ACTIVITY OF LIVER OXIDOREDUCTASES DURING INTERNAL ADMINISTRATION OF RADON WATER

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Under the influence of radon water taken internally, activity of oxidoreductases in the rat liver was increased and the content of lipids and glycogen in the organ was modified. The changes observed were directly dependent on the absorbed dose of radon.

Experimental and clinical investigations [1, 7, 8] have shown that administration of radon and its fission products influence metabolism in the liver, although no information on the histochemistry of metabolic processes in the liver tissue following internal administration of radon water could be found in the accessible literature; only a note on the effect of radon water on lipid metabolism in the liver could be traced [3].

The object of the present investigation was to study activity of the oxidoreductases of liver tissue in healthy experimental animals (rats) receiving radon water internally, and to examine the changes in some indices of carbohydrate, protein, and lipid metabolism under the same experimental conditions.

EXPERIMENTAL METHOD

Experiments were carried out on 180 albino rats subdivided into 7 groups. The control group consisted of intact rats and rats receiving tap water in the same doses and under the same conditions as the rats of the experimental groups. The effect of natural radon water from Pyatigorsk mineral springs with a radon concentration of 0.18 μCi/liter, and also of artificial radon waters with radon concentrations of 0.18, 3.64, 36.4, and 364 μCi/liter, was investigated in the remaining five groups of rats. Radon water was given by gastric tube in a dose of 10 ml daily for 1, 10, and 21 days.

Activity of oxidoreductases, and the contents of glycogen, lipids, proteins, and RNA were studied periodically during and after administration of the water for the three periods mentioned above, and also 15 and 30 days after the end of the 21 day cycle of administration of radon water. Activity and localization of seven enzymes (succinate, malate, glucose-6-phosphate, α-glycerophosphate, and lactate dehydrogenases, NAD- and NADP-diaphorases) were investigated by the methods described in Pearse's textbook [12]. Survey sections were stained with hematoxylin and eosin and by Van Gieson's method. The lipid content was determined with a mixture of Sudan III and Sudan IV, proteins by Danielli's reaction, glycogen by the PAS reaction, and RNA by Brachet's method. The activity of four enzymes (succinate, malate, and lactate dehydrogenases, NAD-diaphorase) was determined in three zones of the hepatic lobules by the quantitative cytophotometric method suggested by Morozov et al. [5], using a microspectrocytophotometer. The numerical results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

Visual examination of the liver of the control rats revealed higher succinate dehydrogenase activity in most lobules in the hepatocytes of the periportal zone (Fig. 1a); activity of malate, glucose-6-phosphate,

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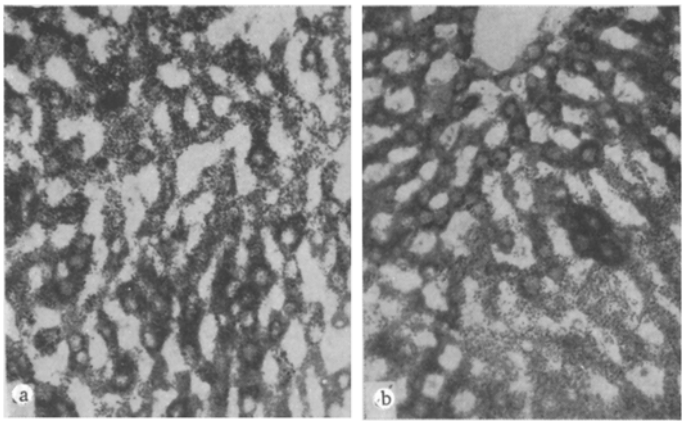

Fig. 1. Liver of control rat: a) succinate dehydrogenase activity higher in hepatocytes of the periportal zone; b) lactate dehydrogenase activity higher in center of hepatic lobule, 200 ×.

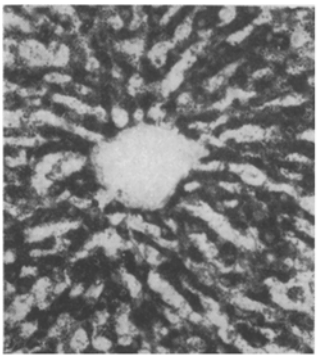

Fig. 2. Marked increase in lactate dehydrogenase activity in hepatic lobule. Administration of radon water with concentration 36.4 μCi/liter for 21 days, 300 ×.

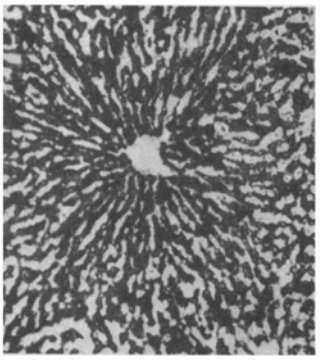

Fig. 3. Sharp increase in NADP-diaphorase activity in hepatocytes of all zones of hepatic lobule. Administration of radon water with concentration 364 μCi/liter for 21 days, 100 ×.

α-glycerophosphate, and lactate dehydrogenases and of NAD- and NADP-diaphorases, was highest in the hepatocytes of the central zone of the hepatic lobule (Fig. 1b). Differences in the activity of respiratory enzymes in different parts of the hepatic lobules have also been reported in the literature [2, 6, 9-11], indicating that the course of metabolism differs among the hepatocytes. Quantitative cytophotometric estimation of the enzyme activity revealed a tendency for an increase in succinate dehydrogenase activity in the periportal zone of the hepatic lobule, and of the activity of malate and lactate dehydrogenases and of NAD-diaphorase in the central zone of the lobule (Table 1). The cytoplasm of the hepatocytes was poor in lipids but very rich in glycogen inclusions; large quantities of protein and RNA also were detected in it, and no zonal differences were observed in the contents of these substances.

Visual investigation of the oxidoreductases of the liver in the experimental animals after administration of natural and artificial radon water with a radon concentration of 0.18 μCi/liter for 1 and 10 days revealed no change in their activity. After administration of radon water of the same concentration for 21 days to the albino rats, quantitative investigation revealed an increase in the activities of succinate and lactate dehydrogenases and of NAD-diaphorase. The increase in activity of succinate and lactate dehydrogenases persisted 15 and 30 days after the beginning of the experiment (Table 1). The activity and localization of the other oxidoreductases investigated in the liver tissue was indistinguishable at all times from the control in this series; no change likewise occurred in the content of protein, RNA, glycogen, and lipids.

TABLE 1. Quantitative Determination of Activity of Oxidoreductases in Rat Liver Tissue in Relation to Radon Concentration in Radon Water and Time of Experiment (in Conventional Units)

Enzyme	Zone of hepatic lobule	Radon concentration in μCi/liter in water and time of experiment (days of administration)							
		control	0,18/1	0,18/10	0,18/21	0,18/30	3,64/21	36,4/21	364/21
Succinate dehydrogenase	Central	25,2±2,2	No change in activity detected visually	29,6±2,1	37,4±0,1	43,1±1,6	46,4±1,3	61,9±0,8	72,6±0,7
	Intermediate	26,6±1,8		31,3±1,8	41,1±1,4	45,6±0,5	48,4±0,6	64,5±0,4	74,6±1,4
	Periportal	27,8±1,9		32,4±2,2	44,7±0,9	49,0±0,4	49,9±0,2	67,6±0,7	77,4±2,1
Malate dehydrogenase	Central	25,4±3,4	21,7±2,8	26,0±2,2	No change in activity detected visually	No change in activity detected visually	26,4±2,2	48,8±1,5	64,3±0,7
	Intermediate	22,4±2,2	20,8±1,6	22,8±1,6			22,9±1,4	47,8±1,2	61,1±0,9
	Periportal	20,5±2,1	21,0±1,9	21,5±2,7			21,7±1,1	45,4±0,8	57,7±1,1
Lactate dehydrogenase	Central	23,6±3,9	No change in activity detected visually	27,3±1,8	43,6±1	51,8±0,5	43,8±1,6	60,8±1,6	74,1±0,8
	Intermediate	17,6±2,6		25,1±2,5	38,9±1,1	47,5±1,2	41,1±1,5	57,5±1,6	69,9±0,2
	Periportal	17,4±1,5		25,0±2,8	35,4±0,9	44,8±1,3	39,5±1,6	53,6±0,9	67,0±0,4
NAD-diaphorase	Central	24,0±1,6	No change in activity detected visually	No change in activity detected visually	32,5±2,6	27,6±0,8	34,1±1,3	63,1±3,3	76,4±0,9
	Intermediate	19,9±1,5			28,1±1,1	24,1±0,7	28,3±1,6	59,6±3	72,3±0,9
	Periportal	19,4±1,3			24,3±1,0	21,0±1,2	24,9±1,2	55,1±2,7	69,1±1,2

Administration of radon water with a radon concentration of 3.64 μCi/liter for 10 or 21 days caused a decrease in the glycogen content and a slight increase in the lipid content in the liver tissue, and these changes persisted at the end of administration. A single dose of radon water in the same concentration caused no changes in activity of the oxidoreductases of the hepatocytes. Administration of radon water for 10 and 21 days caused a more marked (compared with administration of radon water with a radon concentration of 0.18 μCi/liter) increase in activity of succinate and lactate dehydrogenases and NAD-diaphorase (Table 1); the increase in enzyme activity of the liver cells also persisted after administration of radon water. No appreciable abnormalities in the activity of the other oxidoreductases of the liver investigated could be found at any time in this series of experiments.

Administration of radon water with a radon concentration of 36.4 or 364 μCi/liter led to an even more marked and significant increase in the activity of all enzymes studied. Activity of succinate, malate, and lactate dehydrogenases and of NAD-diaphorase increased in all zones of the hepatic lobules to such an extent that visual inspection gave the impression of diffuse staining of the cytoplasm of the hepatocytes and disappearance of the irregular enzyme activity in parts of the lobule (Figs. 2 and 3). However, on the whole the hepatic tissue continued to show irregularity of activity of the respiratory enzymes. In addition, quantitative determination of the enzyme activity showed that the hepatocytes in different zones of the lobules still retained their enzymic heterogeneity (Table 1). Besides the activities of succinate, malate, and lactate dehydrogenases and of NAD-diaphorase, activity of glucose-6-phosphate and α-glycerophosphate dehydrogenases and of NADP-diaphorase also was increased in the hepatocytes of all zones of the hepatic lobules. The content of protein and RNA was unchanged after administration of water containing high radon concentrations; nevertheless, at various times of these series of experiments the glycogen and lipid content in the parenchymatous cells of all three zones of the lobule fell sharply. Basophilia, homogenization of the cytoplasm, and a decrease in the size of some of the cells were observed in the hepatocytes.

These experiments revealed a definite direction of the changes in the liver tissue reflecting changes in the activity of oxidoreductases and some of the basic parameters of carbohydrate and lipid metabolism. The changes observed were directly dependent on the radon concentration in the water, the duration of its administration, and the absorbed dose of radiation reaching the liver. Small doses of radon (0.18 and 3.64 μCi/liter) lowered the glycogen content in the hepatocytes and, at the same time, slightly increased the lipid content and activity of succinate and lactate dehydrogenases and NAD-diaphorase. The decrease in glycogen content was evidently a functional change and was due to the stimulation of metabolism by the radon and mobilization of glycogen from the liver depots [4]. On the other hand, the increase in lactate dehydrogenase activity is evidence of a simultaneous increase in glycolysis in the hepatocytes themselves, in association with increased carbohydrate utilization. The increase in succinate dehydrogenase activity indicated stimulation of tissue respiration. The small increase in lipid content also taking place can probably be attributed to its accumulation as a high-energy material and it was the result of a decrease in the glycogen content in the hepatocytes.

Internal administration of radon water with high radon concentrations (36.4 and 364 μCi/liter) produced even more marked increase in the activities of all oxidoreductases investigated with, at the same time, a decrease in the lipid and glycogen content. The increase in activity of succinate and malate dehydrogenases in the hepatocytes directly reflected stimulation of tissue respiration. Meanwhile the increased activity of glucose-6-phosphate, α-glycerophosphate, and lactate dehydrogenases indicated stimulation of glycolysis. The simultaneous increase in activity of the oxidative and glycolytic enzymes, described in the modern literature as a state of aerobic glycolysis is evidence of inhibition of the pasteur effect. It must therefore be concluded that the absorbed dose of radiation has a substantial influence on metabolic processes in the hepatocytes of the hepatic lobules.

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