PATHOLOGICAL PHYSIOLOGY AND GENERAL PATHOLOGY

PERIPHERAL BLOOD IN MONKEYS IN ACUTE RADIATION SICKNESS

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It has frequently been demonstrated that one of the most constant and early reactions to ionizing radiation consists of changes in the blood system. Studies of the effect of radiation have been made on most laboratory animals, but very little work has been done on monkeys. Some reports [3-5] have shown that the blood reaction of monkeys bears many resemblances to that of other mammals and of man, and differs only in the degree to which different symptoms are developed.

Because the hemopoietic organs in monkeys in radiation sickness have been but little studied, and because certain problems such as changes in the thrombocytes have not been explored, we thought it worthwhile to investigate changes in peripheral blood in monkeys in response to ionizing radiation.

METHOD

The experiments were carried out on Macacus rhesus monkeys at the Sukhumi Medical and Biological Station. The animals were kept in cages. Their ages ranged from $1\frac{1}{2}$ to 2 years. In all, 18 animals, including 11 males and 7 females, were studied; of these, 13 were irradiated with a dose of 700 r, and 5 served as controls.

The conditions of the experiment were as follows: total irradiation dose 700 r; general field with two tubes, distance 78 cm; maximum voltage on tubes 180 kv, current 15 ma; dose 21.8 r/minute; time of irradiation 32 minutes.

RESULTS

For 3-4 hours after the irradiation, diarrhea and vomiting occurred in most animals; they did not eat, but drank copiously. Subsequently, and until the fifth day, their condition was satisfactory. Physical signs of radiation sickness occurred on the 5-7th days, when the animals spent a considerable part of the day lying down; the normal reflexes were absent, and food remained uneaten. Later, there was bleeding from the nose, and in some cases bloody stools were passed.

In the first few hours after irradiation, in spite of their general satisfactory condition, changes in peripheral blood were observed. Three hours after irradiating, the leukocyte count rose sharply, in some cases to 65,000 to 90,000, while by the end of the first 24 hours it had dropped again to 5,000-8,000. Subsequently, the number of leukocytes became progressively reduced; after 7-12 days, it had fallen to 2000-400 per mm^3 or 10-8 % of the initial value. In one animal only, which has survived this period, the leukocyte count again rose, and by the 30th day had reached a value of 15,000.

Changes in the shape of the leukocytes were also observed a few hours after irradiation. The increased leukocyte count found 3 hours after the beginning of the experiment resulted entirely from an increase in the number of neutrophils, which increased by 3.5 times or more; in some cases there were 60,000-80,000, and on average 39,000 cells per mm^3. The increase in the number of neutrophils coincided with an increase in the number of young forms of these cells (Fig. 1).

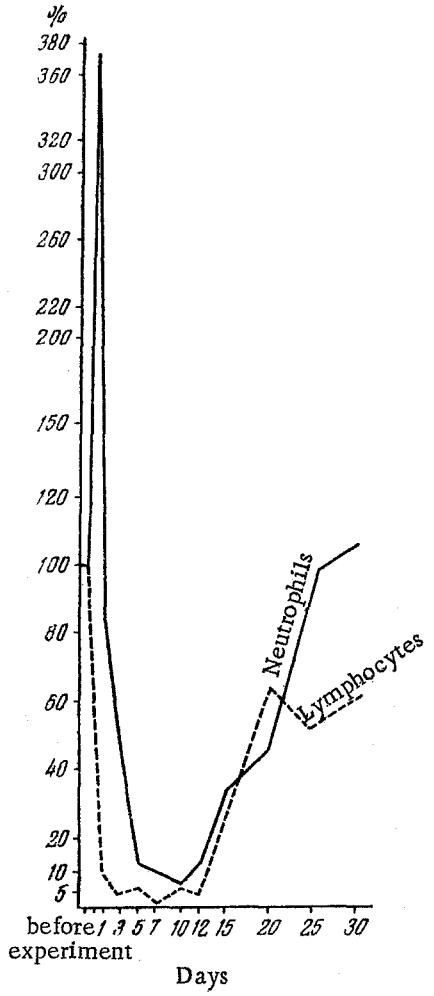

Fig. 1. Changes in average numbers of neutrophils and lymphocytes as a percentage of the original number.

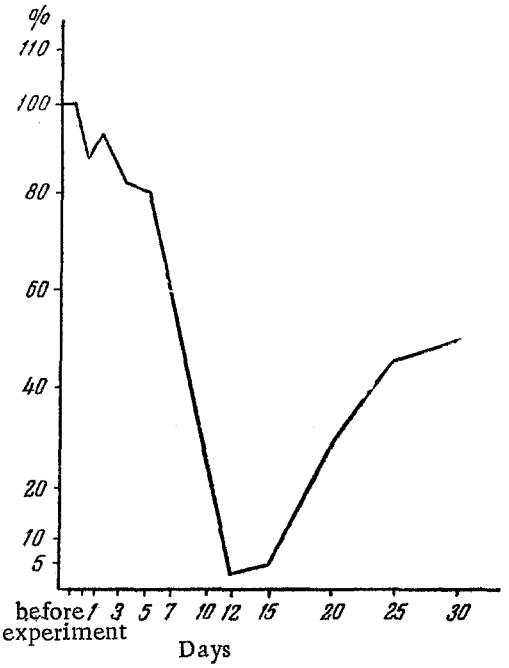

Fig. 2. Changes in thrombocyte count, expressed as a percentage of the original value.

Later, the number of neutrophils fell and reached a minimum value of 1000-700, as compared with an average of 10, 300 cells per mm^3, by the 7-10th day. Subsequent return to normal values was found to occur at the 25-30th day only in the single animal which survived for more than 12 days.

Even as early as 3 hours after the irradiation, the number of lymphocytes was halved: before irradiation it was 5000, and 3 hours later it had fallen to 2500-1500. By the end of the first day, the lymphocyte count was only 10% of the normal (800-400 cells per mm^3) and remained at this level to the end of period of observation.

In the first few days, there was an increase in the number of eosinophils, but later the number fell until only occasional cells could be seen. The changes observed in the monocytes were similar to those in lymphocytes.

On our counts, the average number of thrombocytes was 417,000-474,000. For the first few hours after the irradiation, the number was reduced, and after the 7th day it fell very sharply; by the 10-12th day the minimum value of 20,000-15,000 had been reached. In the single animal which survived to the 31st day, there was some increase after 15 days (Fig. 2).

An increase in the number of young thrombocytes was found 3 hours after irradiating (when there was a fall in the total number of these cells). Subsequently, the number of young and mature platelets became considerably reduced, reaching a minimum value by the 10-12th day. By the 3rd day, there was a marked increase in the number of strongly pyknotic,old thrombocytes, and later these formed the main mass of platelets until the end of the observation period. No thrombocytic irradiation forms were found at any period of the observation (Fig. 3).

The erythrocytes and hemoglobin were much less affected. Whereas no marked changes in the red cells were found, considerable alterations were found in the reticulocytes: 3 hours after irradiation, their number had been halved, and after 5-25 days only a few remained.

In the control group, over the whole period of observation no deviations from the normal blood picture were observed.

From the results presented, it can be seen that as early as 3 hours after the irradiation, the leukocyte count had risen considerably through an increase in the number of neutrophils; the increase was due to the formation of young forms. As has already been pointed out [1, 2, and others], this phenomenon is due to a more rapid maturation of cells in the bone marrow and to an increased rate of entry of these cells into the peripheral blood stream.

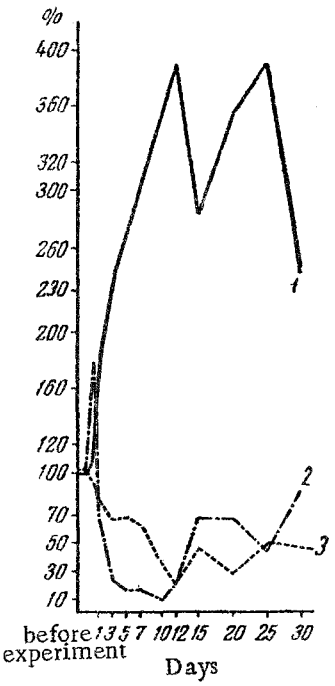

Fig. 3. Changes in the number of thrombocytes as a percentage of the original value. 1) Old thrombocytes; 2) young thrombocytes; 3) mature thrombocytes.

It is well known that lymphocytes are the most vulnerable to radiation, and the considerable reduction in their number found in the first few hours after the treatment evidently results from their increased rate of breakdown.

In the first stage of the reaction, the number of thrombocytes was reduced; however, at this time, owing to an increase in their rate of maturation, the number of young forms in the peripheral blood rose.

It is important to note that no irritation forms were found in any of the irradiated animals; as we have already pointed out, such forms are an unfavorable prognostic sign, and indicate that no regenerative processes are taking place in the megakaryocyte apparatus of the bone marrow.

According to M. Haigh and E. Paterson [5], a progressive reduction in the number of reticulocytes is also a bad prognostic sign in radiation sickness in monkeys. Our investigations confirmed this observation.

From the 3rd. day onwards, there was a reduction of the formed elements of the blood, with the exception of the erythrocytes, whose number was not reduced by more than 20-28% during the whole of the observation period. However, the marked and maintained reduction in the number of reticulocytes shows that the absence of observable changes in the red cells results from the long life of the erythrocytes, taken together with the fact that our observations were not continued for more than 30 days.

In addition to the quantitative changes in the blood cells, qualitative changes were also observed, particularly in the neutrophils and thrombocytes.

The hypersegmentation of the neutrophil nucleus, which is typical of monkey blood, was already well marked by the 3rd day after irradiation. In some of the neutrophils, there were as many as 17-18 segments; occasionally there was a pathological granularity, and a dissociation between the times of maturation of protoplasm and nucleus. The occurrence of pyknotic thrombocytes, the formation of abnormal microforms and pale blue thrombocytes having no granules, and degenerative forms, was an indication that functional changes in the bone marrow had taken place, and that there had been a disturbance in it of hemopoiesis.

SUMMARY

Peripheral blood was studied in 18 monkeys (Macacus rhesus) in acute radiation sickness induced by a single x-ray irradiation with a dose of 600 r.

The principal features of the changes occurring in the blood of these monkeys were, in the main, identical to those revealed in other laboratory animals. In the monkeys, however, typically there were accentuated variations in the number of leukocytes during the first 24 hours, the nuclei formed an abnormally large number of segments, there was a more pronounced microthrombocytosis, and no thrombocytic irritation forms were present.

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