Table. 1. Weight of intact and hypertrophic kidneys, liver, spleen, thymus and bone marrow (g) of rats after administration of cadmium and/or gamma irradiation (± S.E.M.).

Organ	Group	Days after treatment			
		1	7	14	21
Intact kidney	C	0.82 ± 0.05	0.89 ± 0.04	0.89 ± 0.04	0.73 ± 0.1
	Cd	0.73 ± 0.02	0.86 ± 0.03	0.65 ± 0.09^{xx}	0.76 ± 0.07
	Ir	0.8 ± 0.03	0.87 ± 0.02	0.89 ± 0.05*	0.98 ± 0.06^{xx*}
	Cd+Ir	0.82 ± 0.03	0.75 ± 0.03^{xxoo}	0.74 ± 0.06^{xxoo}	0.7 ± 0.08
Hypertrophic kidney	C	0.98 ± 0.05	0.97 ± 0.03	1.12 ± 0.02	1.11 ± 0.04
	Cd	0.75 ± 0.04^{xx}	0.99 ± 0.038	1.01 ± 0.035	1.09 ± 0.03
	Ir	0.93 ± 0.037*	1.06 ± 0.041^{x}	1.04 ± 0.016	1.14 ± 0.07
	Cd+Ir	0.98 ± 0.035**	0.89 ± 0.037^{o}	1.15 ± 0.031	0.96 ± 0.04^{x}
Liver	C	10.02 ± 0.67	10.37 ± 0.45	10.37 ± 0.45	12.3 ± 1.01
	Cd	11.13 ± 1.03	13.02 ± 0.63^{xx}	11.24 ± 0.92	15.4 ± 0.79^{x}
	Ir	10.14 ± 0.3	12.78 ± 0.99^{x}	11.44 ± 0.29	12.5 ± 0.46
	Cd+Ir	12.12 ± 0.61	12.9 ± 0.21^{xx}	11.26 ± 0.67	12.7 ± 0.45
Bone marrow	C	0.041 ± 0.004	0.05 ± 0.004	0.05 ± 0.004	0.052 ± 0.003
	Cd	0.033 ± 0.002	0.048 ± 0.003	0.06 ± 0.003	0.047 ± 0.004
	Ir	0.038 ± 0.003	0.03 ± 0.001^{xx}	0.063 ± 0.008	0.042 ± 0.005
	Cd+Ir	0.037 ± 0.003	0.046 ± 0.002	0.051 ± 0.003	0.049 ± 0.004
Spleen	C	0.97 ± 0.03	1.06 ± 0.032	1.06 ± 0.032	1.01 ± 0.05
	Cd	0.98 ± 0.03	0.75 ± 0.07^{x}	0.81 ± 0.04^{x}	1.22 ± 0.06
	Ir	0.49 ± 0.02^{xx**}	0.38 ± 0.03^{xx**}	0.61 ± 0.03^{xx*}	1.04 ± 0.02
	Cd+Ir	0.48 ± 0.01^{xx**}	0.45 ± 0.04^{xx**}	0.73 ± 0.07^{xx}	0.94 ± 0.03**
Thymus	C	0.36 ± 0.03	0.34 ± 0.07	0.34 ± 0.07	0.37 ± 0.03
	Cd	0.21 ± 0.01^{xx}	0.38 ± 0.03	0.4 ± 0.03	0.49 ± 0.07
	Ir	0.08 ± 0.004^{xx**}	0.26 ± 0.02*	0.24 ± 0.01^{x**}	0.23 ± 0.02^{xx**}
	Cd+Ir	0.12 ± 0.03^{xx*}	0.26 ± 0.01*	0.34 ± 0.05	0.25 ± 0.05^{x**}

C – control; Cd – administration of cadmium (1 mg/rat $CdCl_2$ i.p.); Ir – gamma irradiation (6 Gy); Cd+Ir – combination of cadmium administration and gamma irradiation.
Statistical significance of differences: x = $P < 0.05$; xx = $P < 0.001$ as compared with group C; * = $P < 0.05$; ** = $P < 0.001$ as compared with group Cd; o = $P < 0.05$; oo = $P < 0.001$ as compared with group Ir

Generally, in the intact and hypertrophic kidney, Cd administration alone (1 mg/rat i.p.) caused, especially in the earlier period, more noticeable changes than gamma irradiation (6 Gy) alone.

Liver

In the liver, the concentration and total content of RNA and especially of DNA decreased after Cd administration alone on the 7th and 14th days; later, until the 21st day, the DNA and RNA content increased above the control level (Fig. 3). After Ir alone, no significant decrease in concentration and content of RNA was found, but similarly to the preceding group on the 21st day, we have recorded an increase above the corresponding control level. In the liver of irradiated rats, the decrease in concentration and DNA content was greater on the 7th and 14th days as compared to the Cd-administered ones (Ir *vs.* Cd). Contrary to Cd administration or Ir alone, the combination of these treatments (Cd+Ir) caused a decrease in DNA and RNA concentration and content in the liver also on the 1st day of the investigation.

Bone marrow

In the bone marrow (femur), the Cd administration had no significant influence on DNA and RNA concentration and total content (Fig. 4). After Ir, the concentration and total content of RNA significantly decreased during the 1st day of the investigation; quick temporary recovery of RNA was repeatedly followed by a decrease in RNA concentration and content on the 21st day. The combination of these treatments (Cd+Ir) resulted in later adjustments of RNA concentration and content. DNA changes were less profound than RNA changes and they persisted approximately at the same level during all the period of investigation.

Spleen

After Cd administration alone, the concentration and content of RNA was lower only on the 7th day, but that of DNA was significantly decreased also on the 1st day (Fig. 5). After Ir alone, the RNA concentration temporarily decreased on the 1st day. Because of a significant decrease of spleen weight (Table 1), the decrease in the total RNA content persisted until the 14th day,

with maximal reduction (by 71–72% in comparison with controls) on the 1st and 7th days. In the spleen of irradiated rats, DNA concentration was lower during the whole period of the investigation except for the 14th day after Ir; the total DNA content decreased to a minimum – 18% of control values – on the 7th day, and later only partial adjustment followed. After combination of treatments (Cd+Ir), the DNA and RNA changes in the spleen were similar to those after Ir alone.

Thymus

On the 1st day of investigation, after Cd administration alone, the concentration and especially the total content of RNA and DNA rapidly decreased to 14% and 21% of control values, respectively (Fig. 6). During the next days, complete adjustment of RNA was recorded; DNA changes adjusted more slowly and on the 21st day they became deeper again. After Ir alone, the initial decrease in concentration and content of DNA and RNA in the thymus was even more significant than after Cd administration alone and the repeated decrease was more profound on the 21st day. Cd administration 30 min before Ir (Cd+Ir) made the initial decrease more marked but in the later intervals, the changes of DNA and RNA contents were similar or even lower than after Ir alone.

Discussion

According to the total extent of DNA and RNA and weight changes induced by Cd and/or Ir, the investigated organs can be arranged as follows: intact kidney < liver < hypertrophic kidney and bone marrow < spleen < thymus. In the intact and hypertrophic kidney and in the liver, the Cd administration (1 mg/rat $CdCl_2$ i.p.) caused more significant changes than gamma irradiation (6 Gy) and the effects of combination of the treatments were similar to the effects of Cd alone. On the contrary, in bone marrow, spleen and thymus, more significant changes were induced by Ir than by Cd administration and the effects of combination of both treatments were similar to Ir alone.

In general, the least changes were found in the intact kidney, where no decrease but rather an increase in DNA and RNA content occurred, which in later intervals could be related to the induction of cell proliferation as a consequence of the preceding damage (Otsuka and Meistrich, 1990).

The significant increase in DNA and RNA content, especially in DNA content in the hypertrophic kidney of control animals on the 44th h after UN, reflects cell proliferation, as the compensatory growth of the remaining contralateral kidney after UN is realized not only by hypertrophy but also by hyperplasia (Heine et al., 1971; Choie and Richter, 1972; Zalups et al., 1995; Inda et al., 1997). After treatments applied, the content of nucleic acids in the hypertrophic kidney of experimental rats was lower in comparison with corresponding operated controls, especially in consequence of the inhibition of growth induced by UN and not due to the real decrease in DNA and RNA content evoked by loss of damaged cells. The changes that took place in the hypertrophic kidney on the 7th day after all the treatments (Cd, Ir, Cd+Ir) were an exception, as at that time the values of DNA content decreased not only in comparison with the control hypertrophic kidney, but with control intact kidney, too.

The changes in the hypertrophic kidney after Cd administration and/or Ir were more noticeable than in the intact kidney. This was the result of at least two opposite processes engaged in the damage formation and development in the hypertrophic kidney. On the one side, proliferating cells are, in general, more sensitive to different stimuli, e.g. Ir, because various kinds of damage become manifested during the cell cycle (especially by inhibition of DNA synthesis and mitosis and by formation of chromosome aberrations) and they can lead to the mitotic death of cells. These processes result in more noticeable changes found e.g. in the regenerating liver in comparison with the intact liver of animals after some treatments (Bucher, 1991; Kropáčová and Mišúrová, 1992). On the other side, in proliferating cells of the kidney and liver, in comparison with non-proliferating cells, the level of metallothioneins temporarily increases (Waalkes and Goering, 1990; Zalups et al., 1995; Vašák and Hasler, 2000) and that is why we could expect milder damage after Cd administration and/or Ir in the hypertrophic kidney than in the intact kidney. Metallothioneins are effective scavengers of hydroxyl radicals because of a high content in hydrogensulphide groups, and because of this they participate in very effective protective mechanisms of cells. This kind of mechanism is used in acute response to electrophilic agents, e.g. free radicals and other reactive metabolites (review Waalkes and Goering, 1990), which are formed during irradiation or heavy metal (including Cd) exposure (Koizumi et al., 1996; Ďuračková, 1998; Shaikh et al., 1999). Nucleic acids are especially sensitive to oxidative damage. The oxidation of nitrogen bases can cause mutations and the oxidation damage of deoxyribose can lead to the cleavage of one or both chains of double-stranded DNA. The ionic forms of metals can bound more or less specifically to DNA either by themselves or in the form of complexes. In this way they can induce cleavage of polynucleotide chains (Ďuračková, 1998).

In our experiments, in the case of combined treatment of rats, the time difference between Cd administration and Ir was 30 min, which is too short a period for induction of metallothionein synthesis by a heavy metal (Waalkes and Goering, 1990; Sudo et al., 1996). For this reason, contrary to other papers (Matsubara et al., 1987; Fedoročko et al., 1996; Macková et al., 1996), primary effects of radiation could not be modified in our experiment by metallothioneins induced by preceding Cd administration. Obviously, it was the reason why in the group with combined treatment (Cd+Ir), the radi-