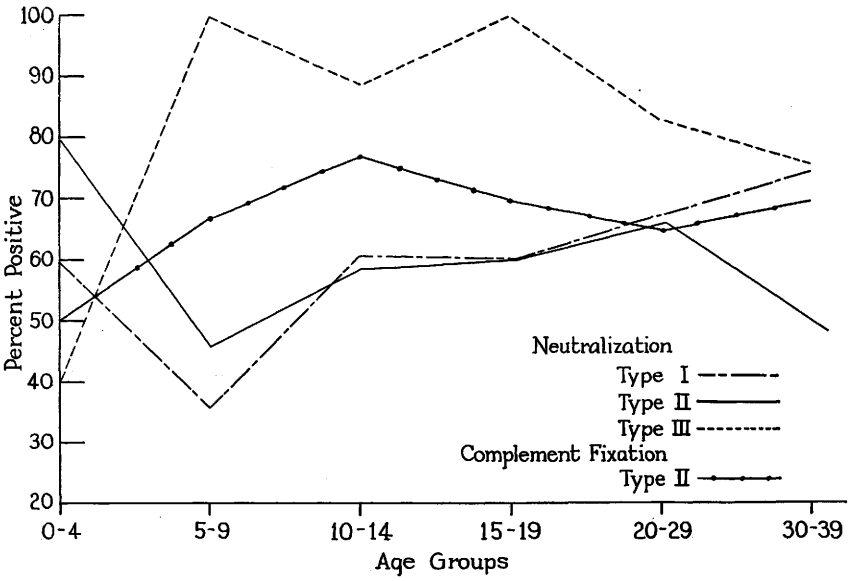

FIG. 3. Neutralizing antibodies by age groups for Types I, II and III and complement fixing antibodies for Type II virus.

fixing antibodies to Type 2 virus may indicate serologic response to the heterologous Type 1 virus, widespread dissemination of Type 1 virus probably occurred at this time. 3. These observations suggest that immunity to poliomyelitis in the Society Islands prior to the epidemic of 1951 was greater to Type 3 virus, and that the outbreak resulted from recent introduction of Type 1 virus, a new type for the area. It is possible that Type 2 virus was present coincidentally.

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Modification of Radiation Injury in the Rabbit. (22190)

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Heterologous tissue transplants or cell suspensions of hematopoietic origin have been reported by Lorenz and his associates(1,2) and Jacobson *et al.*(3) to have a significant effect on survival and hematopoietic regeneration of irradiated rodents. Jacobson first described evidence that suggested the effectiveness of mouse spleen transplants for hastening recovery of the blood-forming tissue of irradiated rabbits(4). Congdon and Lorenz (5) reported that rat bone marrow and rat bone had a significant effect on survival of irradiated mice and that guinea pig marrow likewise afforded a significant increase in survival of irradiated mice. Jacobson and coworkers(3) and more recently Cole *et al.*(6)

corroborated the work of Congdon and Lorenz on effectiveness of rat marrow on survival of irradiated mice, but Loutit(7) has been unable to confirm these positive results with heterospecific material.

In earlier experiments, Jacobson did not observe the effect of mouse hematopoietic tissue transplants on survival of irradiated rabbits(4). Hence, the investigation described in this paper was undertaken to determine whether hematopoietic cells from mice enhance survival of X-irradiated rabbits.

Materials and methods. Swift's snuffle-free, young adult rabbits of both sexes, weighing 1.5 to 2.5 kg, were used as recipient animals. The cells used for postirradiation injection were obtained from tissues of the CF No. 1 mouse embryo or from baby mouse spleens or livers. The donor mice were killed by cervical fracture. Embryo tissue was obtained by making a median incision in the abdominal cavity of the pregnant mouse and removing and plunging the entire embryonic sac into cold Locke's solution. The liver was immediately excised from the embryo and suspended in Locke's solution. A homogeneous cell suspension was produced by drawing the combination into a 2-cc hypodermic syringe and expelling it repeatedly. Before cell counts were made, the suspension was drawn into a syringe and expelled through a 26-gauge needle. No appreciable cell clumping was found. The number of nucleated cells per cu mm was determined by making a dilution with 2% acetic acid in a white blood-counting pipette and counting the cells on a standard hemacytometer. Cell suspensions were diluted with Locke's solution so that each 10 cc contained the required number of cells for each rabbit. All injections were given within a few minutes after final dilutions had been made and were administered intravenously into the marginal ear vein of rabbit with a 24-gauge needle within a few hours (0 to 4) after X irradiation.

Cells from spleen, liver, and other tissues of the mouse were obtained in similar fashion. Cells obtained from baby mouse liver or spleen were not contaminated with other mouse tissue cells.

TABLE I. Outline of Experiment to Study Hematologic Changes in Irradiated Rabbits Treated with Cell Suspensions of Mouse Tissue.

Mouse tissue	Total No. cells ($\times 10^6$)	Rabbits (No.)	X-ray exposure (r)	30-day survivors (No.)
None	None	3	None	3
1-day liver	250	4	900	2
1- to 4-day spleen	209	2	"	1
16-day embryo liver	240–255	6	"	5
None	None	4	"	1

Rabbits were exposed to 900 r total-body X radiation* before administration of the cell suspensions. Irradiated rabbits that were injected with cell suspensions from nonhematopoietic tissue and nonirradiated rabbits that were untreated served as controls. The experiment to study hematologic recovery of irradiated rabbits following injection of cell suspensions obtained from various tissues of the mouse is outlined in Table I. Table II gives a detailed outline of experiments devoted to a study of survival. As indicated in Table I hematologic studies were made on a small number of animals. Only one control irradiated animal survived beyond the 14th day. Leucocyte, hematocrit, and reticulocyte values were determined for irradiated rabbits that had been injected with mouse embryo liver or with baby liver or spleen; for irradiated, untreated rabbits; and for rabbits that were normal, non-irradiated, untreated controls (Table I). Standard hematologic technics were employed. X-rays were administered as a horizontal beam to 2 animals at a time. Measurements were made in air with a Victoreen condenser r-meter equipped with a 100-r chamber at the position occupied by center of the 2 cages. At the midpoint of total exposure, the animals were reversed from top to bottom and from side to side. X-rays were generated by a 250-kvp Maxitron machine operating at 30 ma. A 1.0-mm Al and 0.5-mm Cu filter were used. The half-value layer in copper of the filtered beam was 1.43 mm. Exposure rate averaged 44 r per minute at a

* The 30-day X-ray LD50 for these animals in this laboratory is about 800 r.

TABLE II. Effect of Cell Suspensions of Mouse Tissue on Survival of Rabbits Exposed to 900 r Total-Body X Radiation.

Mouse tissue	Total No. cells ($\times 10^6$)	Rabbits (No.)	Survival			
			28-day		120- to 150-day	
			No.	%	No.	%
Embryo liver	200 to 250	19	11	57.8	10	52.6
1- to 2-day liver	"	10	6	60	6	60
1- to 4-day spleen	25 to 30	8	6	75	6	75
Heart, kidney, lung, placenta	32	9	1	11	1	11
None	X-ray only	50	5	10	4	10

distance of 70 cm.

Results. Survival. As indicated in Table II, cells from the mouse embryo or from baby mouse spleen or liver had an appreciable effect on survival of rabbits that had been exposed previously to 900 r total-body X radiation. Of 8 irradiated rabbits that received from 25 to 30 x 10^6 cells from the spleen of 1- to 4-day-old mice, 6 have survived a period of 150 days, whereas only 1 of 9 has survived 120 days that was injected with cells from nonhematopoietic tissue. All nonsurvivors died within the first 26 days of observation period, and no deaths have occurred since that time. Rabbits that received from 200 to 250 x 10^6 cells from the liver of the mouse embryo or from liver of the 1- to 2-day-old mouse had similar survival. Of 29 thus treated, 17 survived beyond 26 days, and only 1 death has occurred (on day 90) during remaining 120-day period of observation. Of 50 untreated irradiated controls, only 4 survived (Table II).

Hematologic studies. Figs. 1 and 2 indicate that injection of 200 to 240 x 10^6 cells from the mouse embryo or baby liver or spleen had no appreciable effect on recovery of leucocyte and hematocrit values of the peripheral blood of the irradiated rabbit. The normal reticulocyte value of the irradiated cell-injected group at 10 days as compared with controls (Fig. 3) may be significant but should not be considered as evidence of an earlier recovery in these animals unless confirmed by histopathologic findings or a further hematologic study in which values are obtained at additional periods.

Discussion. The data from this investigation indicate that cells from the embryonic mouse liver or from baby mouse liver or

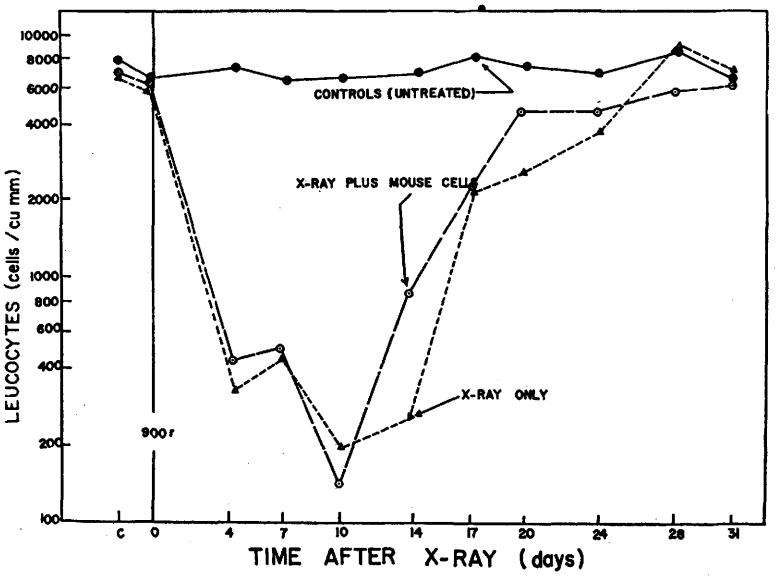

FIG. 1. Effect of cell injections on recovery of irradiated rabbits.

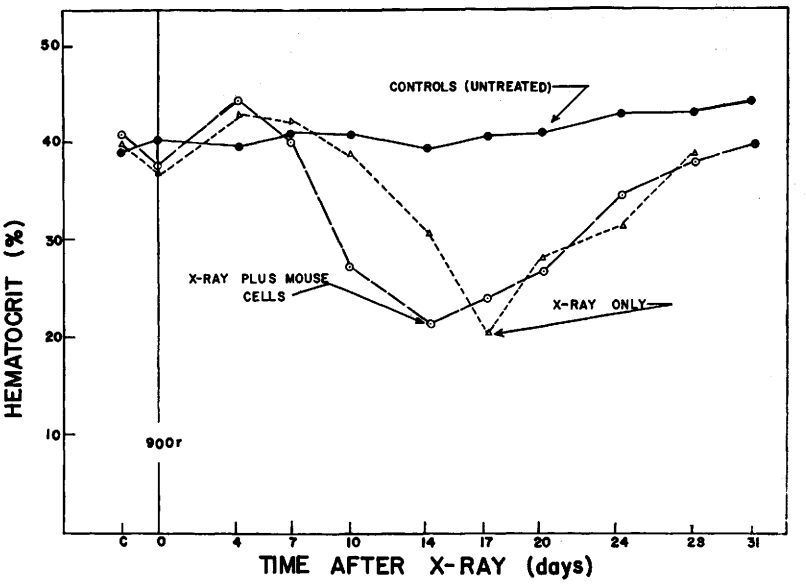

FIG. 2. Effect of cell injections on recovery of irradiated rabbits.

spleen are capable of enhancing the survival of rabbits exposed to 900 r total-body X radiation. These findings supplement those of Lorenz(1,2), Jacobson and his associates (3,4), and Cole *et al.*(6) which show the efficacy of heterologous tissue (rat to mouse, guinea pig to mouse) in prolonging the survival of irradiated mice. Loutit(7), on the contrary, has not been able to increase the survival of irradiated mice by treating them with heterospecific material. In point of fact, his argument against the benefits of homologous suspensions is based upon the number of late deaths that he observed in irradiated mice that had been treated with cell suspensions made from animals of the same species but of a different strain. It is thus important to emphasize that, in our study, late deaths did not

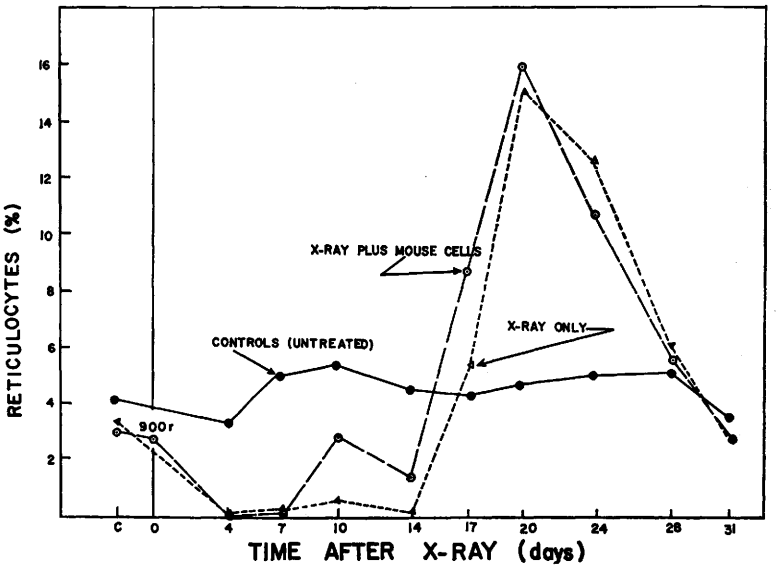

FIG. 3. Effect of cell injections on recovery of irradiated rabbits.

occur in the surviving group of irradiated rabbits that had been treated with mouse tissue.

Previous studies in this laboratory gave evidence that spleen-shielding had only a slight effect on survival of X-irradiated rabbits(8), whereas there was an appreciable effect on survival of mice(4). The possibility that hematopoietic tissue from the mouse is a more potent source of the recovery factor (s) involved in recovery from radiation injury than hematopoietic tissue from the rabbit will require further exploration. Preliminary data in our laboratory suggest that mouse cells from embryonic liver as used in this study are as effective in enhancing survival of irradiated rabbits as are rabbit cells obtained from the liver of 1-day-old rabbits.

The fact that hematologic recovery in the rabbit exposed to 900 r and then treated with cells from the mouse was not appreciably different from that of control rabbits that survived this exposure would seem to indicate that increased survival is not necessarily dependent upon enhanced hematopoietic regeneration. Until histopathologic studies are completed it is perhaps not justified to make such a statement. Evidence of recovery may be present in the bone marrow and elsewhere under conditions of this experiment which are not manifest in peripheral blood.

In some respects, our findings are similar to those from the spleen-shielding splenectomy experiments that have been reported previously(4). Survival of spleen-shielded mice (1025 r) that were splenectomized 1 hour after irradiation spleen-shielding procedure was the same (75%) as that of mice treated similarly, with the exception of splenectomy. Hematopoietic regeneration began by 3 days and was complete in the nonsplectomized spleen-shielded mice in 7 to 9 days, while in mice splenectomized 5 minutes after the spleen-shielding-irradiation procedure, regeneration began at 9 days and was complete at 15 days or longer. These observations suggested that increased survival was not necessarily dependent on early regeneration of the blood-forming tissue. Our finding also suggests that early hematologic recovery is not necessary for increased survival.

Conclusions. Postirradiation injection of mouse embryo cells or baby mouse liver or spleen cells enhances significantly the survival of rabbits exposed previously to 900 r total-body X radiation without producing an appreciable effect upon hematologic recovery as observed in the peripheral blood.

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