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Industrial Pollution Does Not Cause an Increased Incidence of Nephropathies in the Bank Vole

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Abstract—Studies in the vicinities of copper smelters and in undisturbed areas of the Middle Urals have been performed to evaluate the effect of industrial pollution with heavy metals on macro- and micromorphological parameters of kidneys (weight, weight index, the spectrum and frequency of histopathologies) in the bank vole (*Clethrionomys glareolus* Schreber, 1780) and on the accumulation of Cu, Zn, Cd, and Pb in this organ. It has been found that the kidneys of voles from polluted areas accumulate considerable amounts of heavy metals, with their concentrations increasing with age and/or sexual maturation. The kidney weight, index, and the frequency and severity of the majority of observed nephropathies also increase upon change in the reproductive-age status of animals. These parameters show no dependence on the degree of industrial pollution: at individual level, none of the heavy metals accumulated in the kidneys has produced any effect on the frequency and severity of nephropathies. These results contradict the prevailing opinion that toxicants play the determinant role in the development of nephropathies in small mammals inhabiting polluted areas. Therefore, the causes of nephropathies should be sought among other factors, not related to pollution.

Keywords: bank vole, kidneys, morphophysiological indicators, nephropathy, industrial pollution, heavy metals, the Middle Urals

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Analysis of changes in micro- and macromorphological characters is one of possible directions in research on the responses of animals to industrial (chemical) pollution. Special to morphology is a tribute to the tradition to first describe the shape and structure of a biological object, expecting that exposure to a factor of interest will lead to "visible" changes in them. Structural characters are considered to be highly conserved and, hence, most reliable for the diagnosis of such exposure. In evaluating toxic effects, morphological alterations are regarded as integrated and terminal phenomena, compared to changes at the biochemical and cellular levels (Pereira et al., 2006). Today, the prevailing concept is that industrial pollution plays a determinant role in the development of various histopathologies in small mammals inhabiting polluted areas. Histopathological changes in internal organs under toxic load have been repeatedly observed in laboratory experiments as well as in animals from natural populations living in areas with different pollution levels. As a rule, the authors attribute them to the toxic effect of pollution, leaving out of consideration other factors that may be responsible for such changes (Włostowski et al., 2004; Damek-Poprava and Sawicka-Kapusta, 2003, 2004; Pereira et al., 2006; Sánchez-Chardi et al., 2008, 2009).

In our opinion, the concept of strictly deterministic relationship between the external factor (the action of a toxicant) and morphological changes in tissues and organs is a major simplification. Considering that heavy metal intoxication is the only cause of the observed histopathology means to neglect a variety of other endo- and exogenous factors leading to similar disturbances (infections, parasite invasions, etc.). Moreover, most tissue responses to the damaging effect of such factors are unspecific, which makes it still more difficult to reveal the cause of the observed pathology. On this basis, we hypothesized that the frequency and severity of histopathology in the internal organs of animals from polluter areas may be unrelated to the level of pollution.

To verify this hypothesis, we studied the kidneys of small mammals. The main function of this paired organ is to remove metabolic products, thereby maintaining homeostasis of the blood as well as of the entire body. The high level of blood supply to the organ and the great length of kidney tubules account for long-term contact of toxic substances and their metabolites with the renal endothelium, epithelium, and interstitial cells (Gouer, 1989). Along with the liver and bones, the kidneys may be regarded as a model "depot" organ selectively accumulating various xenobiotics. It is generally accepted in ecotoxicology to use

Table 1. Study sites and numbers of samples for chemical and historical analyses

Zone of pollution gradient	Site code	Site, distance from pollution source	Number of samples					
			Cu	Zn	Cd	Pb	macromorphology	micromorphology
Background	Bg-1	Pripyshminskie Bory National Park, Tugulymskii raion, 270 km east of MUCS and KCS	6	6	6	–	–	17
	Bg-2	Shigaevo, Shalinskii raion, 90 km west of MUCS	5	5	17	–	–	–
	Bg-3	Nizhneserginskii raion, 20–30 km west of MUCS	127	126	260	47	339	70
Buffer	B-1	Visim Nature Reserve, Prigorodnyi raion, 18 km from KCS	27	27	115	20	–	6
	B-2	Pervoural'skii raion, 4–6 km west of MUCS	34	34	143	22	57	36
Impact	I	Pervoural'skii raion, 1–2 km west of MUCS	17	17	53	13	23	10

(–) No data.

the concentrations of priority pollutants in such organs for bioindication of environmental pollution and evaluation of individual toxic loads on the organism (Shore and Rattner, 2001; Lodenius et al., 2002; Beernaert et al., 2007; Milton et al., 2003; Lindén et al., 2003; Topolska et al., 2004; Veltman et al., 2007). Being a depot organ for many xenobiotics, the kidneys are especially sensitive to cadmium (Mueller, 1993; Cooke and Johnson, 1996; Griffin et al., 2000).

The purpose of this study was to assess the impact of industrial (chemical) pollution on morphological parameters of the kidneys in small mammals using the example of bank vole, *Clethrionomys glareolus* Schreber, 1780. The kidneys of animals from sites with different levels of industrial pollution were analyzed for the contents of heavy metals, variation in weight (a macromorphological parameter of the organ), the frequency and severity of histopathological (micromorphological) changes (nephropathies), and correlation between these parameters and individual toxic loads.

MATERIAL AND METHODS

Studies were performed in forest ecosystems of the Middle Urals exposed to industrial pollution. Most animals were trapped in the vicinities of the Middle Ural (MUCS) and Kirovgrad (KCS) copper smelters, the Urals' largest nonferrous metal industries that have been in operation for over 70 and 100 years, respectively. Emissions from both smelters have a similar composition: their main components are sulfur dioxide and inorganic dust rich in heavy metals (Cu, Zn, Cd, Pb). Despite modernization of both smelters, their impact on ecosystems is still strong. The test sites were located at different distances from the MUCS (1–2, 4–6, and 20–30 km) and 18 km from the KCS. Control animals were trapped in conditionally clean areas in Shalinskii and Tugulymskii raions of Sverdlovsk oblast, where the contents of pollutants did not exceed the regional background level. Depending on the contents of heavy metals in the soil, forest litter, and snow, each site was assigned to one of the three zones of pollution gradient: the background (Bg), buffer (B), or impact (I) zone (Table 1). The sites and zones were described in detail previously (Vorobeichik et al., 1994, 2006).

The bank vole is one of dominant species in small mammal communities of the study region. The trapped animals were examined for external (body weight and size) and internal characters (the state of the thymus and reproductive system and the weight of internal organs) to determine their reproductive-age status: immature young of the year (im), mature young of the year (m), or overwintered individuals (ow).

The kidneys were weighed and then either dried to air-dry state for determining metal concentrations or fixed in 10% formalin for histological analysis. The chemical and histological analyses were performed in parallel to compare individual toxic loads (heavy metal concentrations) with micromorphological characteristics of animals ($n = 40–106$ for different metals). After drying, the samples were wet-ashed in concentrated (65%) nitric acid using an MWS-2 microwave pressure digestion system (Berghof, Germany). Concentrations of metals (Cu, Zn, Cd, Pb) were measured with an AAS vario 6 atomic absorption spectrometer (Analytik Jena, Germany) in the Laboratory of Population and Community Ecotoxicology, Institute of Plant and Animal Ecology (Ural Branch, Russian Academy of Sciences). The laboratory is certified for technical competence (certificate no. ROSS RU.0001.515630).

The kidney weight and index (kidney-to-body weight ratio, ‰) were regarded both as basic macromorphological characters (along with organ size, weight, texture, etc.) and as a morphophysiological indicator of the state of population (Shvarts et al., 1968).

For micromorphological analysis, the kidneys were processed histologically, embedded in paraffin, and cut along the sagittal plane. Four to six median sections were stained with hematoxylin and eosin or toluidine blue polychrome and examined under a DM1000 LED microscope (Leica Microsystems, Germany). The observed pathomorphological changes were classified into four types, depending on the affected structural component of the kidneys: glomeruli (G), tubules (T), or blood vessels (V), including plasmorrhagia (P) as a particular type of vascular nephropathy. The degree of pathology was scored as follows: (0) no apparent signs of pathology; (1) mild (insignificant or sporadic disturbances); (2) moderate (focal disturbances in less than half of the total section area), and (3) severe (diffuse disturbances in more than half of the section area. Table 1 shows data on the amount of material analyzed.

Analysis for correlations between heavy metal concentrations and nephropathy was performed in two variants. In the first, the animals were divided into "healthy" and "diseased" groups comprising individuals with at most slight nephropathy or without it (grades 0 and 1, $n = 82$) and with moderate or severe nephropathy (grades 2 and 3, $n = 24$) . In the second variant, they were divided into "clean" ($n = 72$) and "contaminated" groups ($n = 27$) by the criterion of Cd accumulation in the kidneys. The threshold was taken at a Cd concentration of 4.0 mg/kg wet weight, which is considered critical for causing nephropathy in small mammals (Leffler and Nyholm, 1996).

Statistical data processing was performed with software packages Statistica v. 6.0 and AtteStat (version of February 24, 2013). The nonparametric Kruskal–Wallis test was used to compare the levels of metal accumulation, and the nonparametric Spearman rank correlation coefficient, to reveal correlations between different types of nephropathies. The dependence of nephropathy on the reproductive-age status of animals and the level of industrial pollution was evaluated by contingency tables with Pearson's χ^2 test. The sparse tables (with frequencies of no more than 5 in some cells) were tested for homogeneity by Simonov–Tsai statistics, with the results being used to determine the validity of approximation by χ^2. In case of problems with this approximation, the Freeman–Halton extension of Fisher's exact test was applied.

RESULTS

Heavy metal concentrations in the kidneys differed between the zones of the pollution gradient, with Cu being an exception ($H(2, 223) = 4.17$, $p = 0.124$). As the distance from the pollution source decreased, the intensification of accumulation in the kidneys was observed for Cd ($H(2, 597) = 216.99$, $p < 0.001$), Zn ($H(2, 221) = 19.53$, $p < 0.001$), and Pb ($H(2, 108) = 19.3$, $p < 0.001$). The levels of pollution in sites within the background and buffer zones were also uneven, reaching a peak in sites Bg-3 and B-2 located in the vicinity of the MUCS. Differences between the sites are illustrated in Fig. 1 using the example of pollution with Cd.

The reproductive-age status of the animals proved to have an effect on the accumulation of Zn ($H(2, 182) = 28.59$, $p < 0.001$) and Cd ($H(2, 460) = 50.02$, $p < 0.001$). The lowest concentrations of these metals in the kidneys were recorded in immature young of the year, and the highest concentrations, in overwintered animals. No such differences were revealed for Cu ($H(2, 184) = 2.57$, $p = 0.277$) and Pb ($H(2, 87) = 3.07$, $p = 0.216$). The concentrations of Cd and Pb in the kidneys of animals from the same reproductive-age group increased along the pollution gradient, reaching the highest values in the immediate proximity to the pollution source (Table 2).

Variation in absolute and relative kidney weight. Both these parameters were found to increase with age and change in animal's reproductive status (maturation and involvement in reproduction): $H(2, n = 419) = 216.09$, $p < 0.001$ and $H(2, n = 412) = 26.12$, $p < 0.001$, respectively. The factor "pollution zone" had no significant effect on these parameters: $H(2, n = 419) = 3.43$, $p = 0.180$; $H(2, n = 412) = 4.10$, $p = 0.129$.

Pathomorphological changes revealed in the kidneys were highly diverse. Glomerular disturbances included cell proliferation, destruction of the glomeruli, or their compaction and compression. The proximal and distal kidney tubules showed epithelial dystrophy, necrosis, and desquamation. Dead epithelial cells and anucleate amorphous structures regularly occurred in tubule lumina, often resulting in their occlusion. Disturbances of major vessels and microvasculature included blood overfilling, blood congestion, vascular thrombosis with the release of free hemoglobin, and plasmorrhagia (plasma infiltration into the vascular wall and then into the surrounding tissues). Since plasmorrhagia affects different structural components of the kidney, it was considered separately from other vascular disturbances. In single instances, foci of inflammation in the kidney medulla and cases of nephrolithiasis were revealed.

Glomerular and tubular disturbances were recorded in all animals examined; microcirculatory disturbances, in 73%; and plasmorrhagia, in 32%. Each type of nephropathy varied in severity (Fig. 2). Glomerular nephropathies in the majority of animals

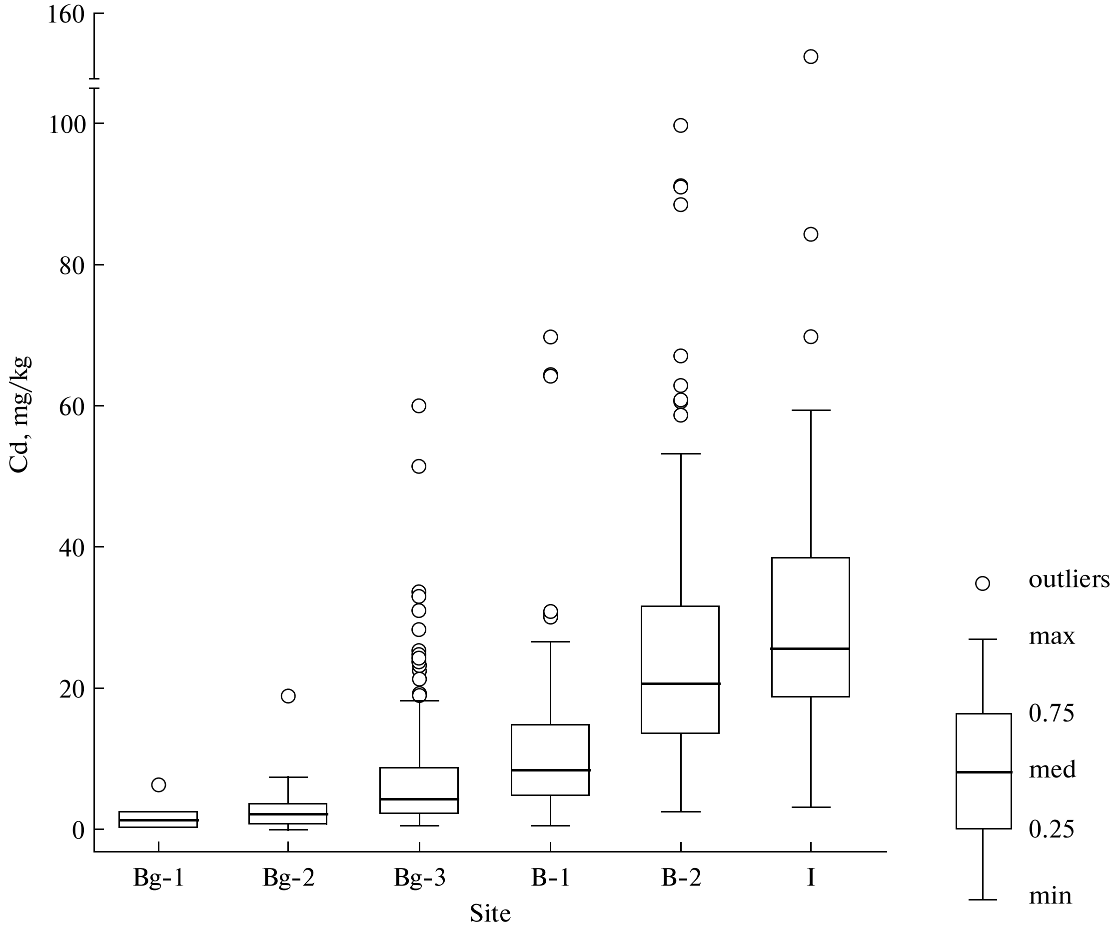

Fig. 1. Concentrations of Cd (mg/kg dry weight) in the kidneys of bank voles from different sites along an industrial pollution gradient.

The median (med) with upper (0.75) and lower (025) quartiles, minimum (min) and maximum (max) values, and outliers are shown. Pollution zones: (Bg) background, (B) buffer, (I) impact (here and in Fig. 2).

were mild (64%) or, less frequently, moderate (31%). Conversely, tubular nephropathies were more often of moderate severity (64%). Mild and moderate vascular nephropathies were recorded in 30 and 39% of animals; plasmorrhagia, in 13 and 15% of animals, respectively. The proportion of animals with severe nephropathies of any type was about 4–6%. All types of nephropathies positively correlated with each other, with the strongest correlation expectedly observed between vascular nephropathies and plasmorrhagia ($r = 0.65$, $p < 0.001$). It should be emphasized that in all cases of pathomorphological changes, whether occurring singly or in complex, portions of normal (functional) tissue were retained in the kidneys.

The dependence on the reproductive-age status of animals was revealed for almost all types of nephropathies: glomerular (χ^2 (6) = 6.65, p = 0.04), tubular (χ^2(6) = 12.14, p = 0.004), and vascular (χ^2 (6) = 16.37, p = 0.0001); but plasmorrhagia was an exception (χ^2 (6) = 26.33, p = 0.367). The frequency and severity of these disturbances were significantly lower in immature young of the year than in mature young of the year and overwintered individuals.

The level of industrial pollution and nephropathy. The level (zone) of pollution was found to have no effect on the frequency and severity of pathological changes in the glomeruli (χ^2 (6) = 2.94, p = 0.823) and tubuli (χ^2 (6) = 3.14, p = 0.797) and of plasmorrhagia (χ^2 (6) = 8.95, p = 0.243). However, vascular disorders (χ^2 (6) = 20.8, p = 0.002) proved to be more strongly manifested in animals from the background zone than in those from the buffer (χ^2 (1) = 13.39, p = 0.004) or impact zone (χ^2 (1) = 14.35, p = 0.008). It is noteworthy that the frequency and severity of pathology in the “cleanest” background site Bg-1 were higher than not only in background site Bg-3 (for vascular disorders: H (1, 71) = 14.25, $p < 0.001$), but also in impact plot 1 (for the same nephropathies: H (1, 27) = 10.04, p = 0.002).

At the individual level, none of the heavy metals accumulated in the kidneys had an effect on the frequency of nephropathies. No differences were

Table 2. Concentrations of Cu, Zn, Cd, and Pb (mg/kg dry weight) in the kidneys of bank voles from zones with different levels of industrial pollution

Reproductive-age group	Zone (site) of pollution gradient		
	background (Bg-3)	buffer (B-2)	impact (I)
	Cu		
im	12.2 (3.7) [51] 4.3–23.0	16.3 (2.5) [16] 12.5–21.6	11.48 (2.3) [2] 9.9–13.1
m	12.8 (3.8) [27] 3.8–20.3	17.1 (7.2) [12] 3.1–31.6	15.0 (5.1) [14] 6.8–27.0
ow	12.8 (4.4) [49] 1.7–26.7	13.8 (2.3) [6] 11.3–17.2	11.1 [1]
	Zn		
im	213.5 (177.2) [51] 48.0–685.7	292.7 (221.7) [16] 45.1–414.3	86.8 (3.6) [2] 83.2–90.4
m	197.2 (140.1) [27] 48.4–657.7	304.9 (174.3) [12] 123.0–503.0	339.8 (174.9) [14] 70.4–622.8
ow	103.6 (53.6) [48] 69.0–326.7	134.5 (67.9) [6] 70.5–230.2	148.8 [1]
	Cd		
im	3.1 (0.2) [137] 0.1–10.8	18.8 (11.5) [85] 2.4–60.4	25.4 (9.4) [29] 7.8–43.4
m	7.1 (3.8) [35] 1.1–14.3	32.6 (23.4) [15] 3.8–99.5	26.7 (17.9) [14] 3.2–59.3
ow	12.5 (10.3) [86] 0.3–59.9	36.2 (21.12) [43] 7.4–90.7	54.1 (41.5) [10] 15.2–81.3
	Pb		
im	6.4 (5.2) [13] 0.1–17.9	6.3 (3.8) [10] 3.2–13.5	30.2 (19.0) [2] 16.8–43.6
m	5.0 (4.3) [16] 0.1–19.0	13.1 (9.3) [11] 3.1–38.2	29.2 (46.3) [10] 3.0–155.7
ow	5.8 (7.0) [18] 0.1–28.4	4.9 [1]	153.0 [1]

Figures above the line are mean values with standard deviations (in parentheses) and the numbers of samples (in square brackets); figures below the line are the minimum and maximum values.

revealed in the content of Cd between "healthy" and "diseased" animals and in the severity of pathology between "clean" and "contaminated" animals: in the first variant, $H(1, 106) = 0.62, p = 0.432$; in the second variant, the values of Kruskal–Wallis test varied from 0.03 ($p = 0.856$, for T) to 3.23 ($p = 0.072$, for G).

DISCUSSION

The recorded concentrations of heavy metals in the kidneys of bank voles generally agree with published data on this species and other small mammals living in areas with different pollution levels (Damek-Poprawa and Sawicka-Kapusta, 2003; Pereira et al., 2006; etc.). Some authors have noted increased concentrations of these elements in the kidneys of breeding animals characterized by a higher metabolic level, compared to immature young of the year (Lodenius et al., 2002; Beernaert et al., 2007; Sánchez-Chardi et al., 2007; Fritch et al., 2010).

It is known that kidney weight and size reflect the level of metabolism: under conditions where its intensification is necessary, an increase in the kidney index is usually observed (Shvarts et al., 1968). Therefore, the increase in kidney weight and index in breeding animals is quite expectable. In the study region, pollu-

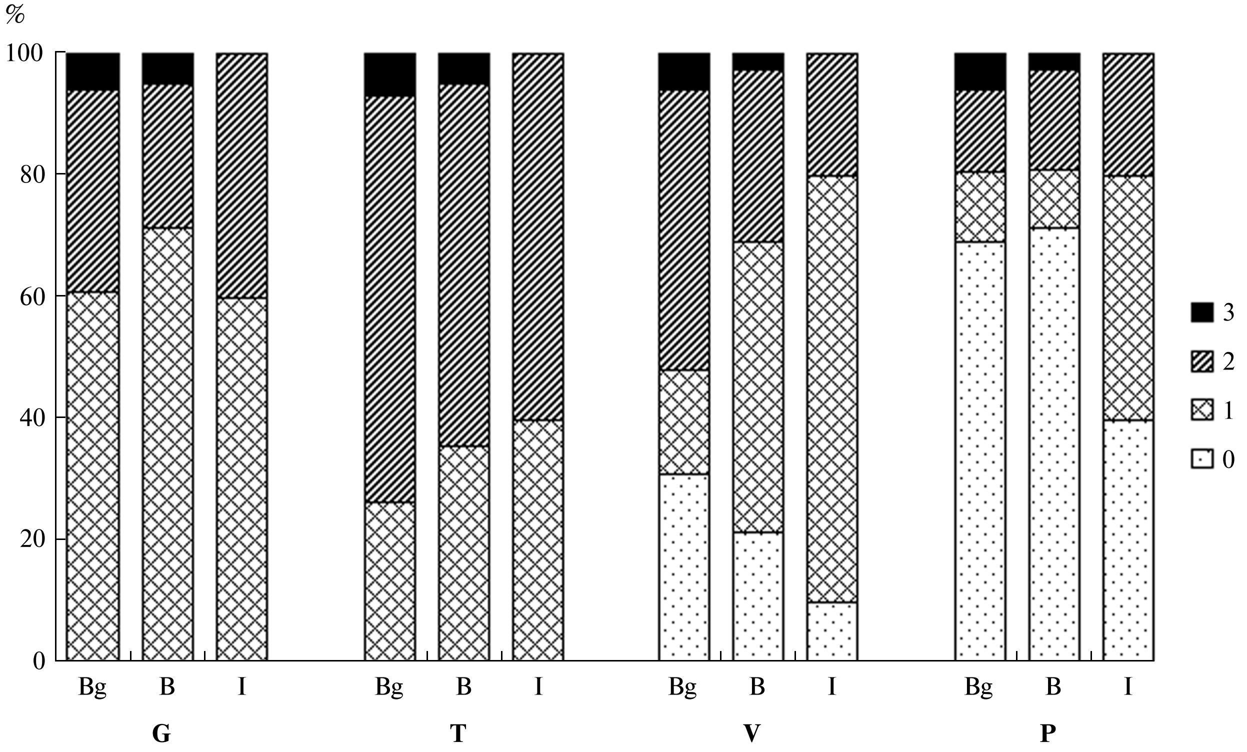

Fig. 2. Proportions (%) of individuals with different types of nephropathies among bank voles from different zones of pollution gradient. Type of pathology: (G) glomerular, (T) tubular, (V) vascular, (P) plasmorrhagia. Degree of pathology: (0) no pathology, (1) mild, (2) moderate, (3) severe.

tion proved to have no effect on either parameter. A probable explanation to this fact is that the influence of the pessimal conditions of technogenically transformed areas on animal metabolism and other physiological characteristics is not as unambiguous as that of conditions at high latitudes and elevations, where the material was obtained that provided a basis for the method of morphophysiological indicators (Shvarts et al., 1968). Other authors also have not revealed any differences in the weight of internal organs (including the kidneys) between animals from the background and impact areas (Pereira et al., 2006).

Analysis of pathomorphological changes in the kidneys was a complicated task in terms of their identification, classification, and quantitative evaluation. Several classifications used in medical practice are based on different criteria (etiology, common pathogenesis, ecological features, etc.). We relied on topographic anatomical criteria, which among others are used in the *International Statistical Classification of Diseases and Related Health Problems* (2010). Among urogenital diseases, this classification distinguishes glomerular and tubulointerstitial nephropathies. It should be noted that we analyzed only a few of many morphological symptoms of renal pathology that were insufficient for its accurate clinical diagnosis. However, any such disturbance as morphological evidence of a pathological process may provide an idea about the character and, in some cases, even the causes of this process (Sheiman, 1999; Fogo et al., 2006).

In our opinion, it is important to discriminate plasmorrhagia from other vascular disorders as a rare but most severe pathology. It is considered that the blood system is one of the first to respond to the influence of heavy metals (Tarakhtii and Mukhacheva, 2011), but we have found that the frequency of vascular disorders as well as of other nephropathies remained unchanged in animals from areas with increased pollution levels.

Identification of different types of nephropathies and evaluation of their severity in grades is an attempt to roughly formalize and generalize very complex combinations of disturbances recorded in the renal tissues of small mammals, which is nevertheless necessary for revealing their possible correlation with the contents of heavy metals. In the majority of ecotoxicological studies, morphological changes in the depot organs are evaluated qualitatively, with their quantitative analysis being reduced to estimation of the proportion of individuals with corresponding disturbances. Data on the degree of their manifestation (severity) are provided very rarely (Sánchez-Chardi et al., 2008), and we are unaware of any studies on the morphometry of pathologically altered structures.

Glomerular and tubulointerstitial nephropathies affect the filtration function of the kidneys and have various etiology (Harrison, 1995). Since the spectrum of possible responses of renal tissues to the damaging effects of various factors is limited, it is necessary to differentiate the toxic impact and associated response from other causes of nephropathy. As repeatedly shown in experiments on small mammals, the frequency of renal pathology correlated with the degree of toxic exposure (Chmielnicka et al., 1989, 2002), with tubulopathies and glomerular nephropathies developing at the early and late stages of intoxication, respectively (Franchini and Mutti, 1990; Gouer, 1989). The series of studies on the F_1 generation of bank voles from a natural population (Włostowski et al., 2004; Salińska et al., 2012) may be regarded as intermediate between laboratory experiments and field observations. Their authors have revealed a correlation between the level of heavy metal accumulation and the proportion of animals with nephropathies and demonstrated the significance of photoperiod and population density for the manifestation of nephrotoxic effects.

Studies demonstrating the relationship between the frequency of nephropathy and the level of heavy metal (mainly Cd) accumulation in animals from natural populations are of special interest to us. Thus, several authors revealed the types of nephropathies similar to those described above in small samples (up to 22 ind.) of small mammals aged 1–9 months from the nearest vicinities of steel works and zinc smelters, but not in samples from background areas. This was interpreted as evidence for the nephrotoxic effect of pollution, although the concentrations of heavy metals in the affected kidneys varied in a wide range: in case of Cd, from 1.2 to 33.0 mg/g dry weight (Damek-Poprawa and Sawicka-Kapusta, 2003, 2004). On the other hand, it has been noted that the absence of correlation between the level of Cd accumulation and the frequency of nephropathies, which is due to high individual variation, imposes limitations on the use of Cd as a biomarker of environmental pollution (Lindén et al., 2003).

Toxic effects do not always manifest themselves in studies based on the paradigm of the determinant role of toxicants in the development of nephropathies. Thus, analysis of black rats (4 ind.) and Algerian mice (4 ind.) from an abandoned copper mine area in southeastern Portugal has revealed no nephropathies in rats (unlike in mice), either in the impact or in the background site (Pereira et al., 2006). The authors attribute this to species-specific differences in the diet, in particular, a higher degree of omnivory in rats, compared to mice. It is difficult to explain the occurrence of nephropathies in yellow-necked and Algerian mice with Cd concentrations in the kidneys not exceeding the background level (1.2 mg/kg dry weight) (Damek-Poprawa and Sawicka-Kapusta, 2003; Pereira et al., 2006) or the absence of nephropathies but the occurrence of liver pathologies in greater white-toothed shrews from polluted regions of southwestern Spain (Sánchez-Chardi et al., 2008). Supposedly, this may be due to the resistance of the kidney to pollutants and its capacity for their effective detoxification. In voles from a mining region in Alaska, nephropathy was revealed in only one out of ten animals (Brumbaugh et al., 2009), and the authors concluded that kidneys are unsuitable for bioindication purposes because of high regeneration capacity and functional reserves of this paired organ.

In studies on the renal tissue response to pollution, many authors have also analyzed other parameters (hematological, genotoxic, biochemical, ultrastructural, etc.). In some cases, animals from zones with different pollution levels proved to differ significantly in these parameters, but no histopathology was revealed in their organs (Leffler and Nyholm, 1996; Damek-Poprawa and Sawicka-Kapusta, 2003). It was proposed to resolve such contradictions by selecting habitats more for comparison in zones with different pollution levels, evaluating a complex of parameters (morphological, physiological, biochemical, etc.) in relation to a complex of pollutants, and analyzing species specificity of responses to pollution in small mammals. It is also apparent that such studies should be performed with large samples of animals.

CONCLUSIONS

The kidneys of bank voles from industrially polluted areas accumulate considerable amounts of heavy metals (primarily Cd), with their concentrations increasing with age and/or sexual maturation. The kidney weight, index, and the frequency and severity of the majority of observed nephropathies also increase upon change in the reproductive-age status of animals. However, the level of toxic load has no effect on the absolute or relative kidney weight; therefore, these parameters cannot be used as indicators of industrial pollution. The frequency and severity of nephropathies also show no dependence on the degree of pollution and individual toxic load. The only exception concerns vascular disorders: unexpectedly, their incidence proved to be higher in the background than in the impact zone.

On the whole, these results contradict the prevailing opinion that the frequency of histopathologies is strongly correlated with the level of pollution. To a certain extent, they reflect difficulties in analyzing toxic effects at the organismal and suborganismal levels that are accounted for by a high level of individual variation and adaptive-compensatory reactions providing for the maintenance of body homeostasis under changing environmental conditions. Therefore, the causes of nephropathies should be sought among other factors, not related to pollution, such as infections, parasite invasions, or metabolic disturbances.

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