Serum Glutamic Oxaloacetic Transaminase Activity after Whole Body Irradiation. (23989)

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As part of a continuing search for biologic phenomena which might give a clue to the amount of total body irradiation absorbed by mammals, the effect of such irradiation upon serum glutamic oxaloacetic transaminase (SGOT) has been examined in 2 different laboratories. SGOT activity is increased in acute myocardial necrosis(1,2,3) and in acute hepatocellular damage(4,5); it was therefore felt that this enzyme system might be a satisfactory index for determining extent of irradiation injury. The following report details the results obtained.

Exp. 1. Method. New Zealand male rabbits, 4½ to 5 lb. in weight were used. Each rabbit was placed in a wooden container, just large enough to accommodate the animal. X-ray was administered toward the lateral aspect of the body, half of the total dose being given from the right, and the other half from the left. Dosages were measured in air at surface of the body. The dose in the midline of the animal was roughly 75% of the air dose. X-ray factors were 200 Kv., 25 Ma., H.V.L. 1.1 mm Cu. Blood specimens were obtained from the heart by direct cardiac puncture.

Results. Table I shows the SGOT levels in the different animals pre- and post-irradiation. The control animal received a sham treatment. With a dose of 500 r, determinations between 6 and 18 hours showed a decrease in the SGOT levels. This phenomenon also was generally seen in those animals given 1000 r. In 2 instances in animals given 1000 r, no appreciable change was noted. One of these rabbits died after a few hours, but the other was followed for 168 hours, and the transaminase level appeared to be quite constant. In this experiment the results appear to be different than those of the subsequent experiment and with those of Milch and Albaum(6). The method of irradiation in this first experiment was directed from the lateral aspects of the body rather than from above and perhaps this may have given a higher dosage to some organ which forms the enzyme and thus might have inhibited enzyme formation.

Another factor was the use of cardiac puncture for blood removal. This was a possible source or error, since one of us (G.K.) found that when specimens were collected by cardiac puncture some of the control animals died. Post-mortem examination revealed the pericardial sac to be filled with clotted blood and there was visible scarring of the myocardium. At times when collecting blood in control animals by intracardiac puncture elevated SGOT levels were obtained even though no other noxious stimuli were applied, indicating a definite reaction on this enzyme system as a result of cardiac puncture. For this reason in the subsequent experiment blood specimens were obtained by the free bleeding technic.

Exp. 2. Method. Male, New Zealand strain rabbits weighing from 5½ to 7 lb were used as the experimental animals. The x-irradiation

TABLE I. SGOT Levels in 9 Rabbits after Various Doses of Whole Body Irradiation (Units/ml).

		Hr after irradiation									
Dose (r)	Pre	1	2	3	6	18	24	48	72	128	168
Control	29			29	35		29				
200	29				46		39	39	32		
500	37					22		13	20		
500	43			17	33		43	29	30		
1000	69	25	35	32			17	17	12		
1000	30	18		Died							
1000	46	26					27	20	Died		
1000	14	12					9	10	9		12
1000	17	17			Died						

TABLE II. SGOT Levels in 28 Rabbits after Various Doses of Whole Body Irradiation (Units/ml).

Dose (r)	Pre	Hr after irradiation						Survival time†
		1	5	11	25	49	73	
1000	25	22	26	28*	12	11		1 wk
	16	27	33	18	20	36	21	1 "
	21	21	35	18	13	19	14	1 "
	14			34	19	21	17	S
	25	25						5 hr
		24	42	70*	137	57	49	S
	15	15	20	20*	32	15		S
	19	20	18	31	19	11	14	S
	29	32	25	30	15	12	17	S
1250	23	20	33	305	500	52	24	S
	33	48	126	2500				24 hr
	19	23	23	86				24 "
	14	23	117	117	75	37		60 "
	16	23	17		22	11	15	S
	15	26	19		12	10	15	S
	22	18	27	68	36	16	68	S
	11	19	21	39				24 hr
	33	30	29	28	32			S
	27	33	19	31	33			S
1500	20	23	37	41		24		S
	9	14	71	534				24 hr
	13	18	71					11 "
	26	21						5 "
	11	27						5 "
	29	28	24	27	24	25	20	S
	47	42	57	134	43	21	27	S
	16	22		38	35			48 hr
	14	15	36	36	48	19	24	S

* 10 hr post-irradiation values.

† S = Survived for 2 wk experimental period.

procedure consisted of placing the animal in a 20x20x20 cm corrugated box. Dose levels of 1000, 1250, and 1500 r in air were administered to the animals. X-ray factors consisted of 200 Kv., 20 Ma., 20x20 cm field, ¼ mm Cu 1 mm Al filter, 50 cm TSD. Irradiation was given from above, one portal being used. The total x-irradiation times for 1000, 1250 and 1500 r (air dose) were 9'32", 11'55", and 14'18" minutes respectively. It should be noted that the actual dose in the midzone of the animal, correcting for the distance according to the inverse square law and neglecting tissue absorption, was approximately 600, 750 and 900 r. All experimental animals served as their own controls by having an initial specimen taken before irradiation. It had been previously determined that irradiation and blood specimens collected serially at specified time intervals did not reveal elevated serum glutamic oxaloacetic transaminase levels. Blood specimens were obtained by a free bleeding technic, *i.e.* cutting the ear vein of the rabbit and collecting approximately 1.5 ml of blood. GOT was determined on sera after centrifugation of the clotted specimens (7).

Results. Average pre-irradiation value for all experimental groups was 21 GOT units (Table II). At one hour post-irradiation there was no perceptible rise in SGOT. For time intervals of 4 to 25 hours post-irradiation, average GOT units were higher than pre- or one hour post-irradiation values. The highest GOT levels occurred 11 hours after total body irradiation. The group of animals receiving 1000 r (air dose) showed the least GOT increase.

The individual SGOT levels of all groups, for the 4 to 25 hour post-irradiation intervals, did not show a consistent increase. Individual values for all groups ranged from that of the pre-irradiation value to an increase of several hundred GOT units. As there was an inconsistent increase in GOT it was decided that statistical groups were not applicable.

Average values of all groups for 25 hours after total body irradiation were still elevated but considerably lower than those for 11 hours post-irradiation. At 49 hours post-irradiation the average values for all groups were the same as that observed for pre- and one hour post-irradiation. After 73 hours average GOT values were similar to the pre-irradiation level.

While the above work was in progress, Milch and Albaum published studies of SGOT levels in x-irradiated animals, using dose levels of 500, 750 and 1000 r. Their data demonstrate significant increase in serum glutamic oxaloacetic transaminase activity within 6 hours after receiving 500 r and within 3 hours after receiving 750 and 1000 r. An exact comparison is not possible, because of differences in time intervals used, but our data indicate an average increase 5 hour post-irradiation. Some animals in all groups did not show any response.

All animals that survived the total body x-irradiation were kept for a maximum of 2 weeks post-irradiation. There was no correlation between GOT changes and survival time, (Table II). The data indicate that some animals survived after an increase of several hundred SGOT units while others died showing only mild GOT increase. More animals in the groups which received dosages of 1250 and 1500 r died during the first 24 hours. Although increased SGOT activities may qualitatively indicate tissue damage inflicted by irradiation, survival of the animal appears to depend on ability to overcome and repair the resultant damage.

Summary. New Zealand strain rabbits were given varying dosages of total body x-irradiation. SGOT determinations were made at various intervals in the post-irradiation period up to 168 hours following irradiation. Initially the blood specimens were drawn by direct cardiac puncture and the results in these instances were too variable to be used for diagnostic or prognostic purposes. When the free bleeding technic was used for obtaining blood specimens, more consistent results were obtained. Average SGOT values for pre- and one hour post-irradiation were of the same order of magnitude. An increase in GOT activity was observed as early as 5 hours after total body irradiation and remained elevated for 25 hours. After 49 hours post-irradiation SGOT levels returned to normal. There was no correlation between SGOT activity and total irradiation or survival time of the animal.

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Effect of Histone on Plasma Unesterified Fatty Acids.* (23990)

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Recognition of the physiological importance of unesterified fatty acids (UFA) followed the observation of the UFA-increasing effect of heparin(1,2,3), and reports establishing UFA as available metabolites(4,5,6,7). Protamine was found to counteract the effects of heparin(7,8,9). In the present studies the effects of histone on UFA metabolism were investigated. Histone, like protamine, is a positively charged molecule, but unlike protamine it is widely distributed physiologically.

Methods. Alimentary lipemia was pro-

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