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- USSR -

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LOWERING THE IMMUNOBIOLOGICAL RESISTANCE OF THE ORGANISM AS A MANIFESTATION OF THE IRREVERSIBLE COMPONENT OF RADIATION SICKNESS

- USSR -

[Following is a translation of an article by I. G. Akoyev and M. A. Lagun in the Russian-language periodical Meditsinskaya Radiologiya (Medical Radiology), Vol VIII, No 2, Moscow, 1963, pages 47-50.]

According to hypotheses of I. F. Kovalyov and Blair — Davidson (G. Davidson; V. N. Korogodin and G. G. Polikarpov; Blair, Storer, H arris, Furshner, Longham; Sparling, Strang, Worman), all affections of an organism caused by ionizing radiation can be divided into two types which are conditionally called reversible and irreversible. By this is meant not only truly irreversible damage (for example, genetic), but also that which is very slowly restored in comparison with reversible damage.

The reversible component of radiation sickness is associated in the first instance with damage to tissue systems which have a high level of physiological regeneration(hematogenic, epithelial, and others). Using the degree of reduction in the organism's immunity to re-irradiation as a criterion of the

amount of remaining radiation damage, it was established that the restoration period of radioresistance of an organism depends directly upon the species peculiarities and first and foremost upon the rate of metabolism processes. The restoration period of radioresistance (which is identified with the reparation period of all reversible injuries) for mice turned out to be 12 to 20 days (Kohn, Kallmen, Rothermel, Woodard, Storer; Stearner, Tyler), and for man, according to the estimation by C. Davidson, this period stretches up to 200 days. According to our data, reparation of injuries in mice takes place in the course of 12 to 15 days. (Diagram 1 and Table 1).

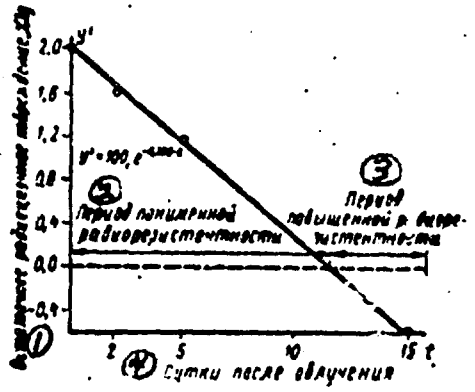

Diagram 1. Dynamics of reparation of reversible radiation injuries of mice after irradiation, dose 400 rontgens. Criterion — displacement of average-lethal doeses upon re-irradiation. (530 female mice, 2 to 3 months of age.)

Legend:

1. Residual radiation damage
2. Period of reduced radioresistance
3. Period of increased radioresistance
4. Days after irradiation

days. Upon double irradiation contamination occurred 30 days after the first irradiation. The animals were subjected to gamma rays Co^{60}, dosage rate 35r/minute. 150 white female mice ranging in age from two to three months were used in experiments.

The basic conditions of irradiation and results of the experiments are shown in Diagram 2 and in Table 2.

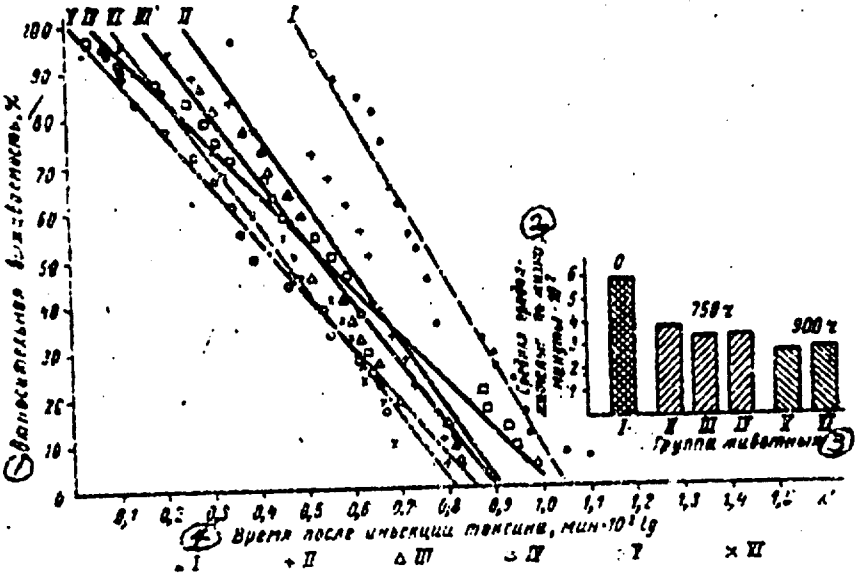

Diagram 2. Influence of conditions of preliminary irradiation on the life span of mice after contamination with toxin Vas. perfringens (contamination subcutaneous, dose 0.8 of experimental unit, 50 days after irradiation).

Probability of differences: Groups I and II, III, IV, V, VI -- R = 0.99; groups II and III, IV-R < 0.5; groups V and VI -- R < 0.5; groups II + III + IV and V + VI R = 0.99.

Legend: 1. Relative survival (%)
2. Average life span, minutes
3. Group of animals
4. Time after toxin injection, minutes.

(1) Группа	(2) Доза облучения, р	(3)	(4) Уравнение кривой	(5) Средняя продолжительность жизни, минуты
I	0	—	$y=187,5-170,5x'$	589±5,5
II	750	—	$y=150,0-135,2x'$	384±38
III	400+400	2	$y=128,4-118,6x'$	336±15
IV	400+400	5	$y=105,8-103,5x'$	342±15
V	400+500	5	$y=101,6-119,9x'$	273±4,1
VI	400+500	15	$y=113,6-136,9x'$	296±14

Table 2

Legend:

1. Group
2. Irradiation dose
3. Interval between irradiations
4. Equation of the curve
5. Average life span, minutes

In all the groups 100% mortality of the preliminarily irradiated animals was observed. The average life span of the controlled animals was 589 ± 5 minutes, but of those exposed to single irradiation, dose 750 r — 384 ± 38 minutes. Consequently, even in the period of time after the restoration of the organism's radioresistance, the immunobiological state remains disrupted. Inasmuch as after irradiation there elapsed more than three times the time necessary for reparation of reversible radiation injuries, it is possible to suppose that reduced immunity of these animals to a bacterial toxin is linked with the irreversible component of radiation sickness. To substantiate this situation it was also necessary to show that the degree of lesion of immunobiological

resistance depends neither upon fractionation of the dose nor upon an increase in time intervals between irradiations. The following experiments were conducted to examine these problems.

In the second series of experiments the animals were subjected to double irradiation of the same total dosage — 750 r (400 + 350 r) — the time interval between exposures two and five days. In this short period of time about 60 and 75% of the reversible radiation injuries is repaired (cf. Diagram 1). The average life span of these mice after contamination by the toxin (339 ± 13 and 342 ± 13 minutes) essentially did not differ from the group exposed to single irradiation. Consequently, the degree of lesion of immunobiological resistance of the organism essentially does not depend upon the conditions ofirradiation.

In the third series of experiments the influence of dosage and increased time interval between irradiations up to a period of time necessary for full reparation of reversible radiation alterations brought about by the first irradiation was examined. The animals of this series were exposed to double irradiation, total dosage 900 r (400 + 500 r). The second irradiation was conducted five and 15 days after the first.

The average life span of the mice in these groups was identical (273 ± 4 and 286 ± 14 minutes), which supports the abovecited observation that the conditions of irradiation (single or double) and time intervals between irradiations do not in-

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fluence the degree of lesion of the organism's immunobiological state. However, the average life span of the animals in the third series exposed to 900 r (279 ± 4.9 minutes) was considerably less than that of the animals in the second series exposed to 750 r (355 ± 14 minutes). This statistically significant difference (R = 0.99) in the life span after contamination by a toxin is apparently linked with a difference in the doses of preliminary irradiation. With an increase of the irradiation dose the degree of lesion of immunobiological resistance of the organism grew, which also led to a greater decrease in the life span.

Our experimental material made it possible to establish that in an irradiated organism and for a period of time after restoration of radioresistance and reparation of reversible radiation injuries, lesions remain in the mechanism of immunobiological resistance for an exceedingly protracted and still unestablished period of time. This mechanism determines the ability of the organism to counteract the influence of bacterial toxins. Manifestation of these lesions, which was displayed in the reduction of the average life span after contamination by the toxin, Vas. perfringens, increased when the irradiation dose was increased. However, the conditions of the influence of radiation (single or double) and increasing the time intervals between irradiations

did not influence the degree of reduction of the organism's immunity. This allows us to associate lesions in the mechanism of immunobiological resistance with the irreversible component of radiation sickness.

It was shown earlier (A. V. Popov with co-authors) that for a protracted time after irradiation of the animals simultaneously with the lowering of immunobiological reactivity, increased hemopoiesis hidden by a normal or anemic pattern of peripheral blood was noted as well as an increase in thyroid activity of the thyroid gland, which was not accompanied by growth of the organ. Continued introduction of thyroid led to normalization of the state of immunobiological resistance and hemopoiesis and brought the histological structure of the thyroid gland and thyroglobulin formation closer to that of healthy animals. Probably, manifestations of the irreversible component of radiation sickness are specifically linked with the state of the endocrine system. Hormone therapy decreases these manifestations and possibly accelerates partial or complete restoration of these radiation injuries, which are repaired with the greatest of difficulty.

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