QUANTITATIVE ASSESSMENT OF RADIATION INJURY TO MOUSE SKIN AFTER SINGLE AND FRACTIONAL IRRADIATION

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The attenuation factor for radiation injury to the skin on fractionation of the dose remains constant over a wide range of doses (128-2850 R). Radiation injury by doses of between 50 and 375 R was assessed from injury to the hair follicles during the period of hair growth, while between doses of 375 and 1900 R it was assessed by means of an integral skin damage characteristic based on visual observation of the course of the radiation reaction. Preparation of the object and the conditions of irradiation were strictly identical in the two series. To increase the accuracy of assessment of the damage, special mathematical methods were used to analyze the data.

Radiation injury to mouse skin was studied after single and fractional irradiation over a wide range of doses (from 50 to 2850 R). The severity of injury was assessed from the state of the hair follicles and the results of intravital observation on changes in the irradiated area of skin. For small and average doses of irradiation the first method of assessment was used; for average and high doses – the second method. In both cases special mathematical methods were used to estimate skin damage in units of dose of standard irradiation.

TABLE 1. Distribution of Hair Follicles by Degree of Injury After Single and Fractional Irradiation with Soft X-Rays

Group	No. of mice	Sessional dose of radiation (in R)	Total dose (with fractional irradiation; in R)	Percent of different types of injuries					
				0	I	II	III	IV	V
		Single irradiation							
1	5	50	—	100	—	—	—	—	—
2	5	75	—	83	17	—	—	—	—
3	5	110	—	36,8	49	13	1,2	—	—
4	5	170	—	1	16	48	30	5	—
5	4	250	—	—	2	9	57	27	5
6	5	300	—	—	—	1,4	24	45	29,6
7	5	375	—	—	—	—	—	—	100 0
		Fractional irradiation							
8	5	22	110	100					
9	5	33	165	82	18				
10	4	50	250	23	41	34	2		
11	5	75	375	—	5	31	41	20	3
12	5	110	550	—	—	—	7	29	64
13	5	130	650	—	—		0,7	9	90.3
14	5	170	850	—	—	—	—	—	100

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TABLE 2. Values of Attenuation Factors of Radiation Injury of the Skin After Fractional Irradiation (results of experiments of series I)

Radiation dose, R		Equiv. dose, single irrad., D_E, R	Attenuation factor, D_Σ/D_E	Mean attenuation factor
Sessional	Total, D_Σ			
33	165	74	2,2	1,88
50	250	128	1,95	
75	375	225	1,66	
110	550	316	1,74	

Both methods showed that the attenuation factor on fractionation of the doses remains constant (1.6-1.8) throughout the dose range studied. The results of the analysis of radiation injury by the state of the hair follicles can thus be extrapolated into the region of high doses producing epidermitis and ulceration.

It is convenient to assess the radiation reaction of the skin by means of methods based on the investigation of injury to the growing hair follicles [1-3]. The most accurate data can be obtained in this way. However, the upper limit of sensitivity of these methods is the dose producing temporary epilation.

The question arises whether results obtained by these methods can be extrapolated into the region of high doses. To examine this problem the relationship between the attenuation factor of the radiation reaction of the skin and fractionation of the dose was investigated over a wide range of doses. With small and average doses, injury was assessed by the epilation test, and for average and high doses by intravital observations on the course of the radiation reaction of the skin.

EXPERIMENTAL METHOD

Experiments were carried out on F_1 (CBA × C57BL) male mice weighing 22-26 g. The skin on the outer surface of the thighs was irradiated in all the experimental mice. Active hair growth was induced by preliminary mechanical epilation during the resting period of the hair cycle [4]. Single irradiation was given 10 days after epilation, and fractional irradiation began 8 days after this process (five sessions with 24-h intervals). The conditions of irradiation were: RUM-7 apparatus, 30 kV, 5 mA, filter 0.48 mm Al, skin-focus distance 75 mm, dose rate 90 R/min, tube 14 × 24 mm.

In the experiments of series I, injury to the hair follicles was studied in 70 animals. Four or five mice were used for each dose. The following doses were given: 50, 75, 110, 170, 250, 300, and 375 R for single irradiation and 22 × 5, 33 × 5, 50 × 5, 75 × 5, 110 × 5, 130 × 5, and 170 × 5 R for fractional irradiation. The mice were killed 3 days after single and 24 h after the fifth session of fractional irradiation. Radiation injury to the follicles was assessed by the method described previously [1, 2]. Five types of radiation injury were distinguished.

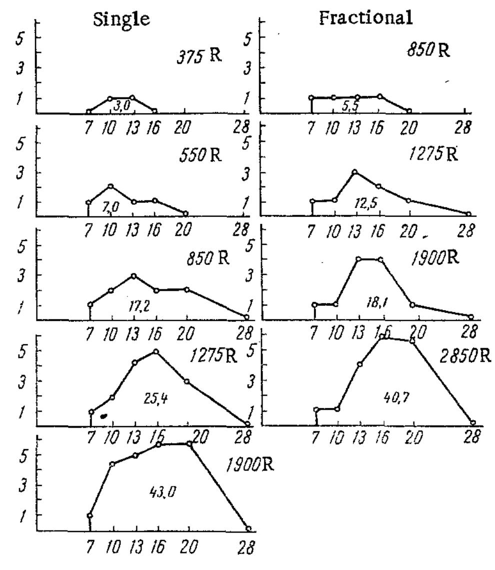

Fig. 1. Dynamics of radiation of mouse skin to single and fractional irradiation with soft x rays. Abscissa, days after beginning or irradiation; ordinate, mean rating, in points, of severity of skin damage. Numbers inside areas bounded by curves indicate their size.

In the experiments of series II the radiation reaction was assessed by intravital observation of the state of the skin, using 43 mice. For each dose, four or five animals were studied. The results of observation were recorded 7, 10, 13, 16, 20, and 28 days after single irradiation or after the first session of fractional irradiation. The following doses were used: 375, 550, 850, 1275, and 1900 R for single irradiation and 170 × 5, 255 × 5, 380 × 5, and 570 × 5 R for fractional irradiation. The severity of radiation injury to the skin was estimated by means of a six-point scale: total epilation 1 point, very slight scaling of the skin (dry epidermitis) – 2 points, severe scaling (dry epidermitis) 3 points, crusts of dried exudate (moist epidermitis) 4 points, scab 5 points, discharging ulcer 6 points, state of the skin before the onset of a visible reaction, scar, or commencing hair growth – 0.

EXPERIMENTAL RESULTS

The results of the experiments of series I are given in Table 1. To calculate the attenuation factor with an accuracy corresponding to the accuracy of experimental determination of the distribution of hair follicles by types of injury, the fol-

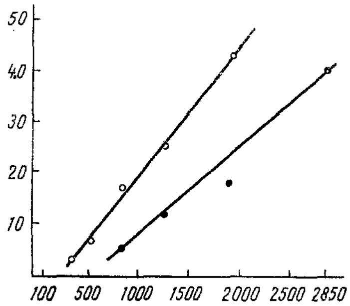

Fig. 2. Severity of radiation injury to skin as a function of dose for single and fractional irradiation. Graphs plotted with the use of an "integral criterion." Empty circles denote single irradiation, filled circles fractional irradiation. Abscissa, dose (in R); ordinate, severity of radiation damage to skin (in conventional units, areas bounded by curves in Fig. 1).

lowing mathematical method was used. A system of linear equations was compiled as follows:

$$D^j = D_0 + \sum_{i=1}^{4} \alpha_i P_i^j,$$

where D^j is the experimental dose of irradiation (in R); D_0 the maximal dose for which no visible damage to the hair follicles is yet produced; P_i^j the percentage of injuries of the i-th degree after irradiation with a dose D^j; α_i a constant with the value of 1% of injuries of the i-th degree expressed in roentgens. The values of D^j and P_i^j are taken from experimental results (Table 1), and D_0 and α_i are calculated by solving a system of linear equations. By using values of 75, 110, 170, 250, and 300 R as single doses of irradiation and taking the fourth and fifth types of injury together, the following rounded values of the coefficients were obtained: $\alpha_1 = 0.65$ R, $\alpha_2 = 1.07$ R, $\alpha_3 = 1.7$ R, and $\alpha_4 = 2.6$ R. It is essential to note that the solution obtained was stable despite variations in the values of D^j and P_i^j within the limits of experimental accuracy of their determination.

It was then easy to determine the attenuation factor for radiation injury to the skin. Any distribution of hair follicles by severity of injury could be estimated in roentgens of standard (in the case concerned, single) irradiation. By comparing this reduced dose with the actual dose of fractional irradiation the attenuation factor could be calculated directly. The results of the appropriate calculations are given in Table 2.

The results of the experiments of series II are illustrated in Fig. 1. For each dose of irradiation a graph reflecting a change in the mean rating of the injury (in points) with time for the group of mice was plotted. To calculate the attenuation factor it was necessary to estimate the degree of injury numerically; as the numerical measure the area bounded by the broken line on the graph and the abscissa (Fig. 1) was chosen. This number is essentially the integral of injury with time.

The severity of injury calculated as described above as a function of dose for single and fractional irradiation is shown in Fig. 2. It is clear from this graph that both with single and with fractional irradiation the severity of skin damage is an approximately linear function of dose. The attenuation factor remained approximately constant: 1.6-1.8.

It can be concluded from a comparison of the results of the experiments of series I and II that the attenuation factor for radiation injury of the skin after fractional irradiation is constant over a very wide range of doses (128-2850 R). Strictly speaking, this conclusion must be accompanied by the qualification "provided that this method is used to assess the severity of radiation injury to the skin." However, this qualification does not detract significantly from the value of the conclusion drawn above, for both methods used to assess the severity of the skin damage are natural and comparable (they are both a question of integral effects over a period of time in each case). The methods described in the paper can be used to study the way in which attenuation factors for radiation skin injury depend on dose or on other variations in the conditions of irradiation.

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