Serum Transaminase Activity in X-Irradiated Rabbits. (22833)

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Increased levels of serum glutamic oxaloacetic transaminase (G-O-T) activity after crushing and tourniquet injury to the rabbit leg were observed in our laboratories and will be reported elsewhere. Preliminary studies indicated that x-irradiation of left chest wall of an otherwise completely shielded rabbit in dosages of 2,500 r and higher, resulted in serum G-O-T elevations as early as 3 hours' post-exposure. It became of immediate interest, therefore, to determine if this very early response could be identified in rabbits after low dosage, whole body x-irradiation.

Methods. Rabbits of New Zealand strain, as in previous studies of traumatic injury(1), were employed. The animal, tied to a board, was placed 135 cm from center line of tube head. Dose levels of 500, 750, and 1,000 r were studied; half the dose was given ventrally and half dorsally in each instance.

Results. At the 500 r level, total irradiation time was 16.1 minutes. In another experiment, an attempt was made to determine if any relationship existed between initially elevated serum G-O-T activity and survival time of the animal.

The combined effects of bleeding and restraint on serum G-O-T activity were recorded in sham controls tied to the board in radiation position, without exposure, and bled serially along with x-rayed rabbits. Bleeding was accomplished by incising the ear vein, and transaminase determinations(2) were made on unhemolyzed sera after separation by low-speed centrifugation. The results are listed in Table I.

It is apparent that bleeding and restraint induce a transitory serum G-O-T activity increase that returns to normal values at 24 hours. However, the data demonstrate that a significant increase in serum G-O-T activity can be identified in the rabbit within 6 hours after 500 r of x-irradiation. At the 750 r and 1,000 r dose levels this alteration was recorded at 3 hours post exposure.

Perhaps the most striking aspect of transaminase change is its discriminating power on an individual basis. Of the 25 animals in the 750 r and 1,000 r experimental groups, 20 survived through 6 hours. In 15 of these 20, the 6-hour G-O-T activity ranged from 23 to 189 units above pre-irradiation levels. In 5 rabbits that died between 3 and 6 hours post-irradiation, the 3-hour determinations ranged from 22 to 196 G-O-T activity units above pre-irradiation values. In 15 sham control rabbits, on the other hand, the maximum change from "pre-irradiation" values at 6-hour sampling was 26 units (one animal) —the next highest change was 17 units (also a single rabbit). At the 500 r level, the significantly increased mean value for the group at 6 hours post-irradiation is not associated with much individual discrimination. Here, only 3 out of 12 rabbits recorded 6-hour G-O-T activity increases in excess of 17 units, although another 5 animals fell in the 14-16 units increase range.

The data in Table II indicate that there exists little relationship between the serum G-O-T change after 625 r of x-irradiation and survival time. The increase of 59 units, within the first 24 hours, recorded for rabbit No. 6 was associated with death on 8th day post-exposure. However, rabbit No. 9 died on 13th day with an observed change of −5 G-O-T units, while animal No. 5 survived the full 30-day term after an observed 24 unit increase within the first 24 hours. It would seem that although the initially elevated serum G-O-T activities may have resulted from increased permeability of irradiated tissue cell membranes, and thus more or less quantitatively reflect the extent of tissue damage, survival of the animal depends, in the main, on its ability to overcome and repair the insult.

Summary. Rabbits were subjected to x-

TABLE I. Serum Transaminase—Pre-irradiation and at Intervals Post-exposure. Means and standard errors.

	Pre-irradiation		+ 3 hr		+ 6 hr		+ 24 hr	
	N	Units/ml	N	Units/ml	N	Units/ml	N	Units/ml
Sham controls	15	22 ± 1.3	15	35 ± 2.2	15	30 ± 2.2	15	24 ± 1.7
500 r	12	24 ± 0.9	12	33 ± 1.3	12	38 ± 2.7*	11	31 ± 2.7*
750 r	12	22 ± 2.7	12	65 ± 14.1*	9	50 ± 5.3*	6	45 ± 7.9*
1,000 r	13	26 ± 1.7	12	52 ± 5.6*	11	66 ± 13.5*	8	42 ± 3.7*

* Difference statistically significant. Difference between means of sham controls and experimentals exceeds the stand. error for the difference by 2 + times.

TABLE II. Serum Transaminase and Time of Death (625 r Total Body Exposure).

Rabbit No.	Pre-irrad., units/ml	Max value 6-24 hr post-irrad., units/ml	△, units/ml	No. days 'til death
1	36	40	+ 4	12
2	26	50	+24	S* 30 d
3	30	50	+20	S 30 d
4	25	73	+46	21
5	26	51	+25	S 30 d
6	28	87	+59	8
7	29	43	+14	7
8	26	39	+13	S 30 d
9	38	33	- 5	13
10	15	50	35	8

* S = Survived.

irradiation in dosages of 500, 750, and 1,000 r. Serum glutamic oxaloacetic transaminase estimations were accomplished at 3, 6, and 24 hours post-irradiation. A significant increase in G-O-T activity could be identified at 6 hours in the rabbit group subjected to 500 r, and as early as 3 hours post-irradiation in the 750 r and 1,000 r animal groups. For the latter animals, the noted increase at 6 hours served to segregate 75% of the group on an individual basis. In rabbits subjected to 625 r of x-irradiation no relation was found between the serum G-O-T elevation and survival time.

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2. Karmen, A., Wroblewski, F., and LaDue, J. S., *J Clin. Invest.*, 1955, v34, 126.

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Pathogenesis of Experimental Arteriosclerosis in the Rat.* (22834)

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We have demonstrated that the standardized production of severe arteriosclerosis (Mönckeberg type) and myocardial necrosis by means of renal injury in the albino rat can be completely prevented by prior thyroparathyroidectomy(1). Studies directed towards elucidation of the mechanism underlying this striking protective effect of thyroparathyroidectomy, led to the conclusion that the cardiovascular injury of intact rats was caused primarily by autointoxication with parathyroid hormone. On further analysis it was inferred that excess function of the parathyroid glands following standard renal damage was mediated through the adrenal cortex. This communication describes experiments which formed the basis for these conclusions, and outlines our present concept of the mechanism of experimental arterial mediosclerosis.

Procedures. The method used for production of lesions has been described previously (2). The procedure consists in a single par-

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