THE BIOLOGICAL ACTION OF HIGH ENERGY RADIATION

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At present an enormous amount of experimental material has accumulated concerning the action of ionizing radiation upon the living organism, but only a small part of the energy spectrum has been systematically and adequately studied. Above all, data concerning the action of X-rays and the γ-radiation of radioactive isotopes are available. Numerous data have also been published concerning the action of thermal and fast neutrons; the effect of supervoltage X-rays and fast electrons obtained on the betaron is less known. The information concerning the effect of high energy neutrons, protons and γ-rays in the range of several hundred or thousand Mev is very scanty. As the technique of nuclear investigations develops and new, more powerful, accelerating apparatus is created, the possibility of exposure to radiation becomes wider and the field of radiobiological investigations extends correspondingly. Reports already available have shown that the primary mechanisms are on the whole similar for all types of ionizing radiation within a very wide range of energy. The response of the animal body to the action is also similar in principle. The degree to which this response becomes manifest and the pattern of its development, however, may vary within a wide range, a fact which determines the specific character of the action exerted by various types of ionizing radiation.

The marked influence exerted by a number of vitamins upon the symptom complex characterizing the response of the animal body to radiation is well known, but the metabolism of the vitamins and the pattern of the relevant reaction within the body, and particularly vitamin C metabolism, have been quite inadequately studied.

Aside from the complete absence of data concerning the pattern of vitamin C metabolism under the influence of high energy radiation (obtained with the aid of contemporary accelerating apparatus), similar observations are extremely scarce even concerning the action of X-rays. At the same time, however, the pattern of distribution of ascorbic acid in the organs and tissues under the influence of one or the other factor represents a particularly sensitive index for the response of individual organ systems as well as of the whole body to the action of the factor in question and yields valuable results. The investigations which have been published in this field mainly concern the response of the adrenal glands [1,4].

It is well known that after exposure of the animal body to radiation, the blood system and the sexual system are involved fairly early in the pathological process. For that reason we thought it worthwhile to study the pattern of changes in some aspects of the response given by these systems to radiation.

METHOD

Rats and mice were given a single exposure to total body radiation with protons of 660 Mev energy, which were obtained on a six meter synchrocyclotron in the Laboratory for Nuclear Problems, United Institute of Nuclear Investigations. The dose for rats was 525-585 rad; for mice about 600 rad. The exposure lasted two-five min. The effect of radiation was in the above experiment judged on the basis of the weight of the organs, the morbid anatomical changes, changes in the total quantity of ascorbic acid in the spleen and the testes and the changes in the concentration of ascorbic acid in the tissue of the spleen, the bone marrow and the testes.

Observations were carried out on nine groups of rats among which one group (nonirradiated control animals) consisted of 21 rats, the other groups - the experimental animals - consisted of 10-11 rats each. The animals were killed for investigation 3,8,15,30,45,60,90 and 120 days after the exposure to radiation.

RESULTS

Well marked and consistent changes were found in the indices selected by us, changes which were fully reproducible in repeated experiments and proved to be highly significant when the numerical material was evaluated statistically.

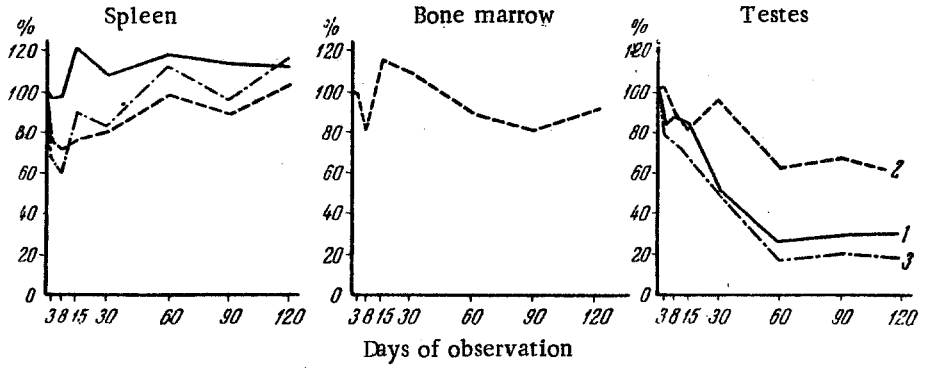

Fig. 1. The pattern of changes in the content of ascorbic acid in the organs of rats after a single exposure to total body radiation. 1) Organ weight; 2) ascorbic acid in mg%; 3) ascorbic acid in mg.

Figure 1 shows the curves which characterize the pattern of changes in the weight of the spleen and testes of rats exposed to radiation as well as the pattern of changes in the content of ascorbic acid in the whole organ and its concentration in the tissue of the organ in question. The content of ascorbic acid in percent was calculated in relation to the control group.

Study of the pattern of changes caused by a single exposure to radiation revealed the following: Three days after radiation, the weight of the spleen fell to 76% of the original weight; later however, it began to increase and within two weeks after exposure to irradiation exceeded the initial weight by 22% and persisted approximately on this level until the end of the four months of observation. The content of ascorbic acid in the spleen decreased considerably (in the whole organ) and the decrease lasted until the eighth day of the experiment when altogether 60% of the original quantity of ascorbic acid was found in the spleen. Later the curve characterizing the content of ascorbic acid began to rise again - by the 15th day it reached 90% of the original level and subsequently showed a further gradual increase. A similar decrease in the concentration of ascorbic acid could be found in the spleen tissue. The minimum concentration persisted for two weeks after the exposure to radiation; later a very gradual increase could be observed. Two months after exposure to radiation the concentration of ascorbic acid in the spleen returned to the original value.

It must be emphasized that in the bone marrow the decrease in the concentration of ascorbic acid was most marked at the same time as in the spleen - on the eighth day after exposure to radiation, with a subsequent return to the normal level.

The results obtained in studies concerning the changes in the testes of the animals exposed to radiation were the following:

By the third day of the experiment a statistically significant decrease in the weight of the testes (approximately by 20%) could be observed. No further decrease in the weight occurred for two weeks after exposure to radiation, later however the curve characterizing the weight of the testes showed a marked fall (with a loss of 74% of the initial weight after two months) and the weight of the testes persisted on this minimal level throughout the period of investigation—up to four months.

The decrease in the concentration of ascorbic acid in the testicular tissue was of more gradual character. It is interesting that the first minimum (80% of the original concentration) was reached within two weeks; then the curve characterizing the concentration of ascorbic acid increased almost to the normal level by one month; after that, however, a renewed fall in the concentration of ascorbic acid, more intensive than in the first period, could be observed. The second minimum (60% of the original concentration) was observed two months after exposure to

radiation and persisted until the end of the period of observation.

Death of the experimental rats was not observed. In the period between the eighth day after irradiation and the end of the experiment, response to irradiation could be observed and judged by changes in the spleen, lymph nodes, and testes. These changes differed depending on the time elapsed since irradiation.

Eight days after exposure to radiation the internal organs were hyperemic, the cervical lymph nodes as well as the mesenteric and retroperitoneal lymph nodes were enlarged and hyperemic; the bone marrow in the sternum, the vertebrae, and the long pipe bones was also hyperemic. The spleen was diminished in size, the testes were slightly hyperemic and edematous. The dose used by us did not produce symptoms of hemorrhagic diathesis.

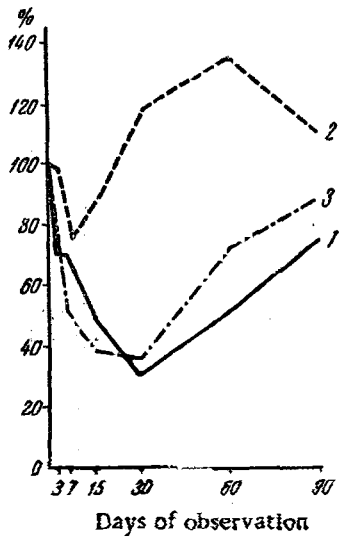

Fig. 2. Pattern of changes in the content of ascorbic acid in the testicles of mice after exposure in one instance to total body radiation. 1) Weight of organ; 2) ascorbic acid in mg%; 3) ascorbic acid in mg.

At later periods, particularly 3-4 months after exposure to radiation, marked atrophy of the testes could be observed; these organs were considerably diminished in size and shrunken. The spleen, lymph nodes, and bone marrow showed no gross changes after one month or during the later periods.

Histological investigation of the spleen eight days after exposure to radiation revealed hyperemia, severe hemosiderosis and a considerable decrease in the number of lymphoid elements with a marked decrease in the size of the follicles; the splenic pulp showed a homogeneous blurred structure. There was a marked polymorphism in the size of the cells and very large cells containing large nuclei could be seen. The arteries showed marked swelling and homogenization of the wall.

After 15 days cells of the plasma cell type began to appear in the spleen in the shape of hyperplasia of the cellular elements in the sinuses and the splenic pulp. After $1\frac{1}{2}$-2 months swelling of the capillary wall, hyperplasia of the follicles as well as sclerotic changes could be observed. Later the structural relations were gradually restored and after four months the spleen was again of the usual appearance. By that time slight deposits of hemosiderin, which gave a positive reaction for iron, could be observed in the reticulo-endothelial elements.

Microscopical investigation of the testes eight days after exposure to radiation revealed hyperemia, edema of the stroma, lymphostasis and also considerable destruction of the spermatogenic epithelium in the majority of tubules. By the 15th day the necrotic changes in the tubular epithelium increased, edema of the capsule and hyperemia could be observed. In the majority of tubules mainly the basal layer of the epithelium was preserved. Later the destruction of the spermatogenic epithelium continued. After $1\frac{1}{2}$ months atrophic changes could be observed in the spermatogenic epithelium. The epithelial cells showed hydropic changes, which became manifest in the vacuolization of the protoplasm; in the remaining epithelium, differences in the size of the nuclei could be observed; some of the nuclei were swollen, others showed pycnosis, still others showed karyorrhexis. Besides, a few giant cells and - in the tubules - deposits of protein could be seen. After two months marked atrophic changes in the spermatogenic epithelium and focal proliferation of the interstitial elements could be observed.

Three to four months after exposure to radiation the testicular tubules were in a state of collapse, the spermatogenic epithelium was almost completely destroyed (only a few cells with hyperchromic nuclei could be seen). In the interstitial tissue an increase in the number of histiocytes and of the cells resembling plasma cells could be seen.

We are thus able to state that the pattern of changes of all indices accepted for the present investigation was similar: changes in the ascorbic acid metabolism precede the morbid anatomical changes.

In addition to the observations on rats, experiments were carried out on mice. Similar to the scheme of experiment used on rats the pattern of changes in the following indices was followed during the development of radiation sickness: the weight of the testes, the total content of ascorbic acid in the testicles as well as its concentration in the testicular tissues.

The changes in the weight of testes in mice were well marked beginning from the earliest stage of investigation. After three days the weight of the testes constituted only 70% of the original weight. The loss of weight of the testes continued until the second month of observation at which time it had fallen to 51% of the original weight.

Later, however, unlike what had been observed in rats, an increase in the weight of the testes up to 75% of the original weight could be observed three months after the exposure to radiation.

The decrease in the total content of ascorbic acid in the testes of mice developed at a much quicker rate than the loss of weight. Fig. 2 shows that after one month the total content of ascorbic acid in the testes constituted only 36% of the original content. Unlike the curve characterizing the weight, however, the curve showing the content of ascorbic acid in the testes began to increase much earlier and after two months reached 74%, and after three months 90% of the original level.

The concentration of ascorbic acid decreased by the seventh day to 75% of the original value remaining more or less on this level until the 15th day of the experiments; then the curve showing the concentration of ascorbic acid rose rapidly and after one month reached a point corresponding to 118% of the original concentration with a subsequent further increase; after three months, however, the curve returned to the original level.

It seems that the compensatory processes in the sexual system of mice connected with the biosynthesis of ascorbic acid in the testes develop at a fairly early stage whereas in the testes of rats such compensatory reaction could not be observed.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
