EFFECT OF THE CHRONIC ACTION OF SMALL DOSES OF IONIZING RADIATION ON THE BLOOD SYSTEM OF THE GROWING ORGANISM

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The object of the present investigation was to study the influence of the chronic action of ionizing radiation on the growing organism and on its hemopoietic system, for the data in the literature [1-7, 12] do not reflect the changes in the character of the course of chronic radiation sickness with age.

EXPERIMENTAL METHOD

Experiments were carried out on 34 puppies, of which 17 were irradiated from the age of 5 days, 9 from the age of 1.5 months, and 8 were controls. X-ray irradiation was given daily in doses of 10 R (22 puppies) and 1 R (4 puppies) on a type RUM-3 apparatus (voltage 180 kV, current 15 and 5 mA, filters 0.5 mm Cu and 1 mm Al, skin-focus distance 155 cm). On all the animals, besides a clinical examination, regular investigations were made of the blood (from the ear), the bone marrow (sternum), and the reactions of the leukocytes to injection of adrenalin. The experiments continued for 2-4 $^1/_2$ years.

EXPERIMENTAL RESULTS

All the puppies receiving chronic irradiation in a dose of 10 R developed radiation sickness, which followed a similar course in both age groups. Of the 22 puppies receiving 10 R each daily, 16 died: 10 during the period of irradiation and 6 at various times after irradiation had ended. In 4 puppies death supervened after comparatively small total doses of irradiation (550-1040 R) from pneumonia, in the absence of any marked disturbance of hemopoiesis. In the remaining 12 puppies, after larger total doses (1590-4320 R) lesions of the blood system developed, mainly affecting the red cells, with the appearance of very severe anemia. In 2 animals hyperplasia of the hemopoietic organs of leukemic type developed before death against the gackground of anemia.

The course of the chronic radiation sickness was cyclic. Three phases could be distinguished in its development.

In the first phase of the disease the external manifestations were very slight, and only an increased excitability of the irradiated animals was observed. The peripheral blood picture was unstable, and marked fluctuations were observed, mainly in the number of leukocytes (more commonly an increase). On the other hand the hemoglobin level fell for a short time. The morphological picture of the bone marrow was indistinguishable from that in the control animals. In the reactions to adrenalin some delay was observed in the increase in the number of leukocytes.

The second phase (the period of relative compensation) in most animals lasted for between a few months and 1.5-3 years. In this period, although the animals' general condition seemed good, an intermittent fall in the hemoglobin concentration and the erythrocyte count and a slight increase in the reticulocyte count were observed. The variations in the number of leukocytes and platelets were within subnormal limits. In the bone marrow the number of erythro-normoblasts was increased. The reactions of the leukocytes to adrenalin showed a sharp increase.

In the third phase (frank clinical manifestations), the duration of which did not exceed 3-5 months, the body weight of the animals fell gradually, they lost their appetite, and they became apathetic. Sometimes trophic ulcers were found on the skin. In the blood a sharp fall occurred in the hemaglobin concentration and the erythrocyte count, and severe destructive changes were observed in the erythrocytes with an accompanying fall in the color in-

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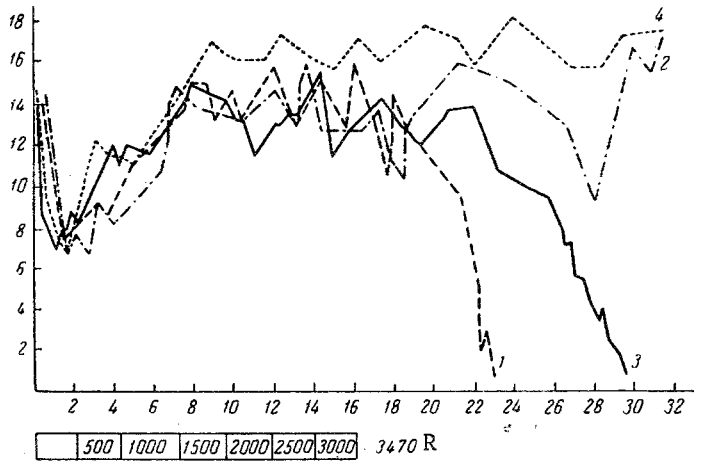

Fig. 1. Changes in hemoglobin concentration in the blood of puppies irradiated with x-rays from the age of 5 days in a daily dose of 10 R. Along the axis of abscissas—age (in months); along the axis of ordinates—hemoglobin concentration (in g %). Here and in Fig. 2: 1) puppy No. 70; 2) No. 71; 3) No. 73; 4) No. 74.

dex. In the bone marrow the number of erythro-normoblasts fell to 3-8%. The reactions of the leukocytes to adrenalin were weak (hardly any increase took place in the number of leukocytes).

Figure 1 shows that during the first 1.5 months of life the hemoglobin level in the control puppies and in the animals irradiated in a dose of 10 R from the age of 5 days fell equally. This was a physiological fall, associated with a replacement of fetal hemoglobin by adult hemoglobin, characteristic of all mammals. Next followed a phase of an increase in the hemoglobin level. In this phase, after total doses of irradiation of 400-700 R, the experimental animals showed some delay in the increase in the hemoglobin concentration by comparison with the control puppy, and repeated waves of a decrease in this index. Later the hemoglobin concentration in the experimental animals varied within the limits of subnormal values (13.5-15.0 g%). In two puppies, despite the cessation or irradiation, the hemoglobin level fell steadily, and they died from severe anemia (one 7 months and the other 14 months

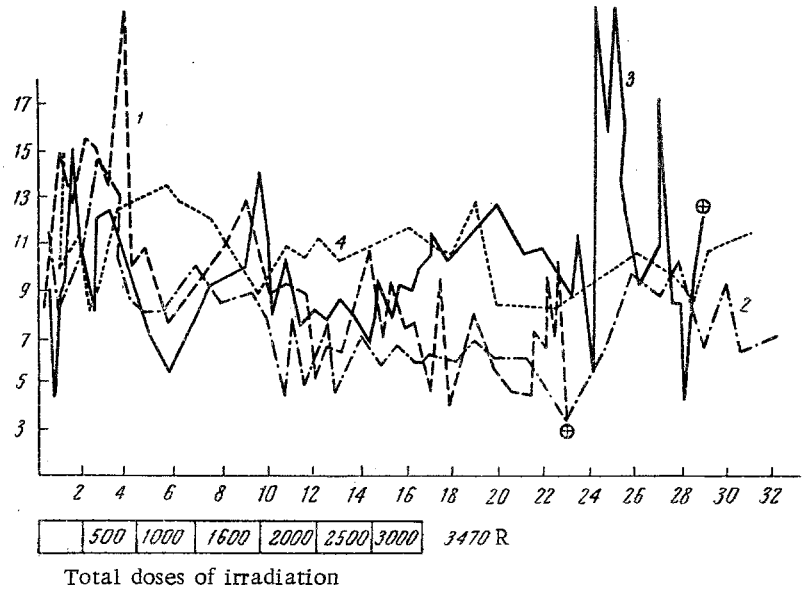

Fig. 2. Changes in the leukocyte count in the blood of puppies irradiated from the age of 5 days with a daily dose of 10 R. Along the axis of abscissas—age (in months); along the axis of ordinates — leukocyte count (in thousands).

after irradiation stopped). The results of the histological investigation of the bone marrow showed considerable destructive changes and a marked fall in the number of erythro-normoblasts. Concurrently with this, marked deposits of hemosiderin were found in the liver, the spleen, and the lymph glands.

Figure 2, which illustrates the changes in the number of lekucoytes in the same puppies, shows that no profound degree of leukopenia was present. However, the morphological changes in the leukocytes were clearly distinguishable. Polysegmented neutrophils with signs of anacytosis appeared. Among the lymphocytes binucleated cells and cells with horseshoe-shaped nuclei were found. In many cells degenerative changes were found (pycnosis of the nuclear substance, karyorrhexis and karyolysis, vacuolation of the cytoplasm).

The platelet count fluctuated in the course of the disease within subnormal limits, and not until shortly before death did the animal develop a thrombocytopenia. The morphological changes in the platelets took the form of anisocytosis (giant forms along with microforms), the appearance of rod-shaped and "tailed" forms, and so on.

Hence, it may be concluded from all the facts described above that in puppies exposed to chronic irradiation (in a daily dose of 10 R) from an early age, the composition of the red blood cells was mainly disturbed, with the development of severe hypochromic anemia. It may be supposed that this anemia in its initial phase is hemolytic. Proof of this is given by the marked destructive changes in the erythrocytes, the absence of a reticulocytopenia, and the periodic increase in the number of reticulocytes in the initial and second phase of the disease, and also the increase in the number of erythro-normoblasts in the bone marrow in the second phase of the disease and the large deposits of hemosiderin in the liver, spleen, and lymph glands.

Later, in the third phase of the disease, the manifestations of breakdown of the erythrocytes increased and, at the same time, signs of a failure of medullary hemopoiesis appeared. At this time, besides a sharp fall in the hemoglobin concentration and in the erythrocyte count, and the developing reticulocytopenia, the number of erythro-normoblasts in the bone marrow fell considerably. Disturbances of erythropoiesis, which develop more readily in growing animals than in adults, were also observed in acute radiation sickness [8-11].

Death of the dogs irradiated from an early age took place after receiving lower total doses of irradiation (550-4320 R) than in the case of sexually mature dogs (900-8600 R) [6].

The results of these investigations also showed that stopping the action of the ionizing radiation did not prevent severe damage in the future to the hemopoietic system in most animals irradiated from an early age and receiving total doses of the order of 1800-3900 R. Of the 16 dogs which died, in 6 deaths occurred 7-14 and 17 months after the irradiation had stopped.

SUMMARY

The paper presents the results of a study of the influence of chronic exposure to x-rays in doses of 1 and 10 R on the state of the blood and bone marrow in dogs irradiated from the age of 5 days and 1.5 months.

Prolonged observation during 2-4½ years has shown that dogs irradiated from an early age develop in the final stage of radiation sickness severe affections of the blood system with prevailing disturbances in red-cell production and severe anemia ending in death.

Cessation of irradiation after attainment of total doses of the order of 1800-3900 R does not prevent severe affections of the hemopoietic system from developing later in most animals irradiated from an early age. Such animals died within 7-14 and 17 months after cessation of irradiation.

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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 the first issue of this year.
