

EFFECT OF X-RAY IRRADIATION ON HEALING
OF EXPERIMENTAL WOUNDS AT HIGH
ALTITUDES

T. G. Chernova

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Experiments on sexually mature rabbits showed that combined irradiation (with a total dose of 500 R, or more, especially local irradiation in a dose of 2000 R) given in one of the first two phases (especially phase I) of adaptation to high altitudes (3379 and 3640 m above sea level), leads to more severe morphological changes in the tissues and to longer delay in the healing of perforating wounds of the pinna than in the plains (820 m above sea level).

KEY WORDS: wound healing; x-ray irradiation; high altitudes; adaptation.

Despite their theoretical importance of the problem of the effect of ionizing radiation on repair processes in organs and tissues at high altitudes and its practical significance for the extensive highland regions of the Soviet Union, until recently its study has been almost completely neglected.

EXPERIMENTAL METHOD

Experiments were carried out on 969 gray rabbits weighing 1800-2600 g. All series of experiments comprised three variants: in the plains (Dushanbe, altitude 820 m above sea level), and in the hills (on Anzobskoe Pass, 3379 m above sea level, and in the region of Murzab, 3640 m); 1) on rabbits completely unadapted to high altitudes, 2) on rabbits relatively adapted (having spent 1 month in the hills and in phase II of adaptation), and 3) on indigenous rabbits born and bred in Khorog (2300 m above sea level). In each variant there were three series of experiments: on unirradiated animals, after whole-body irradiation in a dose of 500 R, and after local irradiation in a dose of 2000 R. Material for histological study was taken 2, 4, 8, 16, 30, and 60 days after trauma, which was inflicted immediately after irradiation. In some animals the time of complete healing of the wounds was noted macroscopically. The irradiation and wounding of the rabbits in space I of high-altitude

TABLE 1. Mortality among Rabbits Following Whole-Body X-Ray Irradiation in a Dose of 500 R

| Index | Number of animals | |
|--------------------------|-------------------|----------------------|
| | irradiated | dying within 1 month |
| In the plains | 33 | 3 |
| In the hills | | |
| indigenous rabbits | 30 | 1 |
| in phase I of adaptation | 93 | 33 |
| in phase II | 70 | 12 |

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TABLE 2. Changes in Body Weight and Peripheral Blood Leukocyte Count after Whole-Body X-Ray Irradiation of Rabbits with a Dose of 500 R (in % of initial level)

| Index | Times after irradiation, days | | | |
|--------------------------|-------------------------------|-------|--------|--------|
| | 2-3 | 7-8 | 16-17 | 29-30 |
| In the plains | 98/40 | 87/74 | 106/78 | 109/88 |
| In the hills | | | | |
| indigenous rabbits | 98/44 | 92/69 | 108/85 | 114/98 |
| in phase I of adaptation | 87/30 | 77/26 | 73/47 | 81/51 |
| in phase II | 89/36 | 88/58 | 90/68 | 102/78 |

Legend. Numerator, body weight; denominator, number of leukocytes

TABLE 3. Times (in days) of Healing of Perforating Wounds of the Pinna in Rabbits ($M \pm m$)

| Index | Without irradiation | Whole-body irradiation, 500 R | Local irradiation, 2000 R |
|--------------------------|---------------------|-------------------------------|---------------------------|
| In the plains | 41,1 \pm 3,4 | 37,7 \pm 1,8 | 72,0 \pm 1,6 |
| In the hills: | | | |
| indigenous rabbits | 34,0 \pm 3,0 | 33,0 \pm 2,3 | 53,6 \pm 4,0 |
| in phase I of adaptation | 58,8 \pm 3,8 | Not healed after 2 months | |
| in phase II | 53,0 \pm 3,5 | Ditto | |

adaptation were carried out 2-3 days after their arrival in the hills from the plains. Healing of perforating wounds formed in the center of the pinna of the left ear by means of a large metal punch, 6 mm in diameter, was studied.

The animals were irradiated both in the plains and in the hills on an RUM-3 therapeutic x-ray apparatus. Whole-body irradiation of the rabbits was given from the ventral aspect. For local irradiation of the pinna a container was used in which the whole body was protected by lead plates 6 mm thick. The conditions of whole-body irradiation were: voltage 180 kV, current 15 mA, filter 0.5 mm Cu + 1 mm Al, HVL (half-value layer), 1.1 Cu, skin-focus distance 50 cm, dose rate 16 R/min, duration of irradiation 31.1 min. The conditions of local irradiation were: voltage 160 kV, current 16 mA, filter 3 mm Al + 1 mm Al, HVL 0.2 Cu, skin-focus distance 20 cm, dose rate 124 R, duration of irradiation 16.1 min. Dosimetry was carried out by a team from the x-ray center of the Ministry of Health of the Tadjik SSR.

EXPERIMENTAL RESULTS

It will be clear from Tables 1 and 2 that animals in phase I of adaptation to high altitudes and irradiated in the hills were the most radiosensitive. The highest mortality and the greatest loss of weight and decrease in the peripheral blood leukocyte count, indicating the greatest severity of radiation sickness, were observed in these animals. Rabbits relatively adapted to high altitudes occupied an intermediate position for all indices. The most radioresistant animals were the indigenous rabbits, irradiated in the hills, in full agreement with data in the literature [1-4, 6, 7], according to which high-altitude acclimatization in the hills increases non-specific resistance. These rabbits were similar in their radioresistance to rabbits irradiated in the plains.

In rabbits irradiated and injured during the first days after their arrival in the hills from the plains considerable delay in regenerative processes was observed. After 2 months their wounds had still not healed (Table 3). Comparison of the state of the wounds in the early stages after trauma and irradiation showed greater inhibition of regeneration after local x-ray irradiation in a dose of 2000 R than after whole-body irradiation in a dose of 500 R.

After the animals had stayed in the hills for 1 month, i.e., in phase II of adaptation to high altitudes, the inhibition of regeneration caused by transportation from the plains into the hills was reduced.

It is interesting to note that after whole-body irradiation of the animals in the plains with a dose of 500 R a tendency was observed for the wounds to heal more quickly, just as Prizhivoit [5] found when studying the healing of perforating wounds of the pinna of rabbits after local irradiation in a dose of 500 R.

The increase in radiosensitivity of rabbits transported from the plains to the hills also was reflected in the greater vulnerability of the tissues to x-ray injury. Radiation burns were frequently observed in these animals, and after irradiation in phase I of adaptation skin lesions of this character also were seen after whole-body irradiation, when the dose of radiation received directly by the skin of the pinna was only 500 R.

The "Miescher reaction" of the irradiated epidermis, manifested as polynuclearity of the cells and a sharp increase in size and polymorphism of the nuclei, was well marked in all series of experiments with local irradiation in a dose of 2000 R. It followed a different time course in the plains and in the hills and in indigenous rabbits and those in phases I and II of adaptation. In most indigenous rabbits and those bred in the plains, the "Miescher reaction" appeared from the 4th day after irradiation and reached its climax in both sets of

animals on the eighth day. By the 30th day only traces of this reaction could still be seen in both cases, and then only in some animals.

Transportation of the rabbits from the plains into the hills delayed the manifestation of the "Miescher reaction" and recovery of the epidermis after radiation injury of this type. In animals irradiated in phase II of adaptation to high altitudes the climax of the "Miescher reaction" was observed between 8 and 16 days after irradiation, and after 30 days it was still considerable. In rabbits irradiated in phase I of adaptation to high altitudes the climax of the "Miescher reaction" generally took place between 16 and 30 days after irradiation, although traces could still be found even 2 months after irradiation. Meanwhile in animals irradiated soon after transportation from the plains into the hills the "Miescher reaction" attained its longest duration and "recovery" of the epidermis was greatly delayed.

To sum up, combined radiation injury (whole-body irradiation in a dose of 500 R or, more especially, local irradiation in a dose of 2000 R) given in one of the first two phases of adaptation to high altitudes (usually in phase I) leads to more severe morphological changes in the tissues than in the plains: A larger area of skin surface is affected and the rejection of necrotic tissues, the formation of granulations, and the epithelization are delayed.

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