THE EFFECT OF IONIZING RADIATION ON THE REGENERATIVE PROCESSES RELATED TO BLOOD LETTING

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The combination of blood letting with irradiation allows an investigation of the character of radiation injury to the erythropoietic system, and the dependence of the reaction to radiation activity on the state of the organism at the moment of irradiation. The literature already contains a body of such works [1, 3-7], but in the majority of cases the authors were limited to investigating only changes in the integral quantity of cells, and the concentration of hemoglobin in the blood.

In this work we studied the changes in the age spectrum of peripheral blood erythrocytes following different combinations of blood letting and irradiation, the purpose being to obtain new data on the character of radiation damage to cells of the erythropoid population.

EXPERIMENTAL METHOD

Male rabbits weighing 2200-2500 g were subjected to the action of Co^{60} γ-radiation in a dose of 350 R. The irradiation was combined with blood letting, which was carried out one day prior to the irradiation, and one day and 6 days after it. As a control, we used rabbits subjected only to the blood letting. In each series we investigated 10 animals. The blood was drawn from the femoral artery in a quantity representing 2.2% of the weight of the rabbit (approximately 40% of the total blood volume of the animal). At 1, 8, 15, 22, and 29 days after the blood letting, blood samples were taken from the rabbits for determination of the hemoglobin concentration, erythrocyte count, and spectrum of erythrocyte distribution according to their dimensions. The procedure for determining the hemoglobin concentration, and number and spectrum of distribution of the erythrocytes, was described earlier [2].

EXPERIMENTAL RESULTS

For graphic rendering of the results obtained, we selected a group of young cells from the spectrum of erythrocyte distribution, equivalent to reticulocytes, and a group of adult cells, within the region of most probable dimensions for the spectrum of erythrocytes of normal animals, and thus entering the greatest contribution in the magnitude of the average characteristics for the population of the peripheral blood erythrocytes. Definition of the concepts "young" and "adult" cells was given earlier [2].

Blood letting caused an increase in the number of young cells in the blood of the irradiated and nonirradiated animals (Fig. 1, a). Irradiation, however, modified the reaction to the blood letting markedly: the rate of increase of the number of young cells and its duration was considerably lower in the irradiated animals than in the nonirradiated. It is easy to understand that a decrease in the rate of the rise represents a lowering of intensity of the sources of young cells, while a decrease in the duration of the rise signifies their earlier depletion. Out of all the cases investigated, the intensity of erythropoiesis was most depressed by irradiation on the day preceding the blood letting. Blood letting preceding irradiation by one day altered the state of the organism in a manner favoring erythropoietic functioning. According to the pitch in the rise of the curve, it may be judged that by the 6th day after irradiation the intensity of erythropoiesis was restored to a large degree, but its forerunning inhibition causes a substantial decrease in the duration of the rise in number of young cells, as compared with the normal.

In the animals that underwent blood letting without irradiation, and in the animals in which the blood letting was carried out one day after the irradiation, we observed an unvarying rise in the number of adult erythrocytes within the peripheral blood (Fig. 1, b). In the other two cases, the number of adult cells first fell and only after a minimum of 8 days began to increase.

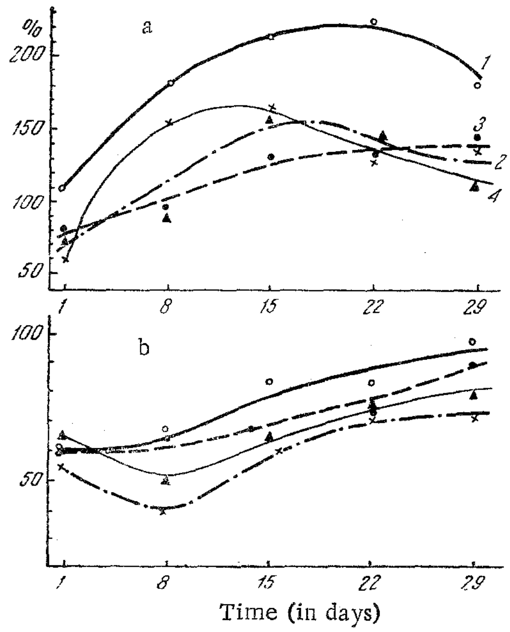


Fig. 1. Curves of restoration of the number of young (a) and adult (b) cells. Meaning of curves: for a – 1) blood letting without irradiation; 2) one day prior to irradiation; 3) one day after irradiation; 4) six days after irradiation; for b – (from above downward): blood letting without irradiation, one day after irradiation, one day prior to irradiation, six days after irradiation.

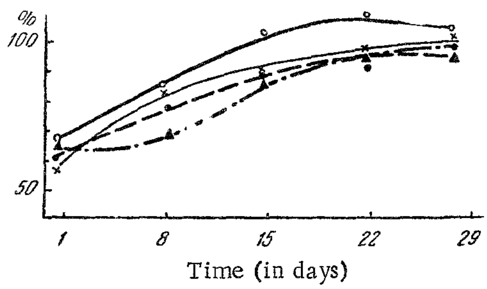


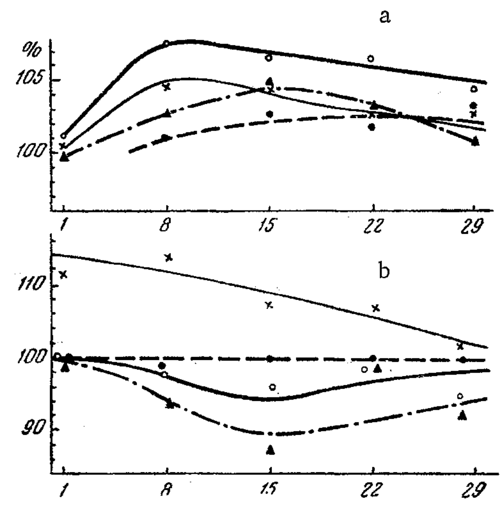
Fig. 2. Curves of restoration of the integral number of erythrocytes. Symbols are the same as in Fig. 1.

From an analysis of the curves shown in Fig. 1, a, it can be established that the intensity of erythropoiesis did not fall below the level characteristic of normal animals in a single one of the cases studied. Hence, the inflow of young cells was more than adequate to compensate for the disappearance of adult cells as a result of aging, provided the latter occurred at the normal rate. It would thus follow that a decrease in the number of adult cells would indicate an acceleration in the natural processes of aging and dying off of the cells during the period in which decreased numbers of adult cells were observed in the blood. With blood letting carried out 6 days after irradiation, this acceleration in the processes of aging and dying of the cells can be attributed to an increase in the average age of the erythrocyte population, related to inhibition of erythropoiesis during the period between the irradiation and the blood letting. Certain arguments for this thesis will be presented below. In the case where the blood letting preceded the irradiation by one day, a direct effect by the radiation on the processes of natural aging and dying of the cells apparently took place. Here the basic role is most likely played by an alteration in the general state of the organism, related to the preceding blood letting, inasmuch as in the very similar case of the blood letting following the irradiation by one day we did not observe a decrease in the number of adult cells.

In conclusion, we will consider the curves of restoration of the integral number of erythrocytes (Fig. 2). Above all, it must be noted that in the series with irradiation there was no essential sign of hyperregeneration of any kind, the latter being characteristic of the process of regeneration in nonirradiated rabbits [2]. This is easy to understand if one remembers that radiation activity markedly lowers the amplitude and duration of the increased intensity of erythropoiesis associated with blood letting. The curve of restoration of the integral number of erythrocytes representing blood letting performed one day before irradiation markedly lags, in the course of the first 10 days, behind the curves of restoration for the remaining series employing irradiation. A comparison with the corresponding curve depicted in Fig. 1, b, serves as a basis for assuming that the reason for this lag is an increase in the death rate of the adult cells during the first 8 days after the blood letting, which is not adequately compensated by the increase in intensity of erythropoiesis.

Measurement of the erythrocyte distribution spectrum according to dimensions makes it possible to investigate the dynamics of the change in mean dimension of the cell (Fig. 3, a). As could be expected, the maximum increase in mean cell dimension, reaching 7% of the original, was observed in association with blood letting without irradiation, when the amplitude and duration of the erythropoiesis stimulation peak were maximal. In the remaining cases, changes in the mean cell dimensions corresponded to the degree of the increase in erythropoiesis intensity. These facts provide a basis for confirming that changes in the mean cell dimensions are not caused so much by changes in the dimensions of cells circulating in the peripheral blood, as by an increase – dependent on the rise in the rate of their output – in the concentration of young cells of greater size.

The dynamics of the mean hemoglobin concentration of the cell is also of interest (Fig. 3, b). A change in the mean hemoglobin concentration of the cell occurs as a result of two processes which are of opposing tendencies. On the one hand, blood letting causes an output of large numbers of young cells into the peripheral blood, with a low



Time (in days)

Fig. 3. Curves for the changes in mean cell dimension (a) and mean hemoglobin concentration (b). Symbols are the same as in Fig. 1.

concentration of hemoglobin, which leads to a decrease in the mean hemoglobin concentration of the cell. On the other hand, radiation inhibition of erythropoiesis causes a decrease in the intensity of erythrocyte renewal, and thus, an increase in their mean age. Because of this, the mean hemoglobin concentration of the cell increases. With irradiation preceding the blood letting by one day, these tendencies compensate for one another, and the mean hemoglobin concentration of the cell remains unchanged, at the same time that blood letting without irradiation causes a decrease in the mean hemoglobin concentration of the cell. At first glance, the curve representing irradiation administered one day after the blood letting appears strange. Despite the fact that the amplitude and duration of the erythropoiesis stimulation peak are notably smaller in this case than in the case of blood letting without irradiation (see Fig. 1, a), the concentration of hemoglobin falls to a lower value. This is easy to understand if one takes into consideration the marked increase in the number of deaths of hemoglobin-rich adult cells observed with irradiation which occurred one day after the blood letting (see Fig. 1, b).

The curve representing blood letting performed 6 days after irradiation is of interest. In the initial period of restoration of the cell numbers, the mean hemoglobin concentration exceeded the normal by approximately 10%, which was caused by a drop in the intensity of erythrocyte renewal during the period between irradiation and blood letting. The output of young cells caused by blood letting increased their concentration in the peripheral blood, which led to a decrease in the mean hemoglobin concentration of the cell.

Thus, blood letting which precedes irradiation by one day favorably affects erythropoietic function, but increases the rate of dying of adult cells in the peripheral blood, as compared with blood letting carried out one day after irradiation. By the 6th day after irradiation with a dose of 350 R, the intensity of erythropoiesis is restored to a considerable degree.

SUMMARY

The effect of radiation on the restorative processes connected with blood letting was studied. An analysis was made of hemoglobin content, number of erythrocytes and the spectrum of their distribution according to sizes, occurring as a result of combined blood letting and irradiation. As demonstrated, irradiation in a dose of 350 R decreased the amplitude and the duration of the erythropoiesis stimulation peak occurring due to blood letting. The latter procedure done 24 hours before irradiation had a favorable effect on the erythropoietic function, but increased the intensity of mature cell disintegration (as compared to the effect of blood letting performed 24 hours after irradiation). The value of the erythropoiesis stimulation peak was largely restored by the 6th day; however, its length was still significantly reduced.

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