 of these women were employed at the smelter. Like the smelter area, the reference area (Holmsund) is situated on the east coast of the Gulf of Bothnia. It is located 130 km south of the smelter and is not con-

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sidered to be influenced by the metal emissions from it. The two areas are similar with regard to both the size of the population and social and economic background factors. Of the women invited to participate in the study from the smelter area and of those similarly invited in the reference area, 85% (209 subjects) and 90% (149 subjects), respectively, agreed to do so. The age distribution was similar in both groups, mean 27.4 (SD 4.8) years for the smelter area and 28.1 (SD 5.0) years in the reference area.

Methods

The pregnant women were asked about their occupation, place of residence, and smoking habits at the beginning of pregnancy (around weeks 10–12). Considered as non- or ex-smokers were those who had never smoked or had not smoked during pregnancy or had stopped smoking at least six months before the onset of pregnancy. Samples of antecubital vein blood were taken from the mothers at about weeks 10 and 32 of pregnancy and at delivery. The blood was collected in heparinized metal-free venoject glass tubes and stored at 4°C until the analysis within 2–4 d. Morning samples of urine were collected in acid-washed polyethylene cups and stored at –20°C. The third urine sample was collected at week 39 of pregnancy.

Lead and cadmium were determined in whole blood after acid digestion by flameless atomic absorption spectroscopy (AAS) on a Perkin Elmer 5000 Zeeman HGA-500 AA spectrophotometer. The method used (standard addition) was a modification according to Stoeppler & Brandt (3). The equipment used (cups and small tubes) was purchased ultraclean from Labasco, Vällingby, Stockholm. The detection limits were 2 nmol · l⁻¹ for cadmium and 0.05 µmol · l⁻¹ for lead. In the statistical analyses samples below the detection limit were given the values 0.03 µmol · l⁻¹ for lead and 1 nmol · l⁻¹ for cadmium. In each run the absorbances of the samples were measured together with those of samples with a standard added and blanks.

For determinations of B-Pb and B-Cd, the laboratory participates in the quality control program of the Swedish National Board of Occupational Health. During the course of the study, agreement with the

target values (0.37–1.57 µmol · l⁻¹) for B-Pb, as measured by the correlation coefficient $r(xy)$, was 0.98. For cadmium (target values 7–49 nmol · l⁻¹), the $r(xy)$ was 0.95. The median value was 104% of the target value for lead and 96% of the target value for cadmium. The day-to-day variation during one year was 7% for the lead analyses and 11% for the cadmium analyses (blood standard Nycomed (Lidingö, Stockholm), batch number 902; lead = 0.3 µmol · l⁻¹, cadmium = 8 nmol · l⁻¹).

Inorganic arsenic and its methylated metabolites, monomethylarsonic acid and dimethylarsinic acid, in urine were analyzed by AAS (Perkin Elmer 5000Z + HGA 500) after hydride generation (MHS-20). The method used was a slight modification of that given in the operator's manual. The test solution contained 500 µl of urine and 100 µl of freshly prepared 2% solution of Antifoam Emulsion RD (Kebo 1.8297) in 5 ml of 10% hydrochloric acid. The evaluation was performed by the standard addition technique, and the peak area of the curve deflections was measured. At the beginning of the study and once during it, double samples were analyzed at the Institute of Environmental Medicine. The agreement between these samples was acceptable [$r(xy) = 0.87$, $P < 0.01$]. The reported values were 1.4–20.4 µg · l⁻¹ (0.02–0.27 µmol · l⁻¹) for the Institute of Environmental Medicine and 2–21 µg · l⁻¹ (0.026–0.28 µmol · l⁻¹) for the laboratory. The detection limit was 2 µg · l⁻¹ (0.026 µmol · l⁻¹) for inorganic arsenic (As⁺³ + As⁺⁵). Samples below the detection limit were given the value 1 µg · l⁻¹.

For the statistical analysis, the computerized program Status II (Foresco AB, Umeå) was used. For the comparison of the groups and for the testing of changes in metal levels during pregnancy, the Wilcoxon rank sum test and the Wilcoxon signed rank test, respectively, were used.

Results

The blood lead levels during pregnancy were higher in the smelter area than in the reference area ($P < 0.01$), and they increased from 0.13 µmol · l⁻¹ at week 10 of pregnancy to 0.16 µmol · l⁻¹ (geometric mean) at delivery (table 2). Five samples were below the detection limit, 0.05 µmol · l⁻¹, at week 10,

Table 2. Lead levels in blood (µmol · l⁻¹)^a during the pregnancies of 209 women from a smelter area and 149 women from a reference area (GM = geometric mean).

Time of sampling	Smelter area			Non-smelter area			P-value
	Arithmetic mean	SD	GM	Arithmetic mean	SD	GM	
Week 10	0.14	0.07	0.13	0.12	0.04	0.11	<0.05
Week 32	0.14	0.05	0.13	0.12	0.04	0.11	<0.01
Delivery ^b	0.17	0.05	0.16	0.14	0.04	0.14	<0.001

^a 0.1 µmol · l⁻¹ = 20 µg · l⁻¹.

^b Statistically significant increase, $P < 0.001$, from week 32 to delivery in both groups.

Table 3. Cadmium levels in blood ($\text{nmol} \cdot \text{l}^{-1}$) during the pregnancies of women from a smelter area (135 non- and ex-smokers and 74 smokers) and from a reference area (96 non- and ex-smokers and 53 smokers). (GM = geometric mean).

Time of sampling	Smelter area			Nonsmelter area			P-value
	Arithmetic mean	SD	GM	Arithmetic mean	SD	GM	
<i>Non- and ex-smokers</i>							
Week 10	6	4	5	5	2	4	<0.05
Week 32	6	3	5	6	3	6	NS
Delivery ^a	7	3	7	7	3	7	NS
<i>Smokers</i>							
Week 10	12	6	11	13	6	12	NS
Week 32	10	5	9	10	4	10	NS
Delivery ^b	10	4	9	9	4	9	NS

^a Statistically significant increase from week 32 to delivery in both groups, $P < 0.01$, and between weeks 10 and 32 in the reference area.

^b Statistically significant decrease between weeks 10 and 32, $P < 0.05$, in the smelter area and $P < 0.001$, in the reference area.

Table 4. Arsenic levels in urine ($\mu\text{mol} \cdot \text{l}^{-1}$) during the pregnancies of 209 women from a smelter area and 149 referents.^a (GM = geometric mean)

Time of sampling	Smelter area			Nonsmelter area		
	Arithmetic mean	SD	GM	Arithmetic mean	SD	GM
Week 10	0.11	0.10	0.08	0.11	0.13	0.07
Week 32	0.12	0.11	0.07	0.09	0.09	0.06
Week 39	0.10	0.13	0.07	0.08	0.08	0.05

^a There were no significant differences between the groups nor among the various gestational stages of pregnancy.

and six at week 32. These samples were equally distributed between the two areas. Only 11 of the women living close to the smelter were employed at it. Their B-Pb levels were, however, significantly higher than those of the rest, one of them having the highest B-Pb value of the study, $0.7 \mu\text{mol} \cdot \text{l}^{-1}$.

There were no significant differences in the B-Cd levels between the two areas, except for the non- and ex-smokers at the onset of pregnancy, $5 \text{ nmol} \cdot \text{l}^{-1}$ versus $4 \text{ nmol} \cdot \text{l}^{-1}$ for the smokers (geometric mean), $P < 0.05$ (table 3). At the beginning of pregnancy, the B-Cd level (geometric mean) was $7 \text{ nmol} \cdot \text{l}^{-1}$ in the smelter area and $6 \text{ nmol} \cdot \text{l}^{-1}$ in the reference area. At delivery, the B-Cd level was $7 \text{ nmol} \cdot \text{l}^{-1}$ in both groups. Altogether 18 samples were below the detection limit, $2 \text{ nmol} \cdot \text{l}^{-1}$, at week 10, seven at week 32, and three at delivery. No difference was seen between the smokers from the two areas. They had B-Cd levels twice as high as those of the non- and ex-smokers.

The B-Cd levels increased from week 32 to delivery among the nonsmokers in both areas, $P < 0.01$. For the smokers, there was a significant decrease during pregnancy in both areas, especially from week 10 to week 32 of pregnancy.

There were no significant differences in the U-As levels, either between the two areas or during pregnancy (table 4). Altogether 19 samples were below

the detection limit, $2 \mu\text{g} \cdot \text{l}^{-1}$, at week 10, 38 at week 32, and 23 at delivery.

Discussion

In the present study, B-Pb, B-Cd, and U-As levels were monitored in 85–90% of the pregnant women in a smelter area and a reference area during a period of one and a half years. The maternal B-Pb levels were lower than in four longitudinal studies from Cincinnati, Cleveland, Port Pirie, and Sydney. (For a review, see reference 4.) In these studies the maternal B-Pb levels ranged from 65 to $95 \mu\text{g} \cdot \text{l}^{-1}$ (0.33 – $0.48 \mu\text{mol} \cdot \text{l}^{-1}$), whereas in our study they were $34 \mu\text{g} \cdot \text{l}^{-1}$ in the smelter area and $28 \mu\text{g} \cdot \text{l}^{-1}$ in the reference area. They were also lower than in a previous study from Sweden (5), including pregnancies from the same area as in the present study, where the B-Pb levels were $87 \mu\text{g} \cdot \text{l}^{-1}$.

The B-Pb levels were, however, significantly higher in the smelter area than in the reference area during the entire pregnancy, though the differences were small. However, the lead concentrations of individual mothers working in some departments of the smelter may reach levels that constitute a risk for adverse effects on the mental development of their children. The highest lead level in this study ($0.7 \mu\text{mol} \cdot \text{l}^{-1}$) is, however, the lowest level for which such risks have been discussed (6). No significant correlation was found between smoking and B-Pb. The increase in B-Pb during pregnancy may be caused by an increased mobilization from the skeleton. It has been suggested, although relatively little is known about this subject, that bone lead is mobilized during pregnancy and is transferred to the more readily bioavailable compartment of maternal circulation (7).

The B-Cd levels during pregnancy were of the same magnitude as in other studies reported from western Europe and the United States (8–10). They

were considerably lower than those accepted for Swedish workers ($50 \text{ nmol} \cdot \text{l}^{-1}$), although they were slightly higher than in a group of 15 nonsmoking Swedish women in Stockholm [mean 3 (SD 1.6) $\text{nmol} \cdot \text{l}^{-1}$] (11). These women were not pregnant, however. There was a tendency towards increased B-Cd levels during pregnancy in non- and ex-smokers, whereas the B-Cd levels decreased in smokers. These changes are considered to be dependent mainly on changes in smoking habits from the beginning of pregnancy to delivery.

There was no significant variation in the U-As levels during pregnancy, nor were there any significant differences between the smelter area and the reference area. The geometric means ($0.05\text{--}0.08 \mu\text{mol} \cdot \text{l}^{-1}$) were 9–12 times lower than the corresponding mean of the exposed workers and of the same magnitude as that of unexposed 52-year-old men (12). The levels found are considered to be normal and are not believed to cause any adverse health effects (13). They are lower than previously reported “normal” urinary levels in Sweden (14).

Concluding remarks

The lead, cadmium, and arsenic levels of pregnant Swedish women were found to be low. The lead levels were significantly higher in the smelter area as compared with those in the nonsmelter one. However, the differences were small. The cadmium levels were influenced by smoking. The arsenic levels were comparable with previously reported values in Sweden, with no significant differences between the two areas.

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References

- Mattson T, Movitz J, Lundberg K, Stenlund H. Bly, kadmium och arsenik i grönsaker odlade kring Rönnskärnsverken, Skelleftehamn [Lead, cadmium and arsenic in vegetables grown in the surroundings of the Rönnskär smelter, Skelleftehamn]. Uppsala (Sweden): National Food Administration, 1986. (Report 1986:2.)
- Jorhem L, Lundberg K, Sundström B. Bly, kadmium och arsenik i vegetabilier odlade kring Rönnskärnsverken, Skelleftehamn [Lead, cadmium and arsenic in vegetables grown in the surroundings of the Rönnskär smelter, Skelleftehamn]. Uppsala (Sweden): National Food Administration, 1991. (Report; no 12.)
- Stoeppeler M, Brandt K. Determination of lead and cadmium in whole blood by electro-thermal atomic absorption spectroscopy. In: Doss M, ed. Diagnosis and therapy of porphyrias and lead intoxication. Heidelberg: Springer Verlag, 1980:185–7.
- Thacker B, 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;47:336–46.
- 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;66:169–75.
- Mushak P, Davis JM, Crocetti AF, Grant LD. Prenatal and postnatal effects of low-level lead exposure: integrated summary of a report to the US congress on childhood lead poisoning. Environ Res 1989;50:11–36.
- Silbergeld EK. Lead in bone: implications for toxicology during pregnancy and lactation. Environ Health Perspect 1991;91:63–70.
- Korpela H, Loueniva R, Yrjänheikki E, Kauppila A. Lead and cadmium concentrations in maternal and umbilical cord blood, amniotic fluid, placenta, and amniotic membranes. Am J Obstet Gynecol 1986;155:1086–9.
- Kuhnert BR, Kuhnert PM, Zarlingo TJ. Associations between placental cadmium and zinc, age and parity in pregnant women who smoke. Obstet Gynecol 1988;71:67–70.
- 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;15:278–89.
- Vahter M, Slorach S. Exposure monitoring of lead and cadmium: an international pilot study within the WHO/UNEP human exposure assessment location (HEAL) programme. Nairobi: World Health Organization and the United Nations Environment Programme, 1990: 82 p.
- Lagerkvist B, Linderholm H, Nordberg GF. Vasospastic tendency and Raynaud's phenomenon in smelter workers exposed to arsenic. Environ Res 1986;39:465–74.
- International Programme on Chemical Safety. Arsenic. Geneva: World Health Organization, 1981. (Environmental health criteria; vol 18.)
- Vahter M, Lind B. Concentrations of arsenic in urine of the general population in Sweden. Sci Total Environ 1986;54:1–12.