bohydrate metabolism [2]. Similar changes in the reproductive and energy producing systems, developing in response to injection of other classes of carcinogens, also arise, it will be noted, during the performance of the neuroendocrine program of development and aging and the formation of age pathology both in animals and in man [3].

It can be postulated from these results that hormonal and metabolic disturbances, creating the conditions necessary for proliferation of the tumor cell, play an essential role in the mechanism of the carcinogenic action of DMH in rats.

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POSSIBILITY OF MIGRATION OF CERTAIN ELEMENTS IN BIOLOGICAL SYSTEMS DURING X-RAY IRRADIATION

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The effect of local x-ray irradiation on the content of certain elements in cell components (nuclei, mitochondria) and blood serum of rats with transplanted sarcoma M-1 in a dose of 250 R during growth of the tumor was shown to lead to a redistribution of Zn from the nuclei into the mitochondria. Statistically significant postradiation changes also were found in the content of Ca, Mg, Cu, and Zn in the blood serum of rats with a transplanted sarcoma M-1 after a single session of local irradiation of the tumor in a dose of 1000 R.

KEY WORDS: *Migration of elements; postradiation changes; neutron-activation and atom-absorption analysis; x-ray irradiation.*

The action of ionizing radiation is known to be accompanied by disturbance of normal metabolic processes taking place in the cell. These disturbances depend on the character of the radiation and on the quantity of absorbed energy. The writers have postulated that changes of concentration of heavy metals can take place in certain structural components of animals with sarcoma under the influence of ionizing radiation [1]. The explanation of the nature of postradiation migration of heavy metals could itself become the key to the study

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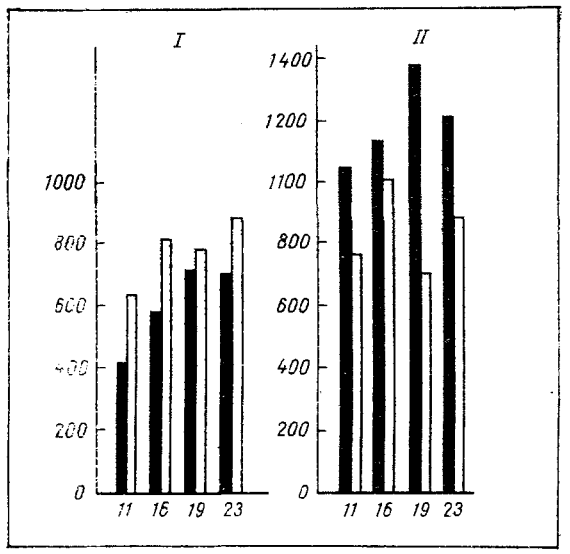

Fig. 1

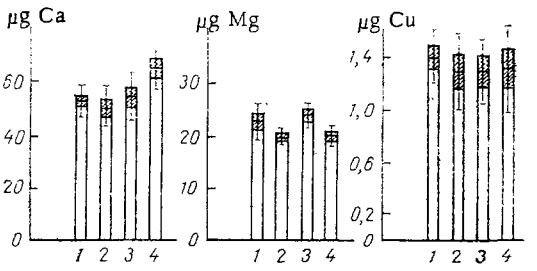

Fig. 2

Fig. 1. Dynamics of changes in Zn content in nuclear (I) and mitochondrial (II) fractions isolated from cells of rat sarcoma M-1 treated by systematic local irradiation during tumor growth. Shaded columns) irradiation; unshaded) control (no irradiation). Ordinate, Zn concentration (in μg/g nitrogen); abscissa, days of development of sarcoma M-1.

Fig. 2. Content of Ca, Mg, and Cu in blood serum of rats after x-ray irradiation (local dose 1000 R). Shaded part with vertical lines) 95% two-way confidence interval of significance of random values. 1) Control (blood serum of rats with transplated sarcome M-1); 2, 3, 4) blood serum of rats with transplated sarcoma M-1 1, 4, and 24 h after irradiation respectively. Mean values of 9-10 experiments given.

of the mechanisms of therapeutic action of ionizing radiation, on the one hand, and of the development of radiation sickness, on the other hand.

This paper gives some results that are evidence of the existence of mechanisms of post-radiation migration of Ca, Mg, Cu, and Zn at the cellular fraction level and in the blood serum of experimental animals after x-ray irradiation.

EXPERIMENTAL METHOD

Two series of experiments were carried out on noninbred albino rats weighing 150-200 g with transplanted sarcoma M-1. In each series the animals were divided into two groups (with and without irradiation). In series I (200 rats) the sarcoma M-1 was treated by local x-ray irradiation in a dose of 250 R on the 11th, 16th, 19th, and 23rd days of tumor growth. At each of the above times 8 to 10 rats were decapitated and nuclear and mitochondrial fractions were separated from the tumor tissue by differential centrifugation, followed by additional purification [5]. The purity of the subcellular components was verified by phase-contrast and electron microscopy. The content of metals in the fractions was determined by neutron activation analysis. Dried preparations were irradiated in the zone of the reactor with an integral flow of neutrons (approximately 10^{19} neutrons/cm^2), after which the γ spectra were measured with a high-resolution spectrometer. A method of comparison with synthetic standards was used for quantitative analysis of the composition of the elements in the samples [2]. In series II 60 rats were irradiated in a dose of 1000 R. Blood serum 1, 4, and 24 h after being obtained was used for the investigations. The content of the metals was determined by atom absorption analysis. The results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

Systematic local irradiation of tumor tissue with x rays in a dose of 250 R led to a redistribution of Zn from the nuclear fraction into the mitochondrial fraction (Fig. 1). This fact goes some way toward explaining the therapeutic value of x-ray irradiation. Since Zn plays an important role in nucleic acid synthesis [3, 4], its removal from the nuclei

could lead to inhibition of DNA synthesis and, consequently, could reduce the rate of multiplication of the tumor cells. The question arises whether concentration changes in the composition of the elements in the blood can be found after local x-ray irradiation of animals in a comparatively small dose (500-1000 R). The experimental results confirmed that this was possible. A steady accumulation of Ca in the blood serum was discovered 1, 4, and 24 h after the end of irradiation (Fig. 2). The change in the concentrations of Mg and Cu did not differ by a statistically significant degree from the control.

Even by investigation of the blood serum differences could thus be found in the concentration of certain elements after local x-ray irradiation of tumor tissue in experimental animals.

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COMPARISON OF THE LEVEL OF MITOTIC ACTIVITY AND DURATION OF MITOSIS IN NORMAL AND NEOPLASTIC MOUSE TISSUES DURING THE 24-HOUR PERIOD

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Diurnal rhythms of cell division in the epithelium of the forestomach and in a transplantable carcinoma of the forestomach were found to be largely similar and the duration of mitosis in both these tissues varied during the course of the 24-hour period. The mean diurnal mitotic activity in the tumor was twice as high as in the normal forestomach. By contrast, in the course of 24 h colchamine (colcemid) led to the accumulation of 121.1 °/₀₀ of mitoses, compared with only 83.8 °/₀₀ in the carcinoma. The larger number of mitoses in the tumor when counted in the ordinary way can be explained by the 2.7 times greater mean diurnal duration of mitosis in carcinoma of the forestomach than in the normal epithelium of the forestomach.

KEY WORDS: *Duration of mitosis; carcinoma of the forestomach; epithelium of the forestomach; colcemid; mitotic index.*

The comparative study of the level of cell proliferation in tumors and in the normal tissues from which these tumors arise is of great importance in the study of the principles governing malignant growth. According to some workers [6-8, 10] the intensity of cell division in tumors is lower than in healthy tissues, and the high mitotic activity can be explained by the slow course of mitosis itself; other workers [4, 5, 9], on the other hand, consider that tumor cells proliferate faster than normal. However, in the study of this problem it is essential to remember that the duration of mitosis in both healthy and tumor tissues varies during the 24-hour period within quite wide limits [1-3].

Changes in mitotic activity and in the duration of mitosis during the 24-h period were investigated in a transplantable carcinoma of the mouse forestomach (strain OZh-5) and, at the same time, in the stratified squamous epithelium of the forestomach of these mice.

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