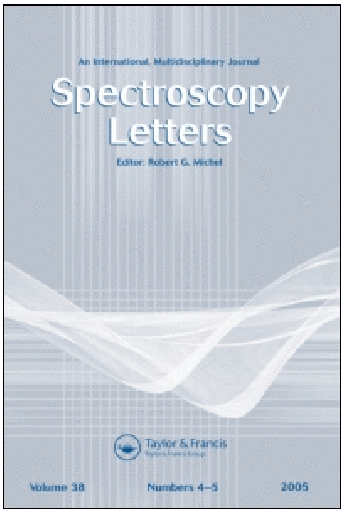

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Distribution of risk elements in the organism of sheep after industrial intoxication with zinc

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Summary

Diagnostics of experimental zinc intoxication by industrial emission from the zinc and copper factory on the basis of accumulation and distribution of Zn, Cu, Fe, Mo, Se, As, Cd and Pb in the liver, kidneys, spleen, musculature, uterus, ovaries, chorioidea of eye and bones in seven experimental and five control sheep is described. A daily intake of Zn from industrial emission was 6158.07 mg/an experimental animal. The first animals died of zinc intoxication on d 42 and the last one on d 58 of the experiment. The highest concentration of zinc in experimental animals died of zinc intoxication was in the liver dry matter (1167.3 ± 314.1 $mg.kg^{-1}$) and in the kidneys (1049.5 ± 283.7 $mg.kg^{-}$). Significantly higher Zn content compared with the control sheep was confirmed in the experimental ones in the liver, kidneys, ovaries and eye chorioidea ($p < 0.01$). The liver, kidneys, uterus were the organs with the highest Cu accumulation. The highest Fe accumulation was found in the spleen, kidneys and liver. Distribution of Mo and Se in the organs analyzed in experimental and control animals was similar. The industrial emission intake from the copper and zinc factory manifested in statistically higher accumulation of As, Cd and Pb in the organism of experimental sheep than in control ones ($p < 0.05$;

$p < 0.01$). Results of accumulation and distributionn of Zn and other toxic elements involved in the substrate tested in the organism of the experimental animals died of Zn intoxication in comparison with the controls have confirmed a significance of their analysis in sheep for estimation of the effect of industrial emission from the zinc and copper factory.

Laboratory diagnostics of zinc intoxication is based upon the knowledge on the biological importance of Zn and its mechanism of toxicicty (Dreosti, 1982; Thompson et al., 1984). Observation of enzymatic systems on the cellular and subcellular level, in which Zn is their component and influences them, is used in the indirect diagnostics of Zn intoxication (O'Dell, 1984; Vallee et al., 1984). Assessment of haemolytical anaemia and leucocytosis in a cumulative, but especially in toxic phase of Zn intoxication is based upon determination of the parameters of the haematological profile (Robinette, 1990). Impairment of functional capability of the liver, kidenys and pancreas gives opportunity, in the course of Zn intoxication, to observe the extent of impairment of the lipid, saccharide and protein metabolism (Llobet et al., 1988; Smith et al., 1984; Allen et al., 1985). Quantification of the parameters of the immune and reproduction profile determines at the chronic intoxication the effect of Zn on defensive and reproduction functions (Bíreš et al., 1990; Kudláč et al., 1990). The tests for mutagenicity, carcinogenicity and teratogenicity are involved into the observation of the toxic effect of Zn on the animal organism (Leonard et al., 1986). An important part of the laboratory diagnostics of zinc intoxication is patho-anatomical and histological evaluation of changes in the liver, kidneys, spleen or other organs (Breitschwerdt et al., 1986). The analysis of Zn in feeds and biological material of animals is inevitable to make an objective diagnosis of zinc intoxication (Leita et al., 1991; Wentink et al., 1985).

Selection of laboratory diagnostic methods depends on the course of intoxication, way and duration of zinc salt intake, animal species, their age as well as the way of breeding. In our work the analysis of feeds, tested substrate and organs for the contents of Zn, Cu, Fe, Mo, Se, As, Cd and Pb was used to make the diagnosis of experimental intoxication with Zn from industrial emission of the zinc and copper factory in sheep.

Material and Methods

Observations were performed under experimental conditions on twelve 18-24 months old Improved Vallachian ewes in the second month of pregnancy. Seven ewes were given the industrial emission from the Cu and Zn factory daily after the morning feeding by an oesophageal tube. Samples of the tested emission were obtained by dedusting of the electrostatic precipitators from the factory chimney. The amount of the emission intaken per an experimental ewe represented according to the initial live weight (40.254 ± 3.55 kg) 31.99 g. A daily intake of Cu, Fe, Zn, Mo, Se, As, Cd and Pb from emission per an experimental animal is given in table 1. Five ewes, with their initial live weight of 40.3 ± 4.38 kg, were included into the control group.

Feeding and treatment of both the experimental and control ewes was the same. The feed ration consisted of meadow hay (1.5 kg/head/day), feed mixture BAK (0.20 kg/head/day) and drinking water (5 l/head/day). The intake of observed elements from feeds in the experimental and control group is listed in table 2. Table 3 shows the intake of Cu, Fe, Zn, Mo, Se, As, Cd and Pb from both the emission and feed in experimental animals.

Application of emission lasted in experimental animals until their death under the symptoms of zinc intoxiation (Bíreš et al., 1996). The mean survival time in experimental animals was 46.28 ± 0.3 days. The first animal died on d 42 and the last one on d 58 of the experiment. The control ewes were killed on d 58 of the experiment. The experimental animals died of zinc intoxication and the control ones, killed at the end of the experiment, were examined *post mortem*. The samples weighing 10-20 g for analysis of risk elements were taken from the right liver lobe, cortical part of the right kideny, spleen, thigh musculature (*m. bicipitis femoris*), uterus (*Corpus uteri*), left ovary, eye chorioidea and carpal bone of the left thoracal limb (*os metacarpale*).

Concetration of Zn, Cu, Fe, Mo, Se, As, Cd and Pb in the examined organs, tested emission and_feeds was determined by the method of the atomic absorption spectrophotometry using the Perkin Elmer, type 1100 and 4100 ZL. Mineralization of emission, examined feeds and organs was carried out in the mixture of HNO_3 and H_2O_2 in the microwave system (Milestone mls 1200). Results of

Table 1. Elements intake in mg from the emission per head and day (experimental group)

Body weight (kg)	Cu	Fe	Zn	Mo	Se	As	Cd	Pb
x ±SD 0.25±3.55	402.02	95.97	6158.07	1.436	2.975	15.38	0.598	22.14

Table 2. Elements intake in mg from the food per head and day experimental group and control group

Daily intake	Cu	Fe	Zn	Mo	Se	As	Cd	Pb
Meadow hay (1.50 kg)	12.66	275.1	79.35	0.601	1.035	2.934	0.005	0.08
Feed mixture (0.20 kg)	18.06	17.4	12.84	0.1	0.45	0.18	0.046	0.367
Drinking water (5 l)	2.43	0.954	1.22	0.14	0.93	t r a c e		
Total	33.15	293.45	93.41	0.841	2.41	3.11	0.051	0.447

Table 3. Elements intake in mg from the emission and food per experimental animal and day

Source intake	Cu	Fe	Zn	Mo	Se	As	Cd	Pb
Emission	402.02	95.97	6158.07	1.436	2.975	15.38	0.598	22.14
Fodder	33.15	293.45	93.41	0.841	2.41	3.14	0.051	0.447
Total	435.17	389.42	6251.48	2.277	5.385	18.52	0.649	22.587

analyses of risk elements in the dry matter of the organs investigated are expressed by the mean values (x) with a standard deviation (±SD). Statistical comparison of the analysis results in the examined organs between experimental and control groups was performed by the Student t-test.

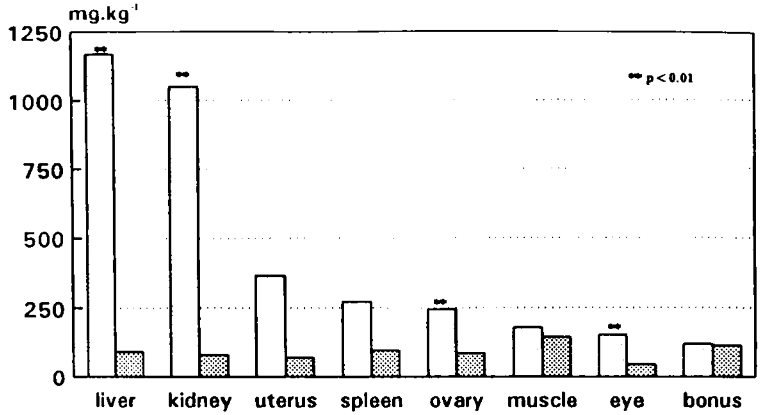
Results

Concentration of Zn in the liver of sheep died of zinc intoxication was 1167.3 ± 314.1 $mg.kg^{-1}$ (Fig. 1). Kidneys appeared to be also the organs with a high zinc cumulation (1049.5 ± 289.7 $mg.kg^{-1}$). The high amount of Zn was also cumulated in the uterus, then in spleen and ovary (367.6 ± 303.9 $mg.kg^{-1}$, 274.0 ± 179.6 $mg.kg^{-1}$ and 245.6 ± 73.5 $mg.kg^{-1}$, respectively). The lowest amount of Zn was found in the eye chorioidea and bone. Significantly higher Zn content compared to the control ewes was confirmed in experimental animals in the liver, kidneys, ovary and eye retina ($p < 0.01$).

The highest levels of Cu were recorded in the liver of sheep died of Zn intoxication (445.6± 238.1 $mg.kg^{-1}$), kidneys (124.7 ± 55.5 $mg.kg^{-1}$) and ovary (124.1 ± 77.6 $mg.kg^{-1}$) (Fig. 2). The uterus and spleen belonged among the organs with the higher Cu cumulation. In the musculature and eye chorioidea, in comparison with the former organs, there were half-values of Cu. The lowest Cu concentration was in experimental sheep in the bone tissue (3.81 ± 1.14 $mg.kg^{-1}$). Statistically significant differences in the Cu levels between experimental and control animals were confirmed in the kidneys ($p < 0.01$) and ovary ($p < 0.05$).

The highest concentration of Fe in experimental sheep was found in the spleen (3784.3 ± 1386.9 $mg.kg^{-1}$; Fig. 3), then in kidneys, liver and ovaries. The Fe content in musculature and uterus was balanced (295.6 ± 59.4 and 290.5 ± 147.4 $mg.kg^{-1}$, respectiely). The lowest level of Fe in experimental animals was found in the bone tissue. Despite that the levels of Fe in the spleen, kidneys, liver and ovary were of half-values in control sheep compared to experimental ones, distribution of Fe in the organs examined, however, corresponded to the experimental group. A statistical difference in cumulation of Fe between both groups was observed in the ovary ($p < 0.05$).

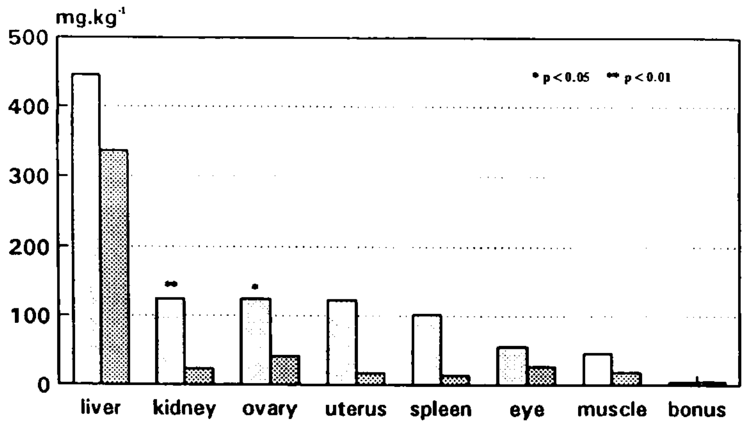
The ovaries, kidneys, liver were the organs with the highest Mo cumulation in experimental sheep; in control ones it was the ovary, liver and bone (Fig. 4). In both groups of animals the lowest values of Mo were found in the uterus and eye chorioidea. Differences in the Mo levels in the organs examined between the experimental and control group were not statistically dependent on the fed industrial emission.



	liver	kidney	uterus	spleen	ovary	muscle	eye	bonus
E (x)	1167.3	1049.5	367.6	274	245.6	180	152.4	119.21
E (SD)	314.1	283.7	303.9	179.6	73.5	37.7	28.3	14.52
C (x)	92.8	81.4	70.54	97.6	87.5	144.8	44.4	113.07
C (SD)	34.8	36.8	43.46	21.6	43.4	38.7	12.7	4.99

E - experiment C - control

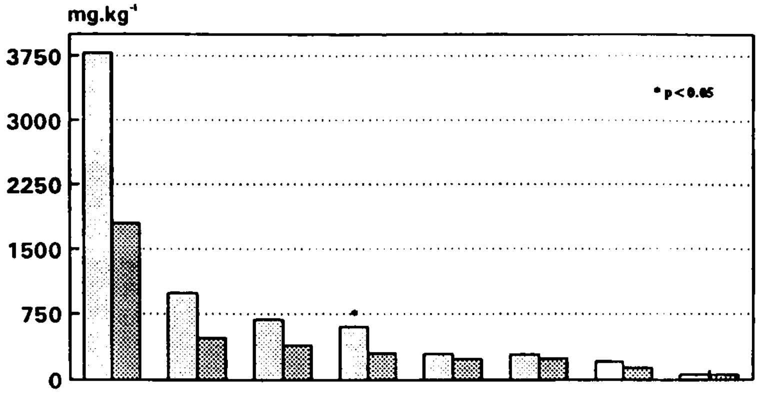
Fig.1. Zinc distribution in the target organs of ewes



	liver	kidney	ovary	uterus	spleen	eye	muscle	bonus
E (x)	445.6	124.7	124.1	122.5	101.8	55.7	45.8	3.812
E (SD)	238.1	55.5	77.6	122.4	150.6	38.8	29.9	1.144
C (x)	336	22.8	41.2	17.05	13.5	26.58	17.9	4.94
C (SD)	102.3	7.61	15.9	10.86	9.27	32.91	4.9	0.3

E - experiment C - control

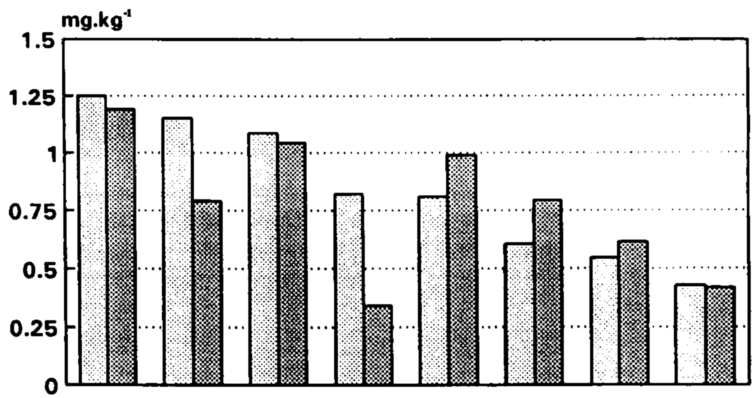
Fig.2. Copper distribution in the target organs of ewes



		spleen	kidney	liver	ovary	muscle	uterus	eye	bonus
E (x)	▭	3784.3	992	685.9	601.6	295.6	290.5	209.7	55.57
E (SD)		1386.9	950.2	303.7	249.3	59.46	147.4	51.9	24.1
C (x)	▩	1799	478.7	393.2	304.9	235.3	245.3	141	60.75
C (SD)		361.6	237.2	102.5	133.4	78.2	97.7	54.3	22.82

E - experiment **C - control**

Fig.3. Iron distribution in the target organs of ewes



		ovary	kidney	liver	muscle	bonus	spleen	uterus	eye
E (x)	▭	1.25	1.15	1.087	0.821	0.809	0.606	0.546	0.428
E (SD)		0.49	0.88	0.83	0.506	0.195	0.263	0.204	0.13
C (x)	▩	1.19	0.791	1.043	0.34	0.992	0.794	0.615	0.419
C (SD)		0.5	0.27	0.202	0.12	0.12	0.457	0.505	0.124

E - experiment **C - control**

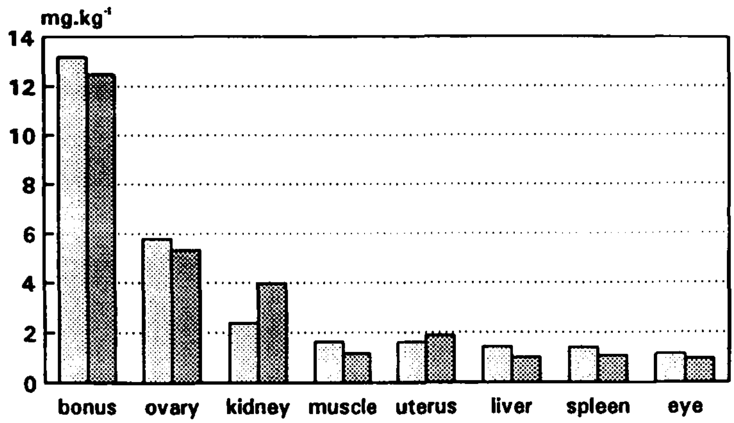
Fig.4. Molybdenum distribution in the target organs of ewes

Distribution of Se in the organs analyzed was the same in both the experimental and control sheep (Fig. 5). The highest concentrations of Se in both the experimental and control ewes were confirmed in their bones (13.17 ± 0.799 $mg.kg^{-1}$ and 12.47 ± 0.365 $mg.kg^{-1}$, respectively). The ovaries were the second organ with a high Se cumulation in both the experimental and control groups (5.78 ± 1.46 $mg.kg^{-1}$ and 5.32 ± 0.73 $mg.kg^{-1}$, respectively), then kidneys, musculature, uterus and liver followed. The lowest Se level was in both groups in the eye chorioidea. Based upon the evaluation of a statistical significance of Se content in the organs of the groups compared, there was no effect of fed emission on its cumulation in the organism of experimental animals.

Concentration of As was significantly higher ($p < 0.01$; $p < 0.05$) in all the organs analyzed in experimental animals in comparison with control ones (Fig. 6). Intake of the tested substrate manifested in experimental sheep in the highest cumulation of As in the ovaries and bone tissue (6.78 ± 1.31 $mg.kg^{-1}$ and 2.83 ± 0.64 $mg.kg^{-1}$, respectively). About the same distribution of As in the experimental group was observed in the uterus, spleen and kidneys. The lowest As levels in this group of animals were in the liver, eye chorioidea and musculature. In the control group the highest amount of As was in the ovary. Differences in the concetration of As in control sheep were minimal.

In experimental sheep the highest Cd content was found in the ovary and kidneys (1.60 ± 0.36 $mg.kg^{-1}$ and 1.17 ± 052 $mg.kg^{-1}$, respectively; Fig. 7). Concentration of Cd in the liver reached the level of 0.95 $mg.kg^{-1}$. In the other organs of experimental animals in comparison with the levels presented, there were half-values of Cd. The lowest Cd content was recorded in the eye chorioidea and musculature of experimental animals. Statistically higher concentration of Cd was in experimental sheep than in control ones in the ovaries, kidneys, liver and bone, and lower in musculature ($p < 0.01$; $p < 0.05$).

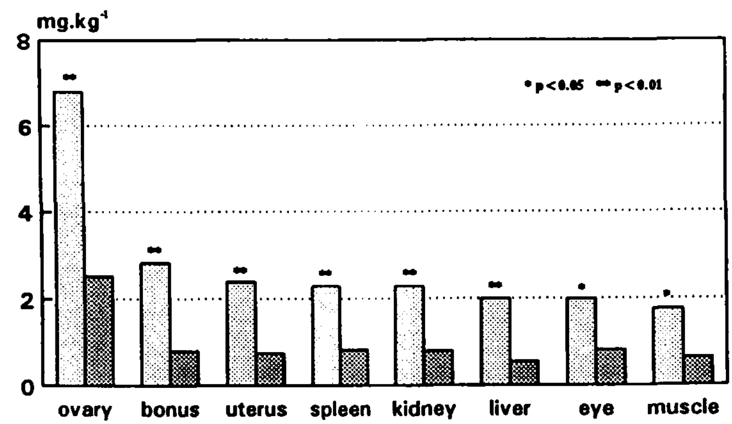
Pb cumulated most in the kidneys of experimental sheep (9.58 ± 1.36 $mg.kg^{-1}$) and in the ovaries of control ones (1.02 ± 0.50 $mg.kg^{-1}$; Fig. 8). Then, the liver, ovaries and spleen of experimental animals were rich in Pb. As well, the lowest amount of Pb was recorded in the eye chorioidea and bone of experimental



	bonus	ovary	kidney	muscle	uterus	liver	spleen	eye
E (x)	13.17	5.78	2.39	1.62	1.61	1.42	1.38	1.13
E (SD)	0.799	1.46	1.29	0.82	0.81	0.75	0.81	0.64
C (x)	12.47	5.321	3.97	1.16	1.88	0.993	1.07	0.94
C (SD)	0.36	0.73	1.54	0.59	1.83	0.894	0.42	0.274

E - experiment **C - control**

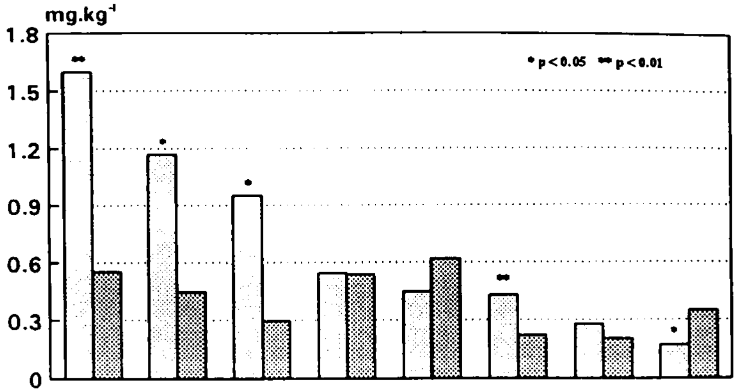
Fig.5. Selenium distribution
in the target organs of ewes



	ovary	bonus	uterus	spleen	kidney	liver	eye	muscle
E (x)	6.78	2.832	2.39	2.29	2.29	2	1.99	1.76
E (SD)	1.31	0.645	0.74	0.67	0.56	0.6	0.78	0.77
C (x)	2.52	0.806	0.758	0.83	0.809	0.557	0.839	0.652
C (SD)	1.25	0.092	0.742	0.527	0.51	0.377	0.446	0.639

E - experiment **C - control**

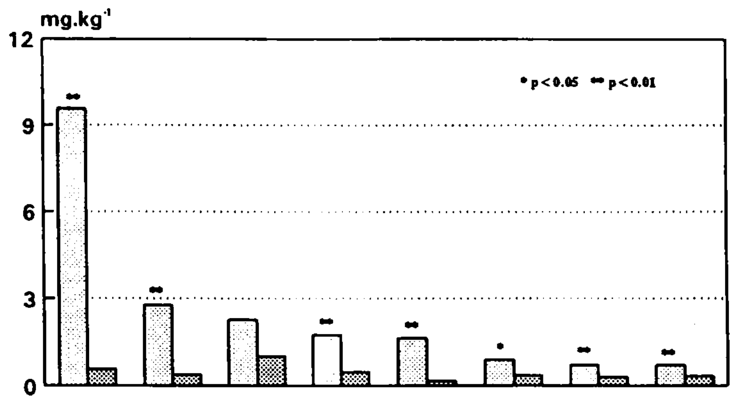
Fig.6. Arsenic distribution
in the target organs of ewes



		ovary	kidney	liver	spleen	uterus	bonus	eye	muscle
E (x)	☐	1.6	1.17	0.951	0.543	0.448	0.429	0.276	0.169
E (SD)		0.36	0.52	0.569	0.623	0.188	0.052	0.077	0.096
C (x)	▩	0.553	0.448	0.296	0.536	0.618	0.219	0.204	0.349
C (SD)		0.265	0.261	0.031	0.371	0.366	0.001	0.09	0.172

E - experiment **C - control**

Fig.7. Cadmium distribution
in the target organs of ewes



		kidney	liver	ovary	spleen	uterus	muscle	eye	bonus
E (x)	☐	9.58	2.76	2.26	1.75	1.64	0.892	0.714	0.707
E (SD)		1.36	1.06	1.39	0.72	0.82	0.424	0.179	0.113
C (x)	▩	0.574	0.369	1.02	0.476	0.15	0.358	0.292	0.327
C (SD)		0.247	0.267	0.5	0.331	0.114	0.294	0.11	0.172

E - experiment **C - control**

Fig.8. Lead distribution
in the target organs of ewes

sheep. Except for ovaries, in all the organs analyzed in experimental animals there was significantly higher cumulation of Pb than in control ones ($p < 0.01$, $p < 0.05$, respectively). In control animals the lowest Pb levels were in the eye chorioidea and uterus.

Discussion

The limiting organ for the metabolism of Zn is the liver (Underwood, 1977). Cumulation of Zn on hepatal metallothionein depends on its dietetical intake and presence of the other elements influencing resorption, intermediary metabolism and secretion of Zn (Lloyd et al., 1993; Pauwels et al., 1994). The Zn level in the liver of sheep died in the experiment has confirmed Zn intoxication. The Zn concentration was higher than that in sheep with Zn intoxication from other sources than industrial emission (Allen et al., 1986). The Zn content in kidneys corresponded to Zn cumulation in the liver of experimental animals, which was also higher than that found by Allen and Masters (1985) in sheep with a daily intake of 2000 to 3000 mg of Zn. In experimental animals in comparison with control ones a high dietetical intake of Zn from industrial emission manifested in the increased levels of Zn also in the other organs examined. From the view point of diagnostics of the effect of industrial emission from the copper and zinc factory, an importance of analysis of Zn in the uterus, spleen and ovaries has been confirmed in sheep died of intoxication. The lowest differences in Zn cumulation between experimental and control sheep were observed in the bone, eye chorioidea and musculature. It means that their examination at judging the Zn toxicity is of secondary significance.

Concentration of Cu in the liver and kidneys reflects best the dietetical intake and metabolic activity of Cu (Soli, 1980). In experimental sheep compared to control ones, a daily intake of Cu from emission at the amount of 10 $mg.kg^{-1}$ of live body weight most markedly manifested in Cu accumulation, especialy in the kidneys, spleen, uterus, ovaries and only then in liver. The presence of Zn and other risk elements in the industrial substrate, entering together with Cu the interreaction relationships on the level of resorption, intermadiary metabolism and secretion was the cause of changes in accumulation as well as in distribution of Cu in experimental animals (Rosa et al., 1986; Bíreš, 1989). Despite the presented, concentration of Cu in the liver and kidneys of sheep died of zinc intoxication approached the levels found by Hidiroglou et al. (1984), Jones et al. (1984) in sheep in the cumulative phase of Cu intoxication. Comparison of Cu levels between experimental and control sheep has not confirmed the diagnostic value of analysis of bones for the Cu content at observation of the effect of industrial emissions from the zinc and copper factory.

Distribution of Fe in the organs examined in experimental and control animals is characteristic for the metabolism of Fe (Underwood, 1977). A high content of Fe in the spleen and other organs observed in the sheep died of zinc intoxication in comparison with the control ones is explained by Fe intake from the industrial substrate, but especially by the mechanism of Zn toxicity (Robinette, 1990).

On the basis of insignificant differences in cumulation and distribution of Mo and Se between experimental and control animals, an insignificant effect of fed emission on the given elements may be judged. Of the elements present in the industrial substrate, the interaction between Cu:Se, Cu:Fe and Zn:Fe have been most studied, (Storey, Greger, 1987; Bíreš et al., 1991) which regarding the presence of other elements did not significantly manifest.

The intake of industrial emission from the copper and zinc factory resulted in a statistically significant higher cumulation of As, Cd and Pb in the organism of experimental sheep than that in control ones. Cumulation of As, Cd and Pb in the organs analysed in experimental animals corresponded to their content in the tested emission and it was in agreement with the knowledge about distribution of these elements in individual tissues (Leita et al., 1991; Massányi et al., 1995a). The highest content of As and Cd was found in the ovaries, Pb in kidneys, then in liver (Pb), kidneys (Cd) and bone tissue (As), which is connected with the mechanism of toxicity of these elements for biological systems (Underwood, 1977; Massányi et al., 1995b). Regarding the dominant representation of Zn in the emission used, the mutual interaction relations, especially between Zn:Cd and Zn:Pb, may be expected. Interinfluencing of Zn and Cd runs through the bond of methallothionein within the process of resorption, retention and metabolic activity (Kojima et al., 1991). The negative interaction between Zn and Pb is, above all, within the process of absorption (Elsenhans et al., 1978). Comparison of cumulation and distribution of As, Cd and Pb in the organs of experimental and control sheep revealed that in experimental animals the significant differences reflected the intake of these elements from industrial emission. Possibility for interaction relations with Zn, regarding the presence of the other toxic elements, appeared to be secondary.

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