

## IMMUNOLOGICAL REACTIVITY OF MONKEYS FOLLOWING ACUTE RADIATION SICKNESS

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There is a vast amount of material in the literature on the effect of strong radiation on natural immunity indices, and particularly on antibody formation. Numerous investigations (1-5, 7-8) indicate that strong irradiation sharply inhibits the phagocytic activity of the leucocytes and reduces bactericidal and complementary indices. The dependence of the disturbances in immunogenesis on the size of the irradiation dose and also on the time elapsing between the radiation and the introduction of an antigenic stimulus has been shown. Thus, the basic principles of the change in immunological reactivity during acute radiation sickness have been established.

Concerning the decrease in the normal nature immunity indices and antibody formation, judging from data in the literature the opinion is held that these processes are normalized in the periods immediately after recovery from radiation sickness (1, 3, 6). It has been established (1, 3, 6) that antibody formation is completely restored 40-65 days after the acute radiation effect. However, during a study of the aftereffects of acute radiation sickness in monkeys it was found that there is a partial inhibition of antibody formation even 2-5 year after irradiation.\*

The purpose of this work was to study the condition of the natural immunity mechanisms, particularly antibody formation, a long time after a single general radiation effect.

### EXPERIMENTAL METHOD

The work was carried out with 77 Macao Rhesus monkeys of various ages and weights. The monkeys were exposed to radiation in doses of 150-700 r for 2, 5, 7 and 11 months and 1-5 years before the experiments. The RUM-3 apparatus and telegammacobalt equipment were used as the source of radiation energy. Of 17 monkeys irradiated with doses of 150-300 r four were treated with antibiotics, while nine irradiated with doses of 400-450 r survived without such treatment. Of 13 monkeys irradiated in doses of 500-550 r, 10 were treated with antibiotics and three were given complex therapy (bone marrow + hemogenesis stimulator). Of 35 irradiated with doses of 600-700 r five were treated with antibiotics, 17 received radiation sickness chemotherapy three survived without treatment, eight received an injection of bone marrow and antibiotics, and five were treated by complex therapy.

The complementary activity and bactericidal properties of the blood serum of 77 irradiated and 63 control animals were examined as natural immunity indices. Bactericidal properties were determined in relation to *E. coli* (strain No. 675) by the usual method. The decrease in antibody production against two kinds of antigens- dead typhoid bacteria and sheep erythrocyte- was studied in the same animals. For determination of agglutinin forming ability the monkeys were immunized with three or four subcutaneous injections of a formalin vaccine of typhoid bacteria (strain TV<sub>2</sub>). During threefold immunization the vaccine was injected in seven-day intervals in doses of 0.25, 0.5 and 1 billion bacteria in one ml. For single immunization a dose of 1 billion bacteria was used. To determine hemolysin forming ability a 50% suspension of sheep erythrocytes in a volume of one ml was injected intravenously. Phagocytic activity of the leucocytes toward Flexner dysentery bacteria (strain No. 2248) was examined in 44 irradiated and 24 control monkeys.

\*Reported at the general session of the Central Medical Radiology Scientific Research Institute of the USSR Ministry of Public Health, April 3-6, 1961 in Leningrad.

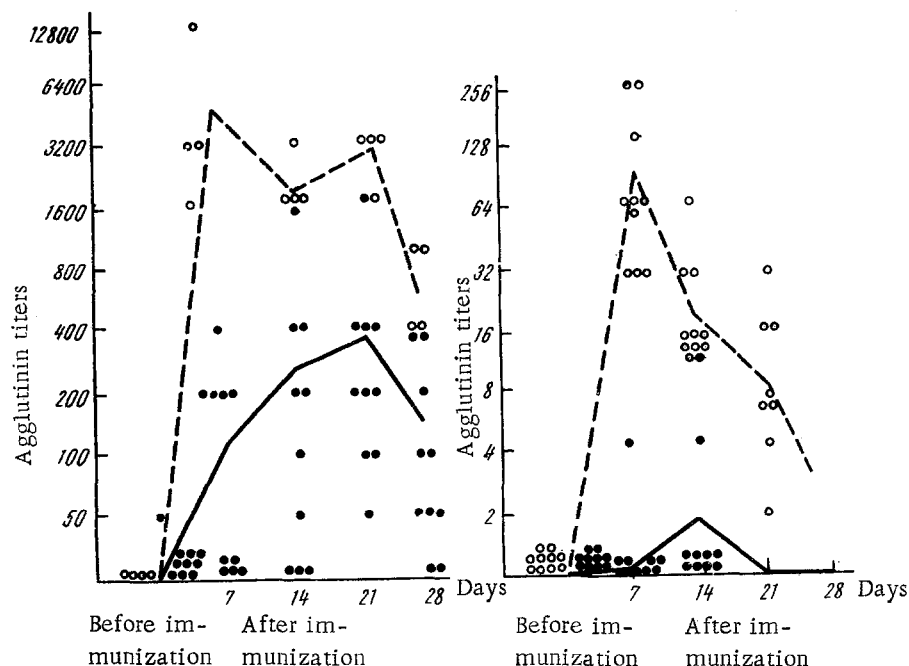


Fig. 1. Dynamics of antibody titers in monkeys 5-10 months after irradiation with doses of 630-700 r. Experimental group: solid line—average titers, dark circles—individual indices; control group: broken line—average titers, light circles—individual indices.

#### EXPERIMENTAL RESULTS

A study of the complementary activity of the blood serum of monkeys irradiated with doses from 300 to 675 r showed that 1, 2, 5 and 7 months after irradiation there were no differences in complement titer in the irradiated and control monkeys.

In the determination of the bactericidal activity of the blood of irradiated and control monkeys no important distinctions appeared. The blood serum of irradiated and intact monkeys showed a high degree of bactericidal activity.

During the investigation of the phagocytic activity of leucocytes—the percent of phagocytosis and the phagocyte index—there were no differences found between the indices obtained during a study of a majority of the monkeys irradiated with doses of 300-675 r and the control animals. In both groups phagocytosis was within the limits of 36-96% and the phagocytic index was 2.2-13.4. However, in individual animals examined 9-11 months after irradiation with doses of 450-675 r the phagocytic properties were lower (phagocytosis 10-18%, phagocytic index 0.16-1.2). During determination of phagocytic properties at much longer periods after irradiation (after 2, 4 and 5 years) significant differences were not found.

A study of the antibody level after irradiation with a dose of 300 r showed that after 1-3 years depression of antibody formation was not observed. Antibody titers in irradiated and control animals were the same. This appeared both with single and three-fold immunization.

Inhibition of antibody formation was observed in monkeys irradiated with a dose of 450 r after 10 months. Thus, on the 7th day after immunization with typhoid bacteria antibody titers varied from 0 to 1:200, on the 14th day from 1:200 to 1:400 and on the 21st day from 1:400 to 1:800, whereas in the control group in these same periods the titers reached 1:3200. Thus, the antibody (agglutinin) titers of irradiated animals sharply decreased in comparison with the controls.

Maximal titers were found not on the 7th day after single immunization but on the 21st day. However, in this period the antibody titer did not reach the same levels as in the control monkeys. Two to five years after irradiation with doses of 450-500 r differences in antibody titers between irradiated and control animals were not observed.

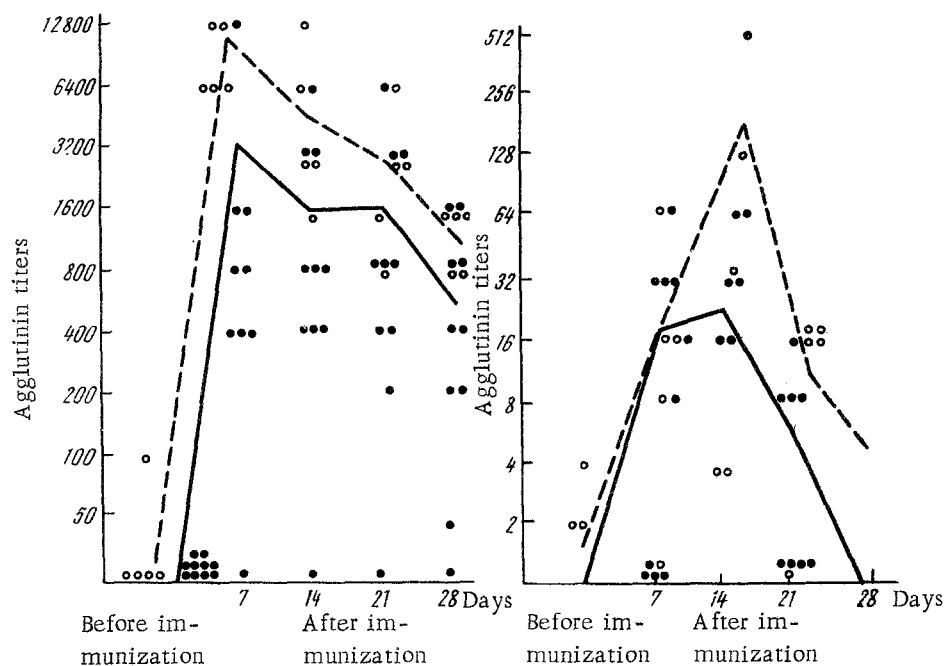


Fig. 2. Dynamics of antibody titers in monkeys 1-2 years after irradiation with a dose of 600 r. Notation same as in Fig. 1.

Inhibition of immunogenesis was found in animals irradiated with doses of 630-700 r upon immunization 2, 5, 7, 9 and 11 months after irradiation. A lower production of antibodies was noted in the majority of the animals after single immunization with typhoid vaccine and sheep erythrocytes. Seven days after immunization in a majority of the animals specific antibodies (hemolysins and agglutinins) were completely absent or the agglutinins were found in low (1:200) titers (in the control 1:1600 to 1:3200). Maximal agglutinin titers were found in most cases 14-21 days after immunization, however they never attained the antibody level of the control animals (Fig. 1).

Antibody production was inhibited during immunization and in later periods—1-2 years after irradiation with doses of 550-600 r (Fig. 2).

If immunization is carried out  $2\frac{1}{2}$ -5 years after irradiation with doses of 550-700 r, differences between the antibody titers in the blood of irradiated and control animals are not found. However, in some irradiated animals antibody buildup proceeds somewhat more slowly than in the controls. This appears particularly on the 7th day after the first antigen injection (with a dose of 0.25 billion bacteria) during three-fold immunization. In these periods the average agglutinin titer in monkeys irradiated with doses of 600-700 r was two times lower than in the controls. This may indicate some functional "inhibition" of the tissues taking part in antibody production.

Noticeable differences in immunological reactivity of the monkeys depending on the character of the treatment (therapy, preventive treatment) are not found.

Thus, our investigations showed that in periods long after acute radiation sickness the humoral indices of natural immunity do not show any kind of serious disturbances while the mechanisms of cellular nonspecific immunity in the first 10-12 months showed some depression in individual animals. The phagocytic indices, with rare exceptions, decreased 1-3 years after radiation damage.

Serious disturbances appeared in the production of antibodies by the animals during the two years after irradiation with doses of 450-800 r. A disturbance in antibody production was greater, the heavier the radiation effect, and was expressed in the varying degree of retardation and depression of the immunological reaction or even in its complete inhibition. An analysis of the results shows that apparent clinical recovery by no means indicates a re-establishment of normal immunological reactivity. Periods for complete reparation of the mechanisms responsible for antibody production after irradiation with doses of 550-700 r exceeded 1-2 years. It is necessary to assume that normalization of immunological reactivity indicates recovery of all the physiological functions damaged by the effect of radiation.

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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.