THE EFFECT OF TOTAL BODY IRRADIATION ON WOUND CLOSURE*

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A NEW PROBLEM has been posed to the surgeon by the potential threat of atomic warfare. Does the local action of irradiation or its effect on the internally situated radiosensitive tissues influence the closure of wounds? If so, is such influence more pronounced immediately following exposure or at the height of the febrile stage of the illness? The answers to these problems would be important in determining the optimum time for operative intervention in atomic bomb casualties.

Previous studies of the influence of irradiation and wound healing by Nathanson[4] and Pohle and Ritchie[5, 6, 7, 8] were directed at the effect of locally applied irradiation. The present study deals with the effect of total body exposure of rats to 250 kv roentgen rays on the rate of closure of excised wounds.

EXPERIMENTAL METHOD

Animals. The total project consisted of three related but distinct experiments. In each experiment 36 albino male rats† of approximately 150 Gm. in weight were segregated equally into two large cages until a weight of over 200 Gm. was attained.‡ Rats from each cage were then selected at random and individually segregated in racks of suspended cages consisting of six tiers of six cages each. Throughout each experiment all 36 rats were handled at the same time and in the same manner to exclude, as far as possible, extraneous environmental effects.

Wounds. Surgically excised wounds, 2.5 cm. in diameter and extending in depth to include the *panniculus carnosus,* were studied. With the animals under ether anesthesia and using sterile technics, the wounds were centrally placed on the dorsal aspect of the thunk, with the superior margin of the wound just distal to the inferior angle of the scapulae. No dressings or bacteriacidal preparations were used.

Measurement of Wound. In order to obtain a precise method for measuring the surface area of each wound, the wounded area was photographed immediately after wounding and at three-day intervals until complete closure had occurred. The apparatus used is shown in Figures 1 and 2. This consists of a stand with two lateral supports for floodlights and a central support for the camera.* Just below the camera is a bridge joined by a sheet of one-quarter-inch leucite with a small rectangle cut out of its center. At one edge of this rectangle a portion of a metric ruler was attached. The animal was then held firmly against the leucite with the wounded area framed within the cut-out area. This arrangement allowed the level of the wound edge to correspond almost exactly with the

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† Rats used were of the Sprague-Dawley strain obtained from the Holtzman Rat Co., Madison, Wisconsin.

‡ The diet consisted entirely of Purina fox chow checkers.

* The camera used was a 35 mm. Kine-Exacta II.

level of the ruler. The print of each picture was enlarged and the precise surface area determined by means of planimeter tracings on the print. When colored film was used, the negatives were projected on a Kodaslide table viewer, the wound edges outlined on Traceoline paper, and the area obtained by planimeter tracings on the paper. A mathematical factor was obtained to correct for the enlargement.

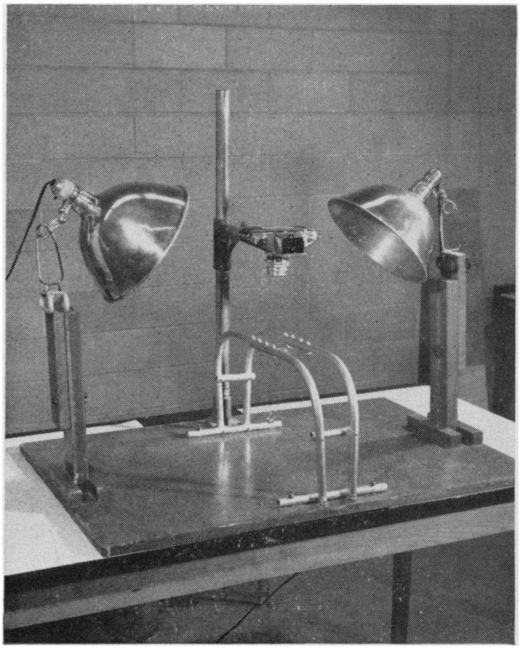

FIG. 1. Equipment designed for photographing wounded areas.

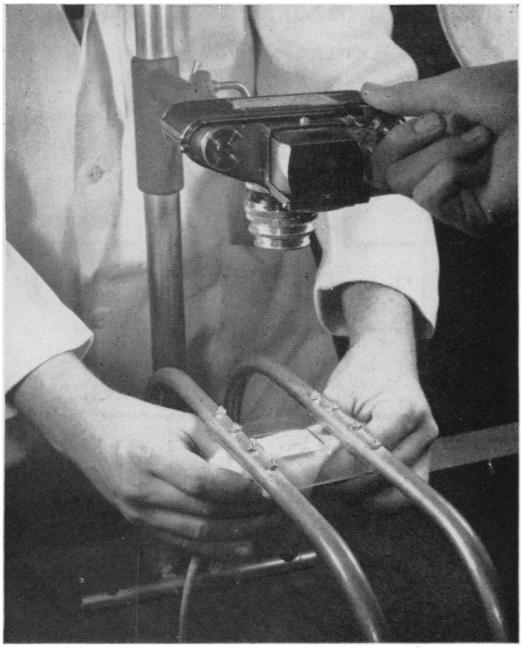

FIG. 2. Close-up of camera and animal with the wounded area outlined within the leucite frame.

Amount of Irradiation. Total body irradiations of 150 r, 450 r and 650 r were delivered with a Picker 250 kv, 15 ma, industrial roentgen ray unit. An aluminum parabolic filter plus 0.5 cm. of copper was used. The animals were placed in separate compartments of a circular, revolving wire cage. The target skin distance in each instance was 25 inches.

Treatment. The first 36 rats were subdivided into six groups of six animals each, and these were labeled A, B, C, D, E and F. Within a group each rat was numbered from one to six. The letters and numbers were assigned at random, according to the Latin square arrangement (Fig. 3). This insured that each treatment group appeared once and only once in each row and in each column of cages.

Groups A and D were used as controls and received no irradiation. Groups B and E were given total body irradiation calculated to be 150 r on the basis of exposure to an intensity of 18.1r/minute for a total time of eight minutes and 17 seconds. Simultaneously, groups C and F were exposed for 24 minutes and 51 seconds at the same intensity, and the total body irradiation was calculated to be 450 r. Groups A, C and E were wounded on the day of irradiation and groups B, D and F two weeks later.

The second 36 rats were divided into six groups designated as G, H, I, J, K and L, and were also assigned numbers according to the Latin square arrangement. G and H were used as controls and received no irradiation. Groups I and J were exposed to an intensity of 16.6 r/minute for nine minutes, receiving a total dosage of 150 r. Groups K and L were exposed to the same intensity for 27 minutes, receiving a total dosage of 450 r. Groups G, I and K were wounded four weeks after groups I and K had been irradiated, and groups H, J and L were wounded after another four weeks.

C1	F1	E1	A1	B1	D1
B2	D2	F2	C2	A2	E2
F3	B3	C3	E3	D3	A3
A4	E4	D4	B4	C4	F4
D5	A5	B5	F5	E5	C5
E6	C6	A6	D6	F6	B6

FIG. 3. Depicting the cage arrangement utilizing the Latin square, thus insuring one of each treatment in each row and each tier of cages.

The third group of 36 rats was divided into six groups of six rats each and designated in an objectively random manner as M, N, O, P, Q and R. Groups M, O and Q were designated as controls and received no irradiation. Groups N, P and R were subjected to an intensity of 18.5 r/minute for 35 minutes, receiving a total dosage of 650 r. Groups M and N were wounded immediately; groups O and P were wounded one week, and groups Q and R were wounded two weeks after the date of irradiation.

All rats were weighed prior to irradiation, at weekly intervals, and just before sacrificing. Each wound was biopsied one week after complete closure.

RESULTS

Animals exposed to 150 r and 450 r. The animals exposed to 150 r and 450 r showed no gastro-intestinal symptoms, weight loss or mortality due to the action of the roentgen rays. Blood counts and the more refined measures of irradiation injury, such as decrease in spleen, thymus and testicular weight and microscopic study of the bone marrow were not attempted. The wounds of the treated animals closed as cleanly as those of the controls, and there was no deceleration in the rate of closure.

Statistically, there was a very slight indication that the animals subjected to the larger irradiation dosage closed their wounds more rapidly.

The data for the control animals and those having received 150 r and 450 r and wounded immediately and two weeks later are found on Table I. Table II represents the same for the groups wounded four and eight weeks after irradiation.

*Animals exposed to 650 r**. The data for the rate of wound closure in the animals given 650 r and their controls are shown on Table III.

The animals subjected to the 650 r level of roentgen ray exposure presented a somewhat different picture. Ten days after exposure every treated rat showed evidence of radioactive illness. This consisted of anorexia, weight loss and varying degrees of bloody diarrhea. Over 20 per cent of the rats (N_2, P_3, P_5 and R_6) died within 30 days after exposure. At autopsy widespread intrapleural, intraperitoneal and gastro-intestinal hemorrhages were found in those

* An LD 20 was actually obtained, but previous studies led us to believe an LD 50 was possible with this dosage.

TABLE I.

Date	A1	A2	A3	A4	A5	A6	Date	B1	B2	B3	B4	B5	B6
3/13	5.88	5.44	5.61	5.85	5.78	5.61	3/27	7.21	6.56	6.60	6.91	6.67	6.60
3/16	4.05	4.25	4.15	4.79	3.84	4.42	3/30	4.97	4.93	4.49	5.17	4.66	4.86
3/19	3.57	3.77	3.13	4.39	3.02	4.15	4/2	4.49	3.09	4.08	3.81	4.05	4.08
3/22	1.872	2.04	1.87	1.77	1.83	2.11	4/5	3.47	1.70	1.70	2.31	2.00	2.14
3/25	1.08	1.02	1.42	1.29	1.02	1.32	4/8	2.00	0.74	1.25	1.32	1.36	1.12
3/28	0.64	0.68	1.05	0.74	0.54	0.74	4/11	1.32	0.54	1.32	0.85	0.57	0.47
3/31	0.34	0.20	0.71	0.37	0.34	0.51	4/14	0.68	0.27	0.47	0.51	0.34	0.17
4/3	0.20	0.06	0.06	0.23	0.06	0.20	4/17	0.17	0.10	0.17	0.40	0.17	0.10
4/6	0.06			0.10		0.17	4/20	0.06			0.30	0.10	
b[1]	−0.2357	−0.2672	−0.2426	−0.2243	−0.2766	−0.2058		−0.2426	−0.2568	−0.2094	−0.1817	−0.2378	−0.2742
	97.3%	93.0%	87.6%	97.4%	94.6%	97.4%		90.5%	98.2%	92.9%	99.0%	98.1%	96.1%
Date	**C1**	**C2**	**C3**	**C4**	**C5**	**C6**	**Date**	**D1**	**D2**	**D3**	**D4**	**D5**	**D6**
3/13	5.85	6.29	6.36	5.85	6.46	5.37	3/27	7.21	6.33	5.85	6.46	6.63	6.53
3/16	4.42	4.05	4.86	5.85	5.27	4.97	3/30	4.73	4.49	3.47	5.48	4.39	4.25
3/19	4.08	3.40	4.83	5.85	4.73	4.42	4/2	3.94	3.30	2.45	4.08	3.47	2.65
3/22	2.89	2.04	3.23	2.96	2.68	2.99	4/5	1.80	1.83	1.08	1.87	2.00	1.08
3/25	1.22	0.78	2.07	1.56	1.56	1.32	4/8	0.74	1.15	0.71	0.74	1.15	0.64
3/28	0.71	0.47	1.53	1.08	0.98	0.68	4/11	0.57	0.71	0.30	0.40	0.71	0.51
3/31	0.44	0.23	0.88	0.44	0.51	0.47	4/14	0.30	0.51	0.20	0.13	0.40	0.17
4/3	0.20	0.10	0.51	0.10	0.13	0.10	4/17	0.17	0.17	0.06		0.27	
4/6	0.10		0.37										
b[1]	−0.2263	−0.2579	−0.1610	−0.2498	−0.2272	−0.2539		−0.2407	−0.2132	−0.2689	−0.2865	−0.2114	−0.2473
	96.4%	97.4%	97.0%	89.2%	92.5%	93.1%		98.4%	97.4%	98.6%	95.4%	99.3%	98.5%
Date	**E1**	**E2**	**E3**	**E4**	**E5**	**E6**	**Date**	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
3/13	6.09	5.17	5.44	6.29	6.29	6.09	3/27	6.33	6.29	7.45	5.41	6.94	6.50
3/16	4.76	4.28	4.69	4.97	4.86	4.08	3/30	4.35	4.76	5.17	3.94	4.90	4.90
3/19	4.15	3.84	4.25	4.15	4.15	3.74	4/2	3.71	4.08	4.59	3.57	3.84	3.94
3/22	2.55	3.13	1.36	1.90	1.87	1.83	4/5	1.80	2.41	2.72	2.00	2.41	2.58
3/25	1.05	0.85	1.02	0.68	1.39	1.08	4/8	1.15	1.32	1.46	1.12	1.36	1.77
3/28	0.81	0.44	0.64	0.47	0.98	0.68	4/11	0.44	0.85	0.78	0.51	0.71	0.85
3/31	0.51	0.30	0.44	0.23	0.40	0.30	4/14	0.30	0.37	0.51	0.30	0.40	0.50
4/3	0.34	0.13	0.17	0.17	0.17	0.10	4/17	0.17	0.17	0.30	0.06	0.06	0.30
4/6	0.17												
b[1]	−0.1995	−0.2401	−0.2105	−0.2481	−0.2185	−0.2357		−0.2227	−0.2239	−0.1800	−0.2576	−0.2607	−0.2010
	97.9%	93.4%	96.7%	97.1%	76.8%	89.1%		87.6%	96.0%	96.6%	93.0%	91.5%	96.0%

Dated figures represent the area of the wound in square centimeters.
b[1]—is the average rate of change of the logarithms of the area per observation period.
%—is the percentage of total sum of squares of deviations from the mean explained by the linear fit—a measure of the goodness of fit of the straight line.

animals which died presumably from the action of irradiation. The gross appearance of the wounds of the treated animals did not differ from the controls. Statistical consideration of the data indicated quite strongly that the wounds of the treated animals closed more rapidly than did those of the controls.

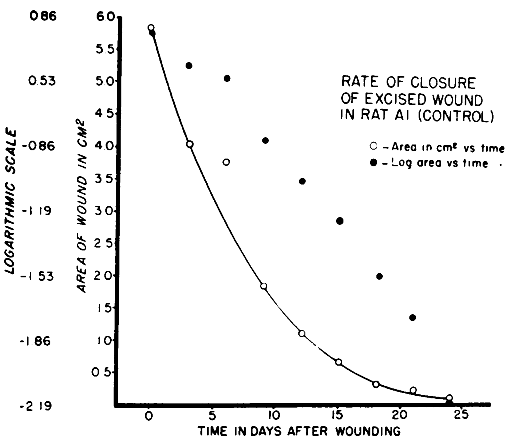

FIG. 4. Shows typical closure curve for an excised wound in a control animal.

STATISTICAL ANALYSIS

The data consist of the successively measured wound areas on each animal. These are presented in Tables I, II and III.

The set of measurements for each animal was treated as a unit. It was noted that the area of the wound plotted against time gave an approximately exponential relationship for each animal. Therefore, the logarithms of the areas plotted against time were almost linear (Fig. 4).

Straight lines were fitted to the transformed (logarithmic) data for each animal by the method of least squares. The time axis was measured in observation period (3 days) units. The slope of each of these fitted lines represents an estimated wound closure rate (*i.e.*, the time rate of change of the logarithms of the areas). The slope (multiplied by 100) may also be interpreted as an estimate of the instantaneous percentage change in actual wound area. These slopes are indicated by the row labeled b_1 in Tables I, II and III.

Higher ordered polynomials (quadratic and cubic) fitted to the transformed data did not significantly reduce the variation in most cases. The amount of the variation of the transformed data which is taken out or "explained" by the straight line can be conveniently expressed as the ratio of the reduction in the sum of squares effected by fitting a straight line to the total sum of squares of deviations from the mean. These ratios for each animal, expressed as percentages, are given in Tables I, II and III. The fact that they are all in the neighborhood of 90 per cent indicates that the straight lines explain a large amount of the area variation for each animal.

The group means of the estimated closure rates and their standard errors are presented in Table IV.

The set of experimental treatments used in each of the three experiments was factorial in nature. Thus, in each of the first two experiments all possible combinations of three irradiation doses and two wounding dates were used, and in the last experiment all combinations of two doses and three times of wounding were used. The effect of time of wounding and the irradiation dosage effect and their interaction can be tested by well-known statistical methods.*

In the first experiment the evidence indicates that the rate of wound closure is the same for all the groups considered.

In the second experiment there is no strict evidence that the closing rate is not the same for all groups considered. There is a slight indication, however, that heavy irradiation may actually accelerate the rate of closure.

In the final experiment the difference between the mean of the irradiated group

* See, for example, G. W. Snedecor, *Statistical Methods*, 4th ed., 1946, p. 423.

Table II.

Date	G1	G2	G3	G4	G5	G6	Date	H1	H2	H3	H4	H5	H6
5/24	6.43	6.46	6.05	6.77	6.19	6.05	6/21	6.43	5.88	5.95	6.12	6.36	5.85
5/27	4.73	4.69	4.05	4.86	4.59	4.59	6/24	4.79	4.56	5.00	4.42	4.66	4.83
5/30	4.22	3.74	3.54	4.45	4.49	4.42	6/27	4.49	3.91	4.59	4.05	4.08	4.11
6/2	2.48	1.97	1.87	1.56	2.79	2.34	6/30	3.47	1.87	2.17	2.11	2.00	1.87
6/5	1.08	1.39	1.02	1.22	1.32	1.29	7/3	1.77	1.19	1.19	1.08	0.88	1.22
6/8	0.68	0.88	0.64	0.74	0.85	0.81	7/6	1.36	0.74	0.64	0.74	0.71	0.61
6/11	0.37	0.74	0.44	0.51	0.44	0.68	7/9	0.85	0.47	0.34	0.34	0.37	0.27
6/14	0.27	0.68	0.23	0.27	0.13	0.27	7/12	0.61	0.10	0.13	0.17	0.10	0.23
6/17	0.27	0.54	0.17	0.13	0.29	0.10	7/15	0.47	0.06	0.06		0.13	0.40
6/20		0.28	0.13		0.13		7/18	0.30				0.06	0.13
							7/21	0.20					
b¹	−0.1908	−0.1243	−0.1964	−0.2124	−0.2081	−0.2143		−0.1474	−0.2487	−0.2477	−0.2256	−0.2155	−0.1892
	96.7%	91.4%	99.0%	98.1%	94.9%	95.3%		98.1%	94.8%	97.2%	97.0%	94.9%	83.2%

Date	I1	I2	I3	I4	I5	I6	Date	J1	J2	J3	J4	J5	J6
5/24	6.19	6.16	6.53	7.50	5.78	6.09	6/21	6.09	6.56	6.22	6.02	6.12	5.31
5/27	5.10	4.73	5.27	4.90	4.73	4.35	6/24	4.76	5.20	5.48	4.76	5.07	4.73
5/30	4.76	4.01	5.17	4.42	4.49	4.22	6/27	4.15	4.56	5.27	4.69	4.66	4.15
6/2	2.28	2.00	2.14	2.79	2.31	2.11	6/30	2.65	2.45	3.84	3.02	2.75	2.45
6/5	1.25	1.29	1.42	1.73	1.32	0.68	7/3	2.00	0.98	1.77	1.25	1.42	1.46
6/8	1.08	0.74	0.85	0.68	0.91	0.47	7/6	1.53	0.61	1.29	1.19	1.08	0.95
6/11	0.54	0.61	0.44	0.71	0.57	0.34	7/9	1.29	0.34	0.71	0.51	0.61	0.64
6/14	0.27	0.30	0.13	0.47	0.17	0.17	7/12	1.02	0.17	0.30	0.30	0.40	0.47
6/17	0.27	0.27		0.34		0.06	7/15	0.71		0.47	0.17	0.34	0.30
6/20	0.23	0.13		0.27			7/18	0.27		0.44	0.06	0.10	0.34
							7/21	0.20		0.40			0.27
							7/24	0.10		0.37			0.17
b¹	−0.1805	−0.1875	−0.3239	−0.1635	−0.2094	−0.2477		−0.1536	−0.2386	−0.1306	−0.2177	−0.1914	−0.1513
	96.6%	98.7%	94.1%	96.6%	93.7%	97.0%		95.5%	96.9%	90.5%	96.1%	96.6%	88.5%

Date	K1	K2	K3	K4	K5	K6	Date	L1	L2	L3	L4	L5	L6
5/24	6.43	6.29	6.22	6.22	6.60	6.94	6/21	6.84	6.39	6.05	6.91	5.95	6.19
5/27	4.39	4.28	4.66	4.73	4.76	5.07	6/24	4.35	4.76	4.83	5.85	4.79	5.10
5/30	4.08	4.15	4.73	4.49	4.15	4.39	6/27	4.32	3.81	3.94	5.68	4.42	5.07
6/2	2.14	2.58	2.31	2.24	1.90	1.63	6/30	2.96	1.70	1.77	4.25	2.34	3.40
6/5	1.02	1.53	1.46	1.29	1.36	0.64	7/3	1.36	0.98	0.74	2.34	1.32	2.00
6/8	0.78	0.78	1.08	0.74	0.98	0.23	7/6	0.78	0.54	0.27	1.29	0.74	1.19
6/11	0.17	0.47	0.68	0.17	0.44	0.06	7/9	0.51	0.44	0.06	0.98	0.44	0.47
6/14	0.06	0.17	0.30		0.37		7/12	0.20	0.17		0.57	0.40	0.40
6/17		0.10	0.13		0.23		7/15	0.10			0.61	0.37	0.34
6/20					0.13		7/18				0.30	0.34	0.20
							7/21				0.27	0.10	
b¹	−0.2781	−0.2294	−0.2033	−0.2440	−0.1912	−0.3398		−0.2288	−0.2257	−0.3239	−0.1515	−0.1579	−0.1808
	92.8%	95.9%	95.8%	90.2%	98.8%	94.4%		96.3%	97.9%	92.8%	97.9%	96.2%	96.2%

TABLE III.

Date	M1	M2	M3	M4	M5	M6
7/25	7.22	7.61	7.64	7.05	7.65	6.46
7/28	5.42	4.69	5.53	5.22	5.32	5.00
7/31	4.50	4.43	4.43	4.52	4.46	4.16
8/3	2.32	2.03	2.12	2.59	1.97	3.03
8/6	1.57	1.03	1.56	1.60	0.60	1.22
8/9	0.87	0.86	1.40	1.50	0.43	0.57
8/12	0.47	0.50	0.93	1.16		0.60
8/15	0.17	0.13	0.46	0.99		0.49
8/18		0.03	0.17	0.50		0.31
8/21				0.31		
b'	−0.2229	−0.2775	−0.2494	−0.1434		−0.1472
	97.2%	92.4%	85.2%	97.5%		90.0%

Date	N1	N2	N3	N4	N5	N6
7/25	7.14	7.41	6.84	7.71	7.59	6.86
7/28	5.61	4.78	4.89	5.01	6.01	5.03
7/31	5.41	3.68	3.13	4.43	4.69	4.36
8/3	2.72	2.33	2.72	3.36	3.65	2.60
8/6	1.54		0.60	1.46	1.27	1.04
8/9	0.74		0.40	1.09	0.74	0.57
8/12	0.44		0.14	0.78	0.37	0.39
8/15	0.27		0.01	0.37	0.27	0.16
8/18	0.13					
8/21						
	−0.1750		−0.3543	−0.1955	−0.2369	−0.3001
	94.4%		90.3%	94.3%	97.0%	90.0%

Date	O1	O2	O3	O4	O5	O6
8/1	6.32	5.91	6.85	6.94	7.46	5.86
8/4	4.95	4.49	5.26	5.16	5.05	4.42
8/7	4.83	3.58	4.79	4.70	3.58	4.18
8/10	2.83	1.89	2.59	2.27	1.50	2.07
8/13	1.69	1.36	1.66	1.34	1.07	1.22
8/16	1.14	1.19	1.37	0.82	0.70	0.73
8/19	1.02	0.79	0.97	0.50	0.33	0.34
8/22	0.63	0.57	0.40	0.60	0.24	0.33
8/25	0.43	0.29	0.21	0.57	0.07	0.16
8/28	0.27	0.20	0.17	0.14	0.01	0.10
b'	−0.1552	−0.1518	−0.1822	−0.1690	−0.2816	−0.2369
	98.8%	98.8%	97.5%	94.8%	96.1%	94.4%

Date	P1	P2	P3	P4	P5	P6
8/1	6.65	7.69		7.31	6.79	6.51
8/4	5.69	5.36		5.41	6.01	5.48
8/7	5.08	4.86		4.53	5.49	5.22
8/10	2.87	2.02		2.55		3.32
8/13	1.76	1.14		1.30		1.93
8/16	1.12	0.87		0.74		1.07
8/19	0.89	0.59		0.59		0.72
8/22	0.56	0.41		0.14		0.26
8/25	0.41	0.29				0.19
8/28	0.30	0.17				
	−0.1697	−0.1765		−0.2980		−0.2063
	98.4%	98.0%		87.7%		95.3%

Date	Q1	Q2	Q3	Q4	Q5	Q6
8/8	6.65	5.69	6.31	5.61	6.86	7.18
8/11	5.05	4.29	4.93	5.03	4.68	4.86
8/14	4.06	3.79	4.32	3.88	4.13	3.80
8/17	1.90	1.89	3.73	2.89	2.12	2.26
8/20	1.19	0.73	3.23	1.36	1.74	1.36
8/23	0.86	0.59	0.89	0.74	1.79	1.02
8/26	0.51	0.43	0.41	0.41	1.16	0.33
8/29	0.70	0.40	0.29	0.30	0.96	0.31
9/1	0.34	0.19	0.07	0.07	0.07	0.19
b'	−0.1472	−0.1922	−0.2199	−0.2280	−0.1831	−0.2065
	92.6%	97.2%	89.3%	95.0%	81.7%	97.8%

Date	R1	R2	R3	R4	R5	R6
8/8	6.36	7.12	5.78	7.24	6.71	
8/11	5.03	5.72	4.45	5.40	5.58	
8/14	4.79	4.99	3.89	5.06	4.42	
8/17	3.40	3.06	1.37	1.87	2.29	
8/20	1.93	2.29	0.54	1.46	1.29	
8/23	0.84	1.13	0.27	0.94	0.60	
8/26	0.50	0.63	0.13	0.72	0.34	
8/29	0.46	0.34	0.01	0.47	0.11	
9/1	0.30	0.16		0.30		
	−0.1833	−0.2237	−0.3799	−0.2243	−0.3079	
	95.8%	93.9%	89.4%	89.1%	95.4%	

(650 r) and the non-irradiated group is significant at the 0.05 level. There is thus a strong indication that the high dose actually increases the rate at which the wounds close.

The second aspect is by far the more interesting. In view of the proneness of irradiated animals to develop serious infections, the failure of the systemic effects of the total body irradiation to influence wound closure is significant. C. P. Miller[3] has found that irradiated mice have a high incidence of septicemia as well as positive bacterial cultures from certain organs. The septicemia in these cases is the result of (1) the invasion of the damaged gut by the normally non-pathogenic bacteria of the lower bowel and (2) lowered resistance of the animal to infection due to the agranulocytosis and the diminished immunologic reactions. The importance of the increased susceptibility to infection is shown by the experiments of Shechmaister, *et al.*,[9] who found that the LD 50 for S. enteritides in the normal rat is 10 million organisms injected intraperitoneally, whereas that for rats given 350 r dosage is 100 organisms. Thus, any break in the skin or mucous

TABLE IV. *Average Rates of Closure for Treated Groups.*

1st Experiment					
A	No Radiation		Wounded Immediately	−0.2420	Standard error of each of these means is 0.0122
B	150r		Wounded after 2 wks.	−0.2338	
C	450r		Wounded Immediately	−0.2294	
D	No Radiation		Wounded after 2 wks.	−0.2447	
E	150r		Wounded Immediately	−0.2254	
F	450r		Wounded after 2 wks.	−0.2243	
2nd Experiment					
G	No Radiation		Wounded after 4 wks.	−0.1925	Standard error of each of these means is 0.0164
H	No Radiation		Wounded after 8 wks.	−0.2124	
I	150r		Wounded after 4 wks.	−0.2038	
J	150r		Wounded after 8 wks.	−0.1805	
K	450r		Wounded after 4 wks.	−0.2476	
L	450r		Wounded after 8 wks.	−0.2114	
	No Radiation	G+H		−0.2024	Standard error of each of these means is 0.0116
	150r	I+J		−0.1922	
	450r	K+L		−0.2295	
3rd Experiment					
M	No Radiation		Wounded Immediately	−0.2081 ±0.0269	
N	650r		Wounded Immediately	−0.2524 ±0.0269	
O	No Radiation		Wounded after 1 wk.	−0.1961 ±0.0245	
P	650r		Wounded after 1 wk.	−0.2126 ±0.0300	
Q	No Radiation		Wounded after 2 wks.	−0.1962 ±0.0245	
R	650r		Wounded after 2 wks.	−0.2632 ±0.0269	
	No Radiation	M+O+Q		−0.1997 ±0.0146	
	650r	N+P+R		−0.2451 ±0.0160	
	Difference			0.0454 ±0.0197	

(This difference is significant at the 0.05 probability level).

DISCUSSION

This study has encompassed two aspects affecting wound closure. The first is the local effect of the ionizing irradiation on the wound. Previous studies by Nathanson[4] and by Pohle and Ritchie[5-8] indicated retardation in wound healing when a large dose, approximately 1000 r applied as roentgen rays or up to 1000 mg. hours of radium, was applied locally to a linear wound. The effects were noted only after high dosages and when the irradiation had been applied immediately after wounding. This effect was not noted in the present experiments, where the irradiation applied to any one area of the skin was not in the high dosages used by the previous investigators.

membrane barriers is potentially serious in an irradiated animal. Evans[1] has found that dogs receiving thermal burns plus a sublethal dose of total body irradiation also show a high incidence of septicemia due to organisms which normally exist on the skin. He also found that the presence of a burn of 20 per cent of the body caused a high mortality in animals given 200 r (about one-half of a lethal dose). It is evident from our experiments that there was no gross evidence of local infection or increased mortality due to septicemia, even in the highest exposure group.

Perhaps the most interesting observation is that there was no correlation between the rate of wound closure and the nutritional state of the animals. The irradiated animals were in a poor nutritional state. It has been shown that most, if not all, of the weight loss in irradiated animals is due to decreased food intake.[2, 10] Our observations indicate that closure of wounds must have a high priority in the nutritional economy of the body.

CONCLUSIONS

The effect of total body irradiation on the rate of closure of surgically excised wounds was studied on rats.

The amount of total body irradiation used was 150 r, 450 r and 650 r.

No retardation of wound closure was noted.

In the animals receiving 650 r and surviving the lethal effects of the irradiation, a slight increase in the rate of wound closure was demonstrated.

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