ISSN 1067-4136, Russian Journal of Ecology, 2015, Vol. 46, No. 6, pp. 564–572. © Pleiades Publishing, Ltd., 2015.
Original Russian Text © S.V. Mukhacheva, V.S. Bezel', 2015, published in Ekologiya, 2015, No. 6, pp. 444–453.

Heavy Metals in the Mother–Placenta–Fetus System in Bank Voles under Conditions of Environmental Pollution from Copper Plant Emissions

S. V. Mukhacheva and V. S. Bezel'

Institute of Plant and Animal Ecology, Ural Branch, Russian Academy of Sciences, ul. Vos'mogo Marta 202, Yekaterinburg, 620144 Russia

e-mail: msv@ipae.uran.ru

Received November 20, 2014

Abstract—Accumulation of heavy metals (Cu, Zn, Cd, and Pb) in the mother–placenta–fetus system has been studied in small mammals (based on a case study of bank voles) living under conditions of environmental pollution from copper production emissions (Middle Ural). The role of gastrointestinal and placental barriers has been assessed in translocation of the studied elements from pregnant female diets to embryos. It has been shown that, with existing environmental pollution levels, the entry of toxicants into the organisms of female individuals does not necessarily lead to significant fetal losses during pregnancy, but it may affect the quality of progeny and its vital capacity in the early postnatal period.

Keywords: small mammals, industrial pollution, heavy metals, embryo, placenta, copper smelter, Middle Urals

DOI: 10.1134/S1067413615060120

The ability of natural populations of any species to maintain a high level of abundance under unfavorable environmental changes, including intensive anthropogenic impact, is a prerequisite for their stable functioning. This fully pertains to small mammals (rodents and small insectivores) living under conditions of environmental pollution from different pollutants (heavy metals, radioactive elements, and organic compounds), and they are often used as model objects both in population ecology (Schwarz, 1980) and ecotoxicology (Talmage and Walton, 1991).

The majority of authors associate the observed toxic effects with the effects of direct impact of pollutants on reproduction (Dinerman, 1980; Moskvitina et al., 2011; Domingo, 1994; and Thompson and Bannigan, 2008). While it is possible to accurately assess the toxic effect in a laboratory experiment, depending on dose loads, it is necessary to take into account a variety of additional factors when studying natural populations: the mosaical structure of pollution fields, variation of diets, the spatial movement of animals in the pollution gradient, etc. under the circumstances, one can assess the contribution of the direct impact of pollutants using the values of toxic elements that enter an organism along with food and their accumulation thereof. In this case, it is necessary to take into account the presence of effective histohematogenous barriers in an organism that enable implementation of intensive selective transport and the protection of progeny from the impact of various chemical factors.

There are very few studies dedicated to translocation of chemical elements in the diet–maternal organism–placenta–fetus chain under chronic impact of toxicants on animals in experimental conditions, and there are almost no studies on natural populations. The purpose of this work is to assess the role of gastrointestinal and placental barriers in the translocation of heavy metals in the mother–placenta–fetus system in small mammals (based on a case study of bank voles) living under conditions of environmental pollution from copper production emissions. The hypothesis tested by us assumes that, with existing environmental pollution levels, the entry of toxicants into the organisms of female individuals does not necessarily lead to significant embryonal losses during pregnancy, but it may affect the quality of progeny and its vital capacity in the early postnatal period.

MATERIAL AND METHODS

This work uses materials obtained in the course of numerous (1990–2007) studies of small mammal communities inhabiting the area in the vicinity of the Middle Ural copper smelter (MUCS) and background areas. The plant, located 50 km west of Yekaterinburg, has been the largest source of atmospheric pollution for many decades (since 1940). The main components of emissions are gaseous S, F, and N compounds, as well as dust particles with sorbed metals (Cu, Pb, Zn, Cd, Fe, Hg, etc.) and metalloids (As). Despite a significant decrease in the volume of atmospheric emissions

Table 1. Volume of studied material

Period, years	Trap days processed	Females obtained[1]	Number of samples for measuring heavy metal concentrations				Assessment of embryo weight[3]
			diet[2]	liver	placenta	embryo[3]	
1990–1994	23365	144	82	101	0	7 (2)	34 (6)
1995–2000	18115	135	134	70	52	63 (9)	68 (13)
2003–2007	13725	190	61[4]	26	80	92 (18)	198 (28)
Total	55205	469	216	197	132	162 (29)	300 (47)

[1], the total number of breeding females in traps is given; [2], the contents of stomachs were used to assess the concentration of elements in the diet; [3], number of analyzed embryos, number of litters in parentheses; [4], data over the period from 2012 to 2014 are given to assess long-term changes.

in recent decades (141000 t/yr since 1989; 25000 t/yr since 2005; and less than 5000 t/yr since 2010), the heavy metal content in the soil (Trubina et al., 2014) and food objects for bank voles (from 1990 to 2014, according to our data) changed insignificantly, which allowed us to subsequently consider combined samples.

The study areas are located west of the emission source within the area in the vicinity of copper smelter (1–2 and 4–6 km) and are significantly distant from this source (20–30 km). Based on an analysis of the heavy metal content in natural deposit environments (soil, forest litter, and snow cover), areas were accordingly classified as impact (Imp) or background (Bg). Detailed characteristics of areas are given in earlier works (Vorobeichik et al., 1994; Mukhacheva, 2007).

As a model object, we used the bank vole (*Clethrionomys* (*Myodes*) *glareolus* Schreber, 1780), which is the dominant species in communities of small mammals in the compared areas. The animals were caught using lines of snap-traps (25 traps every 5–7 m, which were simultaneously set at all sites for 4–5 days with a daily single check) during the mass breeding period (from May to August). More than 55000 trap days were processed and 469 breeding bank vole females were obtained (Table 1).

The embryonic development stage was determined by the Tupikova technique (1964). Embryos and the respective placentas were extracted from fetal membranes, and amniotic fluid was removed, weighed on the electronic balance Tanita (with an accuracy to 0.001), and dried at a temperature of 65°C for chemical analysis. Data on 300 embryos from 47 litters were used to assess the weight of embryos during pregnancy (from 12 to 20 days).

The content of priority pollutants in the study area (Cu, Zn, Cd, and Pb) was studied in the diet (content of stomach) and organism (liver) of pregnant bank voles, as well as in placentas and embryos in the second half of pregnancy. The individual levels of accumulation were analyzed in 216 samples of gastric contents, 197 samples of liver, 162 embryos, and 132 placentas. To assess the barrier function of the gastrointestinal tract and placenta, only "pair" substrates were used, i.e., the gastric content and liver of the same females (n = 140) and embryos with the respective placentas (n = 132).

The samples were chopped, weighed (about 0.1 g) on a KERN-770 analytical balance with an accuracy of 0.00001 g, and incinerated in a MWS-2 microwave oven (Berghof, Germany) by the wet mineralization method in 65% nitric acid. The concentration of elements (μg/g dry weight) was determined on an AAS 6 Vario spectrometer (Analitik Jena AG, Germany) by the atomic absorption method using flame (for Cu and Zn) or electrothermal (Cd, Pb) atomization. The analyses were performed at the Laboratory of Ecotoxicology of Populations and Communities (Institute of Plant and Animal Ecology, Ural Branch, Russian Academy of Sciences) accredited for technical competence (accreditation certificate no. ROSS. RU0001.515630). The measurement quality was assessed according to the international CRM standard sample 185R (bull liver). 707 samples (see Table 1) were analyzed and about 2600 element identifications were performed.

Statistical analysis was carried out in Statistica v. 8.0. We used the no-parametric Mann–Whitney (U) test to assess differences in the content of elements, and the Spearman correlation coefficient was used to identify relations between the concentrations of elements in substrates, as well as the weight of embryos with concentrations of heavy metals in them. Multiple comparisons were made according to the Tukey test, and differences were considered significant at $p < 0.05$. The coefficient of variation *CV* was used to assess the variability of weight of viable embryos (without resorption traits) in one litter.

RESULTS

Long-term changes in the content of heavy metals in bank vole food objects were assessed based on data on animal stomach contents that most adequately reflects the diet of voles in a specific area (Mukhacheva and Bezel', 1995; Bezel' et al., 2007). Multiple comparisons showed that the Zn, Cd, and Pb concentrations in

Table 2. Concentrations of heavy metals (μg/g dry weight) in diet, liver, embryos, and placenta of pregnant bank voles living in background (Bg) and impact (Imp) areas

Substrate	Trapping area	Element concentration, mg/g dry weight			
		Cu	Zn	Cd	Pb
Stomach contents	Bg	16.37 [73] / 5.08–83.20	89.24 [72] / 19.06–452.91	0.91 [73] / 0.01–9.38	7.67 [70] / 0.01–59.47
	Imp	148.30 [140] / 11.85–087.12	191.53 [139] / 22.98–1516.78	4.27 [143] / 0.10–17.30	38.37 [135] / 0.12–287.38
Liver	Bg	11.71 [84] / 3.78–26.51	94.73 [83] / 21.31–187.45	1.55 [84] / 0.01–8.08	1.57 [69] / 0.01–10.86
	Imp	13.55 [111] / 4.32–63.62	100.92 [112] / 25.70–154.53	8.75 [111] / 0.49–54.82	3.57 [97] / 0.22–19.65
Placenta	Bg	12.12 [99] / 2.51–32.13	84.70 [99] / 16.11–395.77	0.12 [99] / 0.01–0.94	0.65 [46] / 0.10–3.72
	Imp	14.90 [33] / 2.04–38.22	80.50 [33] / 36.27–164.57	0.70 [33] / 0.25–1.17	0.41 [11] / 0.09–1.30
Embryo	Bg	6.88 [113] / 1.39–19.56	90.04 [112] / 68.39–296.80	0.04 [98] / 0.01–0.75	1.13 [47] / 0.11–6.11
	Imp	8.07 [50] / 1.60–17.11	86.84 [50] / 39.53–311.19	0.06 [41] / 0.01–1.22	4.32 [19] / 1.13–9.49

The numerator indicates the median and sample size (in brackets), and the denominator indicates the minim and maximum values.

the diet of voles trapped in one areas in different periods did not show significant differences. For instance, the Cd concentration in the food of voles from the background area was 1.34 ± 0.30 μg/g dry weight in 1990–1994 and 1.97 ± 0.22 in 1995–2000; 1.70 ± 0.16 in 2012–2014; and 4.34 ± 0.39, 5.72 ± 0.42, and 3.45 ± 0.67 in an impact area, respectively. And only in the female food from an impact area did the Cu concentration decrease three times over the study period: from 198.9 ± 22.2 μg/g dry weight in 1990–1994 to 64.4 ± 8.7 in 2012–2014. However, this did not have a significant effect on copper accumulation in an organism, since its content is effectively regulated by homeostatic mechanisms.

The concentrations of heavy metals in analyzable substrates are given in Table 2. The *diets* of breeding females from impact areas, which were determined by the stomach contents, contained all elements in amounts exceeding those from background areas: Cu, 9 times ($U_{Cu} = 288$, $p < 0.0001$); Pb, 5 times ($U_{Pb} = 1661$, $p < 0.0001$); Cd, 4.6 times ($U_{Cd} = 1606$, $p < 0.0001$); and Zn, 2 times ($U_{Zn} = 1929$, $p < 0.0001$). The concentrations of all elements positively correlated with each other ($r = 0.51–0.77$, $p < 0.05$).

A similar trend was also found for accumulation of heavy metals *in the organism of maternal individuals* (*liver*); however, the intensity of accumulation of essential (Cu and Zn) and toxic (Cd and Pb) elements was different. With the approach to the source of emission, Zn and Cu concentrations increased only by 7–15% of the background values ($U_{Zn} = 3598$, $p = 0.007$; $U_{Cu} = 3242$, $p < 0.0003$), while Cd increased 5.6 times ($U_{Cd} = 710$, $p < 0.0001$) and Pb increased 2.3 times ($U_{Pb} = 1885$, $p < 0.0001$). The content of most of heavy metals in the liver and food is closely related ($r_{Cu} = 0.57$, $r_{Cd} = 0.50$, $r_{Pb} = 0.49$, $p < 0.05$), except for Zn whose concentration in the liver did not depend on its amount in the diet ($r = 0.22$).

The content of most of the studied elements *in the placenta* did not depend on the level of pollution of the area. The exception was Cd ($U_{Cd} = 158$, $p < 0.0001$), whose concentration in the placenta in impact areas exceeded the background values almost by 6 times. A negative correlation ($r = –0.52$, $n = 189$, $p < 0.05$) between the levels of toxic elements (Cd and Pb) was identified in the placenta, while a positive correlation ($r = 0.32$, $n = 262$, $p < 0.05$) was determined for essential elements (Cu and Zn).

Cd and Pb concentrations were 2–4 times higher *in embryos* from impact areas than their respective values for background areas ($U_{Cd} = 1505$, $p = 0.019$; $U_{Pb} = 132$, $p < 0.0001$) and positively correlated with each other ($r = 0.29$, $n = 205$, $p < 0.05$). Independently of the area, the Cd concentration in the embryo was always lower than that in the respective placenta; an inverse dependence was recorded for Pb. The levels of

Cu and Zn accumulation in an embryo varied insignificantly and increased in proportion to their change in placentas. Negative correlations in Cd–Cu ($r = -0.29$, $n = 302$, $p < 0.05$) and Pb–Zn ($r = -0.36$, $n = 228$, $p < 0.05$) pairs were also recorded.

Embryo weight. During the period of pregnancy, a relative decrease (compared with the background values) in progeny weight, which reached 6–10% by the end of prenatal development, was observed in voles from impact areas, and in some litters the weight decreased by 20% (Fig. 1). Multiple comparisons showed that differences are significant ($p = 0.013$) only at the final stage of pregnancy (18–20 days): in terms of wet weight, an embryo has an average weight of 1.27 ± 0.05 g ($n = 123$) in the background area and 1.05 ± 0.06 g ($n = 53$) in the impact area.

Increase in the concentrations of toxicants (Cd and Pb) in embryos was accompanied by a relative decrease in their weight in second half of pregnancy (Fig. 2). However, due to considerable variability of the weight of separate embryos (both among litters and within one litter), the relation is weak ($r = 0.25$–0.32). According to our estimates, the variability of weight of viable embryos in a litter was, on average, 10% (*CV* from 2.2% to 25.4%) and did not depend on the contamination level of the area.

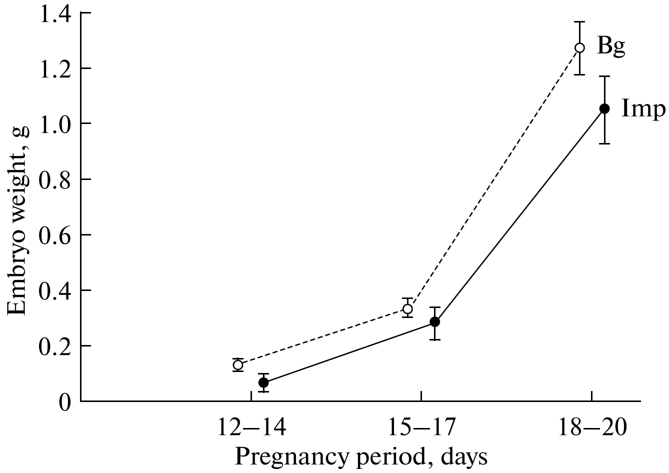

Fig. 1. Change in embryo weight (average and 95% confidence interval) in bank voles inhabiting background (Bg) and impact (Imp) areas, in the second half of pregnancy.

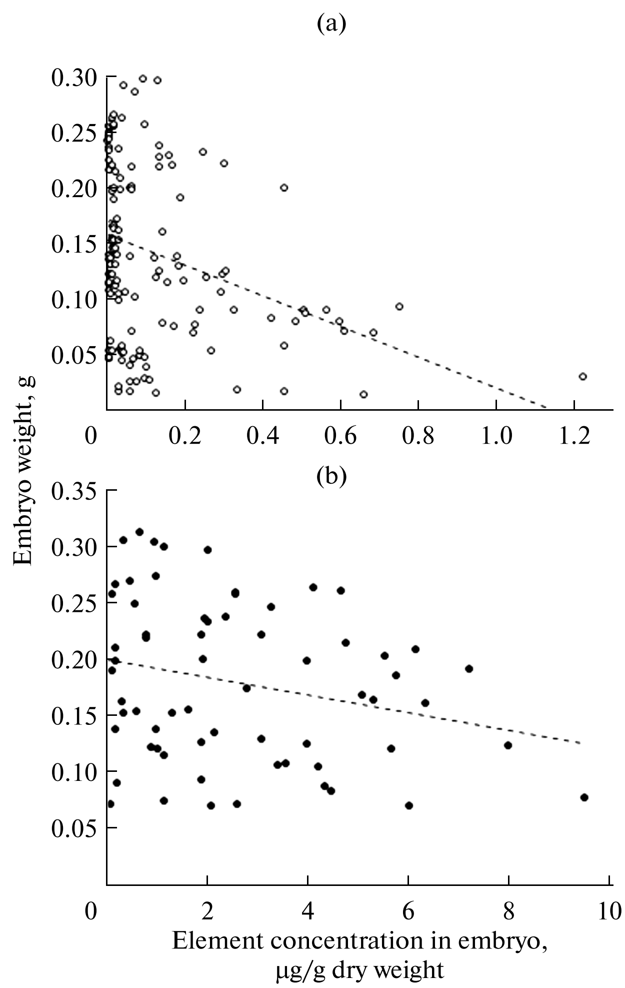

Fig. 2. Change in weight of bank vole embryos during the second half of pregnancy depending on Cd (a) and Pb (b) concentration in them.

DISCUSSION

The role of the gastrointestinal barrier. The barrier at the level of gastrointestinal tract is one of the unique gistohematogenous barriers in an organism, in which intensive selective transport is implemented based on intertissue and intercellular cooperation and which ensures protection from various mechanical, chemical, and biological factors (Mogil'naya and Mogil'nyi, 2007). Its role can be assessed by the ratio of heavy metal concentrations in the diet and liver of the same individuals (Fig. 3): the dashed line (bisector) denotes a direct proportional relationship of metal concentration in these substrates; the points below the bisector indicate the discrimination of an element, while the points above the bisector indicate its accumulation in an organism.

Despite high Cu, Zn, and Pb concentrations in bank vole food in contaminated areas, the toxic load of these elements on the organism (liver) is insignificant. Independently of a study area, Cd had heavily accumulated in the liver of animals: its concentration in the liver was about 2 times higher than that in the diet.

Therefore, Cu, Zn, and Pb are characterized by the discrimination of elements at the level of the gastrointestinal barrier, while Cd easily overcomes it. A similar dependence is shown for small mammals of different trophic groups (Bezel' et al., 2007; Nesterkova et al., 2014).

The role of the placental barrier. The placenta is the link between a developing embryo and the maternal organism, performing a double function: providing

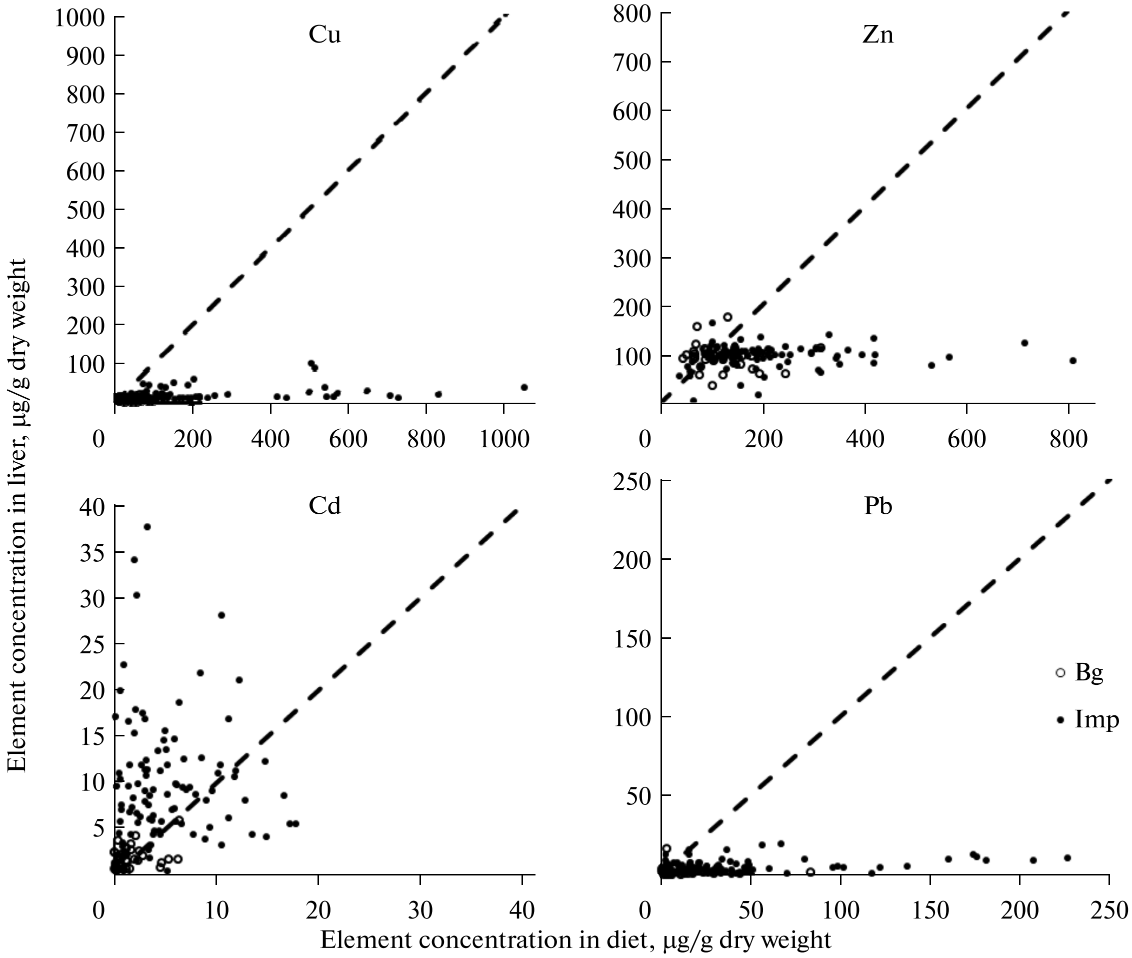

Fig. 3. Change in concentration of heavy metals in liver and diet of bank voles from background (Bg) and impact (Imp) areas.

free passage for some substances (nutrition and gaseous exchange) and serving as a barrier for other substances. However, some xenobiotics (including heavy metals) penetrate through the placenta and have a negative effect on the fetus (Iyengar and Rapp, 2001; Stawarz et al., 2011; Amaya et al., 2013).

The barrier role of the placenta in process of translocation of chemical elements from the maternal organism to the developing embryo can be assessed by considering the ratio of concentrations of heavy metals in placentas and the respective embryos (Fig. 4). This dependence makes it possible to determine the range of critical concentrations of elements, the excess of which leads to their accumulation in the embryo. Cu was proportionally accumulated in the placenta and embryo up to a level of 10 μg/g dry weight, and its excess lead to restricted entry of the element into the embryo. A different change was observed in the concentration of another essential element, Zn: its accumulation was recorded in the embryo as compared with the placenta. Its supply to the fetus was restricted only when Zn levels in the placenta reached significant values (200 μg/g dry weight). According to the literature data (Lindsay et al., 1994), the Zn content in the embryo increases over the entire pregnancy period.

For toxic elements, the discriminatory function of the placenta is less pronounced than that for essential elements: for Cd, it serves as a partial barrier, and Pb easily overcomes it (see Fig. 4). This agrees with the literature data (Osman et al., 2000; Iyengar and Rapp, 2001; and Stawarz et al., 2011). According to information from some authors (Loiacono et al., 1992; Baranowska, 1995; Diaz-Barriga et al., 1995; and Zakrzewska et al., 2002), the average Cd content in placentas in industrialized areas significantly (from 50 to 800%) exceeds the background values, while other authors (Truska et al., 1989) did not observe such changes. According to our data, by the end of pregnancy, the average Cd content was 5 times higher in the placenta of animals from impact areas than in those from background ones, while there were no significant differences recorded for Pb (Table 2).

Accumulation of chemical elements in developing embryos in areas with different pollution levels can be represented as frequency distributions the shift of which toward high concentrations reflects an increased accu-

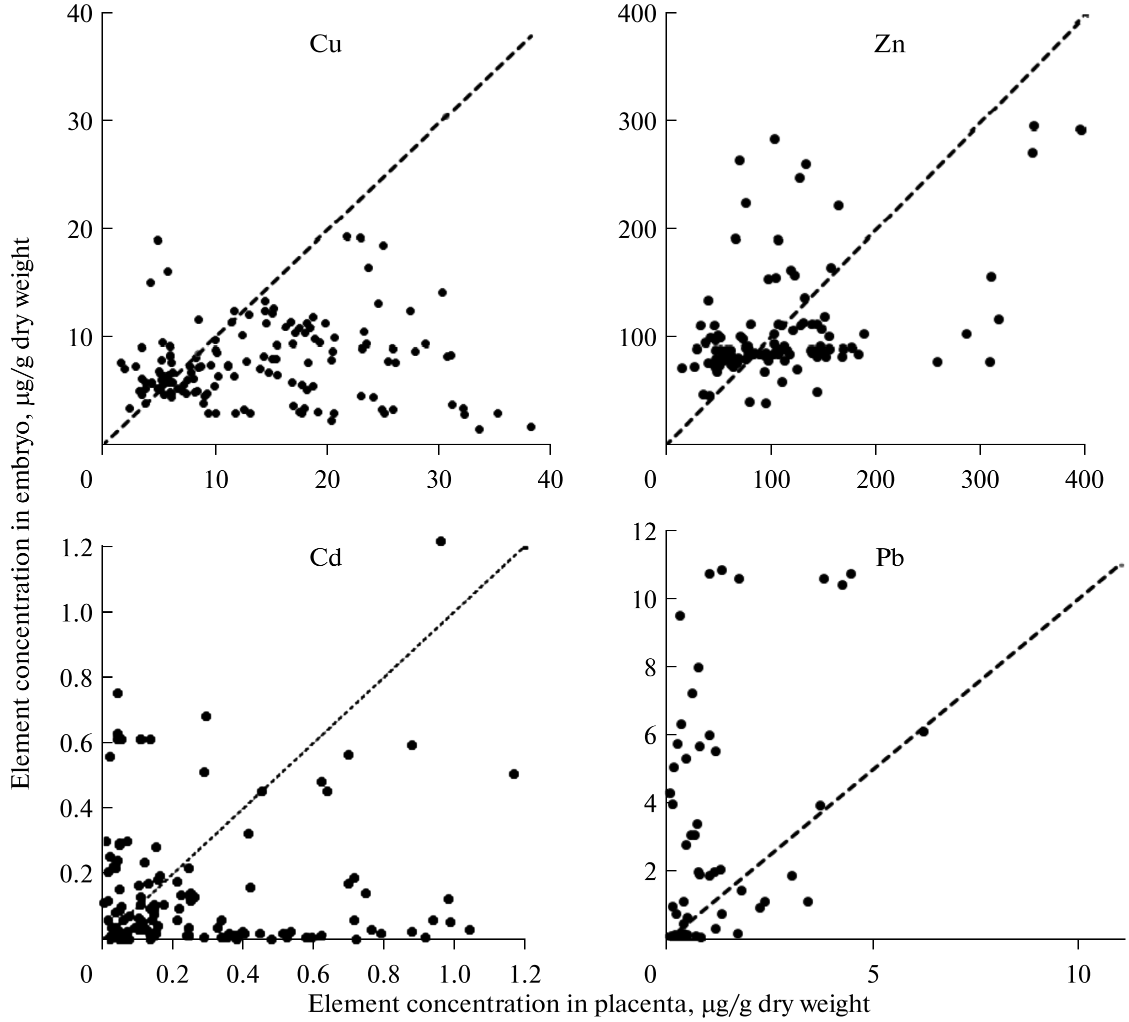

Fig. 4. Change in heavy metal concentrations in embryos and respective placentas of bank voles.

mulation of elements in impact areas (Fig. 5). Despite high levels of elements in the diet of animals living in the impact area (Cu, 9 times higher, and Zn, 2 times higher), the almost complete coincidence of the distribution curves of Cu and Zn concentrations in the samples from background and impact areas reflects the discrimination of these elements at the level of the above-considered barriers. In the distribution of Cd and Pb concentrations, we can clearly see the effect of their heavier accumulation in embryos from impact areas, which completely corresponds to increased concentrations of these toxic elements (by 5 times) in the maternal diet and the absence of a "hard" barrier at the placenta level. Thus, the number of embryos with a Cd concentration of more than 0.45 μg/g is 4 times larger in the impact area than in the background one. With respect to Pb, the share of embryos that accumulated Pb in amounts more than 4.0 μg/g is 7 times higher in the impact area than in the background one (see Fig. 5).

Therefore, under the above-considered contamination levels, the pronounced discrimination of separate essential elements and its absence in the case of toxicants forms in mammal organisms based on the barrier function of the gastrointestinal tract and placenta.

Population effects. The toxic Cd and Pb effect on the reproductive function of mammals is evident (Domingo, 1994; Thompson and Bannigan, 2008). These effects can have an impact both on the gonads of parental individuals and developing progeny, causing a complete failure of pregnancy. In our case, in terms of population ecotoxicology, translocations of chemical elements in the diet–maternal organism–placenta–embryo system not only have an indicative value, but also reflect the key aspects of the well-being of a population, and, first of all, its ability to provide the necessary reproduction level of qualitative progeny. Despite increased levels of heavy metals supplied with foods, the presence of the histohematogenous barrier system at the organism level in bank vole

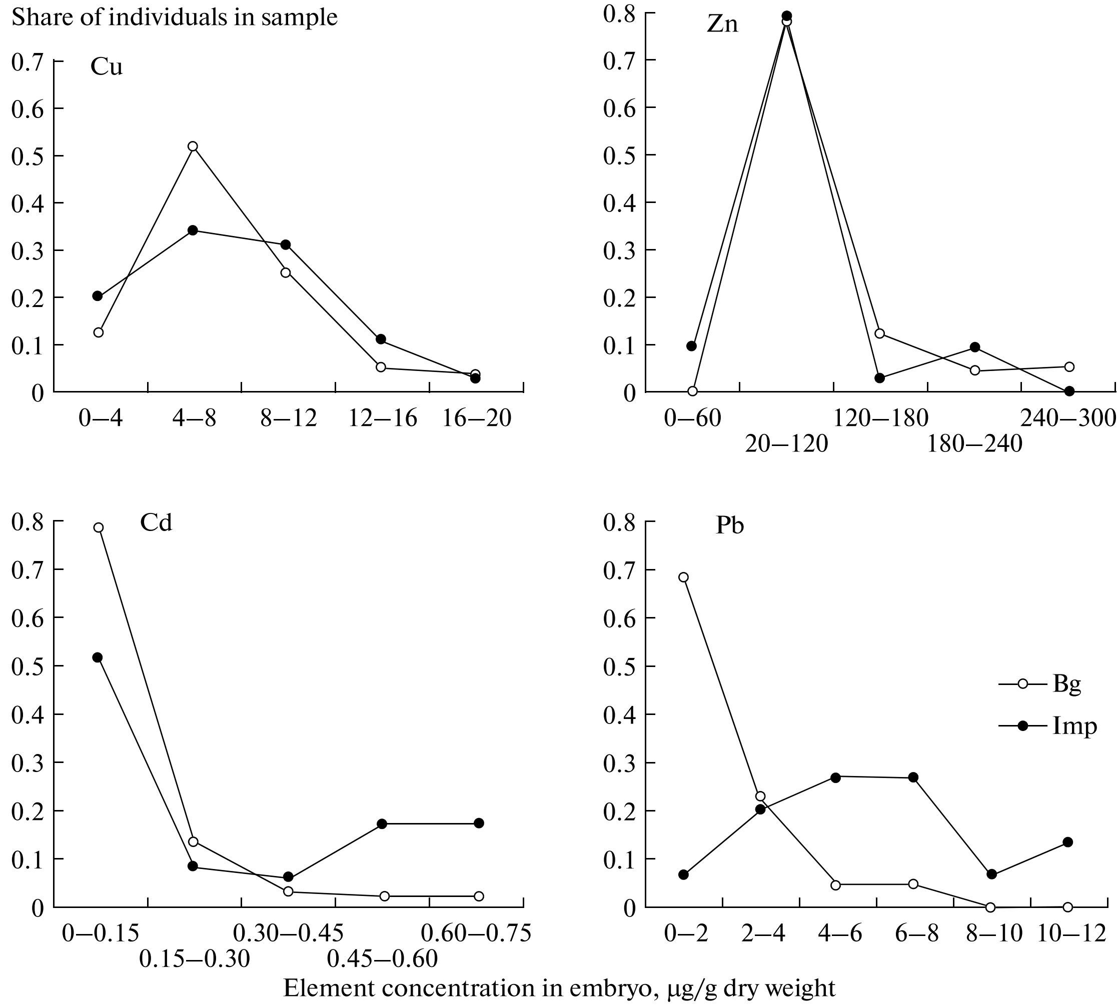

Fig. 5. Distribution curves of concentration of essential and toxic elements in embryos in background (Bg) and impact (Imp) areas.

maternal individuals living in impact areas significantly decreases toxicant concentrations in organs and tissues, as well as in developing embryos. According to our data, taking into account the levels of industrial pollution under consideration, separate stages of embryogenesis in bank voles are distinguished by a high resistance to the impact of heavy metals, and we did not observe their significant influence on such reproductive indicators as potential fecundity and embryonic mortality during the prenatal period (Mukhacheva, 2001).

However, simple calculation of the number of viable embryos, which is sufficient in the course of a standard zoological study of animals from natural populations, does not allow one to take into account the quality of progeny. Attention is rarely paid to deviations from normal development (the presence of malformations, size and weight embryo, peculiarities of placenta location, etc.) determining the health of progeny (Moskvitina et al., 2011). At the same time, when there is a chronic impact of heavy metals on the maternal organism during pregnancy, up to 30 types of serious pathological changes can develop in the embryos of small mammals (Moskvitina et al., 2011; Salomeina and Mashak, 2012; Mirzoev et al., 2014; Domingo, 1994; Zakrzewska et al., 2002; and Thompson and Bannigan, 2008): many of them lead to birth of fragile progeny, while others are fatal.

One of the major indicators determining a young vole's life potential is its weight. It is known that the weight of embryos (newborns) is negatively associated with concentrations of toxicants in the placenta (Ward et al., 1987; Loiacono et al., 1992; and Benitez et al., 2009). When there is a chronic impact of pollutants during pregnancy and lactation, weight decrease can reach 6–10% and, in some cases, 25% of the reference values (Salomeina and Mashak, 2012; Zakrzewska, 1988).

In our case, by the end of the prenatal period, an increase in the level of Pb and Cd (to a lesser degree) in bank voles from impact areas is accompanied a decrease in weight, compared with those from background areas. By the end of pregnancy (18–20 days), the number of embryos with a weight of less than 1 g is about 40% in background areas and more than 50% in impact areas. This inevitably leads to a generation of fragile progeny and its increased mortality in the early postnatal period. Unlike the level of embryonic losses, the weight of embryos indicates a change in the population reproductive potential more adequately, which is confirmed by our data (Bezel' et al., 1998; Mukhacheva, 2001), according to which the relative survival of juvenile voles in the summer and autumn period is 1.5–1.8 times lower in impact areas than in background ones.

CONCLUSIONS

Based on chemical analysis of the diets, liver, and progeny (embryos and placentas) of female bank voles living under conditions of environmental pollutions from copper plant emissions, the entry of essential (Cu and Zn) and toxic (Cd and Pb) elements with diet and their accumulation in an organism were assessed. It was shown that there is Cu, Zn, and Pb discrimination at the gastrointestinal tract level, while Cd easily overcomes it. The placental barrier restricts excessive entry of Cu, Zn, and Cd; however, it is permeable to Pb.

It was established that, during the prenatal development, the Pb and Cd concentrations increase in embryos from polluted areas, while the relative weight of developing progeny decreases. This can lead to a reduction in the adaptive potential and increased elimination of progeny in the early postnatal period.

The hypothesis tested by us assumes that, with the existing levels of environmental pollution, the entry of toxicants into the organisms of maternal individuals does not necessarily lead to significant embryonic losses during pregnancy, but it may affect the quality of progeny and its vital capacity in the early postnatal period.

Under specific conditions of environmental pollution, the observed phenomena of the main reproductive indicators of voles are only marginally associated with the direct toxic effect of pollutants, which possibly results in decreasing weight of embryos during second half of pregnancy; this completely confirms our current hypothesis. The decisive role in the implementation of population reproductive potential is played by such factors as quality of habitat, age structure, and level of local animal abundance.

ACKNOWLEDGMENTS

This work was partially supported by the Basic Research Program of the Ural Branch, Russian Academy of Sciences (15-3-4-28), the Program for in Support of Leading Scientific Schools (NSh-2840.2014.4), and the Russian Foundation for Basic Research (project nos. 12-0500811 and 13-04-01229). The authors are grateful to E.L. Vorobeichik for constructive comments in the writing of this article, as well as to E.A. Akhunova and A.V. Shchepetkin, who performed analytical work.

REFERENCES

Amaya, E., Gil, F., Freire, C., et al., Placental concentrations of heavy metals in a mother-child cohort, *Environ. Res*, 2013, vol. 120, pp. 63–70.

Baranowska, I., Lead and cadmium in human placentas and maternal and neonatal blood in heavily polluted area, measured by graphite furnace atomic absorption spectrometry, *Occup. Environ. Med.*, 1995, vol. 51, no. 1, pp. 229–232.

Benitez, M.A., Mendez-Armenta, M., Montes, S., et al., Mother–fetus transference of lead and cadmium in rats: Involvement of metallothionein, *Histol. Histopathol.*, 2009, vol. 24, pp. 1523–1530.

Bezel, V.S., Belskii, E.A., and Mukhacheva, S.V., On the problem of variability in reproductive parameters of animal populations under toxic pollution of the environment, *Russ. J. Ecol.*, 1998, vol. 29, no. 3, pp. 186–191.

Bezel, V.S., Kutsenogii, K.P., Mukhacheva, S.V., et al., Elemental composition of the diets and tissues of small mammals at different trophic levels as a biological indicator of chemical pollution of the environment, *Chemistry for Sustainable Development*, 2007, no. 1, pp. 33–42.

Diaz-Barriga, F., Carrizeles, L., Calderon, J., et al., Measurement of placental levels of arsenic, lead and cadmium as a biomarker of exposure to mixtures, in *Biomonitors and Biomarkers as Indicators of Environmental Change*, New York: Plenum, 1995, pp. 139–148.

Dinerman, A.A., *Rol' zagryaznitelei okruzhayushchei sredy v narushenii embrional'nogo razvitiya* (The Role of Environmental Pollutants in Disturbances of Embryonic Development), Moscow: Meditsina, 1980.

Domingo, J.L., Metal-induced developmental toxicity in mammals: A review, *J. Toxic. Environ. Health: Current Issues*, 1994, vol. 42, no. 2, pp. 123–141.

Iyengar, G.V. and Rapp, A., Human placenta as a 'dual' biomarker for monitoring fetal and maternal environment, with special reference to potentially toxic trace elements: Part 3. Toxic trace elements in placenta and placenta as a biomarker for these elements, *Sci. Tot. Environ.*, 2001, vol. 280, pp. 221–238.

Lindsay, Y., Duthie, L.M., and Mcardle, H., Zinc levels in the rat fetal liver are not determined by transport across the placental microvillar membrane or the fatal liver plasma membrane, *Biol. Reprod.*, 1994, no. 51, pp. 358–365.

Loiacono, N.J., Graziano, J.H., Kline, J.K., et al., Placental cadmium and birthweight in women living near a lead smelter, *Arch. Environ. Health*, 1992, vol. 47, pp. 250–255.

Mirzoev, E.B., Kobyako, V.O., Gubina, O.A., and Frolova, N.A., Responses of F1 rats to chronic exposure to small doses of cadmium in the antenatal period of development, *Toksik. Vestn.*, 2014, no. 4, pp. 29–33.

Mogil'naya, G.M. and Mogil'nyi, V.L., The gastrointestinal protective barrier, *Morfologiya*, 2007, no. 6, pp. 9–16.

Moskvitina, N.S., Kuranova, V.N., and Savel'ev, S.V., Disturbances of embryonic development in vertebrates under conditions of technogenic environmental pollution, *Sib. Ekol. Zh.*, 2011, no. 4, pp. 489–495.

Mukhacheva, S.V., Bank vole population reproduction in a gradient of technogenic environmental pollution, *Zool. Zh.*, 2001, vol. 80, no. 12, pp. 1509–1517.

Mukhacheva, S.V., Spatiotemporal population structure of the bank vole in a gradient of technogenic environmental pollution, *Russ. J. Ecol.*, 2007, vol. 38, no. 3, pp. 161–167.

Mukhacheva, S.V., and Bezel, V.S., Levels of toxic elements and functional structure in population of small mammals under conditions of technogenic pollution (with reference to the bank vole), *Russ. J. Ecol.*, 1995, vol. 26, no. 3, pp. 212–215.

Nesterkova, D.V., Vorobeichik, E.L., and Reznichenko, I.S., The effect of heavy metals on the soil–earthworm–european mole food chain under the conditions of environmental pollution caused by the emissions of a copper smelting plant, *Sib. Ekol. Zh.*, 2014, no. 5, pp. 777–788.

Osman, K., Akesson, A., Berglund, M., et al., Toxic and essential elements in placentas of Swedish women, *Clin. Biochem.*, 2000, vol. 33, p. 131–138.

Salomeina, N.V. and Mashak, S.V., Structural bases of mother–fetus relationships under chemical impact during embryonic development, *Med. Obraz. Sibiri*, 2012, no. 1, pp. 10–15.

Shvarts, S.S., *Ekologicheskie zakonomernosti evolyutsii* (Ecological Patterns of Evolution), Moscow: Nauka, 1980.

Stawarz, R., Formcki, G., Chrobaczynska, M., et al., Accumulation of cadmium and lead in placenta and amnion of women from upper Silesian region, Poland, *J. Environ. Res. Dev.*, 2011, vol. 5, no. 4, pp. 871–879.

Talmage, S.S. and Walton, B.T., Small mammals as monitors of environmental contaminants, *Rev. Environ. Contam. Toxicol.*, 1991, vol. 119, pp. 47–145.

Thompson, J. and Bannigan, J., Cadmium: Toxic effects on the reproductive system and the embryo, *Reprod. Toxicol.*, 2008, vol. 25, pp. 304–315.

Trubina, M.R., Vorobeichik, E.L., Khantemirova, E.V., et al., Dynamics of forest vegetation after the reduction of industrial emissions: Fast recovery or continued degradation?, *Dokl. Biol. Sci.*, 2014, vol. 458, pp. 302–305.

Truska, P., Rosival, L., Balazova, G., et al., Blood and placental concentrations of cadmium, lead and mercury in mother and their newborns, *J. Hyg. Epidemiol. Microbiol. Immunol.*, 1989, vol. 33, no. 2, pp. 141–147.

Tupikova, N.V., Analysis of reproduction and age composition of small mammal populations, in *Metody izucheniya prirodnykh ochagov boleznei cheloveka* (Methods of Studies on Natural Foci of Human Diseases), Moscow: Meditsina, 1964, pp. 154–191

Vorobeichik, E.L., Sadykov, O.F., and Farafontov, M.G., *Ekologicheskoe normirovanie tekhnogennykh zagryaznenii ekosistem (lokal'nyi uroven')* (Ecological Rating of Technogenic Pollutants in Ecosystems: Local Level), Yekaterinburg: Nauka, 1994.

Ward, N.I., Watson, R., and Bryce-Smith, D., Placental element levels in relation to fetal development for obstetrically 'normal' births: A study of 37 elements. Evidence for effects of cadmium, lead and zinc on fetal growth, and for smoking as a source of cadmium, *J. Biosoc. Res.*, 1987, no. 9, pp. 63–81.

Zakrzewska, M., Bialoriska, D., and Sawicka-Kapusta, K., Cadmium accumulation in fetus and placenta of bank voles (*Clethrionomys glareolus*), *Bull. Environ. Contam.*, 2002, no. 69, pp. 829–834.

Zakrzewska, M., Effect of lead on postnatal development of the bank vole (*Clethrionomys glareolus*), *Arch. Envoron. Contam. Toxicol.*, 1988, no. 17, pp. 365–371.

Translated by D. Zabolotny