Effect of Partial Shielding by Grids on Survival of X-irradiated Rats. (21036)

J. G. KEREIAKES, W. H. PARR, J. B. STORER, AND A. T. KREBS.
From the Army Medical Research Laboratory, Ft. Knox, Ky.

There appear to be at least two general mechanisms by which partial body shielding protects animals from x-radiation. The first of these, which may be termed "remote" effect, has been thoroughly investigated by a number of workers(1-7). In studies on this mechanism of protection a single organ or portion of the body is shielded with lead and the "remote" effects such as effect on survival, white cell count, rate of regeneration of the marrow, etc., are studied. Whether or not the results can be explained by a humoral substance(1), cell seeding(1,6,7), or a temporary maintenance of the animal's defense mechanisms(6) is not yet established. In any event it is clear that reparative processes are stimulated at a distance from, but under the influence of, the shielded normal tissue. The second general mechanism may be called the "local" effect of shielding. Here the area of interest is located at the interface between shielded and irradiated tissues. Kohler(8), Liberson(9), Goldfeder(10), Grynkraut(11), Jolles(12), Marks(13), and others have shown that when radiation is delivered through multiple holes in a shielding material, *i.e.* through a grid, doses which would not ordinarily be tolerated by the skin if given over the entire area can be delivered with relative safety. It is generally believed that this phenomenon can be best explained on the basis of the normal shielded skin(9,14) and/or connective tissue (12) adjacent to the irradiated tissue initiating repair of the damaged area. No information is available as to whether this protective effect is limited to the skin and underlying connective tissue or is a property of tissues in general which might be utilized to protect animals against total body irradiation.

The present study was undertaken to determine whether or not irradiation of entire animals through a grid is less effective in producing lethality than direct total body irradiation and if so, to determine the relation of effectiveness to grid hole size.

Experimental. A total of 104 adult male Sprague-Dawley rats weighing 250 ± 25 g each were used in the present study. Prior to and following irradiation the rats were housed 2 or 3 to a cage and given water and Purina Laboratory chow *ad libitum*. The rats were anesthetized with pentobarbital prior to irradiation exposure. They were then placed, 2 at a time, on their left sides in a shallow lucite cage. A lucite lid, with or without a lead grid attached, was placed on top of the cage in close proximity to the surface of the rats. Following radiation exposure the animals were observed daily for 30 days and the survival noted. The grids used in the present study were constructed from lead sheets 1.6 mm thick. Previous measurements showed that lead of this thickness transmitted only 1% of the incident radiation dose. The closed to open areas were kept constant at 60 to 40%, respectively, and only the hole size was varied. The holes were distributed as uniformly as possible over a circular area of 189 cm^2. X-rays were delivered from a Keleket Deep Therapy Model machine operated at 200 KVP and 9 ma with added filters of 1.0 mm Al and 0.5 mm Cu. The target-specimen distance was 29.5 cm and the dose rate 62.0 r/min. measured in air. The grid transmission dose rates were measured by rotating a Victoreen ionization chamber under the grids on an eccentric axis. Data on hole sizes, transmission rates, etc., for the various grids are given in Table I. To determine the approximate extent of scatter of the radiation in passing through a rat, films were placed immediately beneath the grid and immediately beneath the rats. The assembly was then exposed to radiation. The results of this study indicated that scattering was minimal and that when a grid was used, the radiation was delivered essentially as sharply defined cylinders. Since rats exposed through the grid received only about 40% of the dose incident to the grid, it was necessary to com-

TABLE I. Physical Data on Grid Hole Sizes, % Open Area, and Dose Rates Transmitted.

Shielding	Hole size (diam. cm)	Hole area (cm^2)	Distance between centers (cm)	Calculated % open area	Measured % open area	Dose rate through grid (r/min.)
0 (open portal)				100	100	62.0
Grid 1	1.0	.79	1.40	40	46	28.3
2	.66	.34	.93	40	44	27.5
3	.44	.15	.61	40	42	26.2
4	.32	.08	.44	40	46	28.6

pensate for this lower dose rate to the shielded animals by increasing the exposure times. For this purpose the concept of volume dose as discussed by Hempelmann *et al.*(15) was used. According to these authors the integral or volume dose "is the product of the radiation dose in energy units multiplied by the mass of irradiated tissue in grams." The unshielded control rats (avg wt 250 g) were given a total body exposure of 800 r or an average volume dose of 200 kg roentgens per rat. Approximately 40% or about 100 g of the rats irradiated through the various grids were exposed to radiation. To make the total energy absorption or average volume dose per rat equal to the dose received by the controls it was necessary to increase the dose incident through the holes in the grids to about 1740 to 1900 r (the exact dose depending on the measured percent open area).

Results. Exposure of rats to equal volume doses of x-radiation through grids having various diameter hole sizes but a constant open area to closed area ratio resulted in increasingly greater survival as the hole size was decreased. These data are shown in Table II. Of the 24 control rats exposed to a total body radiation dose of 800 r (or 200 kg roentgens volume dose) only 5 or 21% survived for 30 days. Rats irradiated with the same volume dose (2000 r to 40% of the body or 200 kg roentgens) showed no increase in survival when the radiation was delivered through a grid having holes 1 cm in diameter. When the hole size was reduced to 0.66, 0.44, and 0.32 cm in diameter, however, 30-day survivals of 37, 68, and 84%, respectively, were found. In Fig. 1 the per cent survival is plotted against log of hole areas. The resulting straight line indicates a simple exponential relationship over the range of hole sizes studied.

TABLE II. Effect of X-Irradiation through Various Grids on Survival of Rats. Volume dose 200, kg roentgens/250 g rat.

Shielding	Hole size (diam. cm)	No. rats	30-day survival	% survival
0 (open portal)		24	5	21
Grid 1	1.0	19	3	16
2	.66	19	7	37
3	.44	19	13	68
4	.32	19	16	84

Discussion. Exposure of rats to x-radiation delivered through grids has been shown, in the present study, to increase survival significantly over that found in control rats exposed to equal volume doses of total body x-irradiation. Grid hole size was found to be of critical importance in altering survival. Rats exposed through grids having openings of 0.66 cm or less in diameter showed increasing survival with decreasing hole size even though the ratio of total open area to closed area was kept constant at a 40 to 60% ratio.

Other investigators have found similar protection of skin and underlying connective tissue of men and experimental animals when radiation was delivered through a grid(8,14). Presumably this protective effect, which may be called the local effect of partial shielding as opposed to the remote effects obtained by spleen or marrow shielding, may be explained as being due to the initiation of repair in the irradiated area by the surrounding unirradiated tissues. This conclusion is supported by the fact that greater protection was obtained as hole sizes in the grids were decreased. Such decrease in size had the effect of increasing the total area of the interface between irradiated and normal tissues. If protection is due to reparative changes induced at these interfaces then it would be expected that degree of pro-

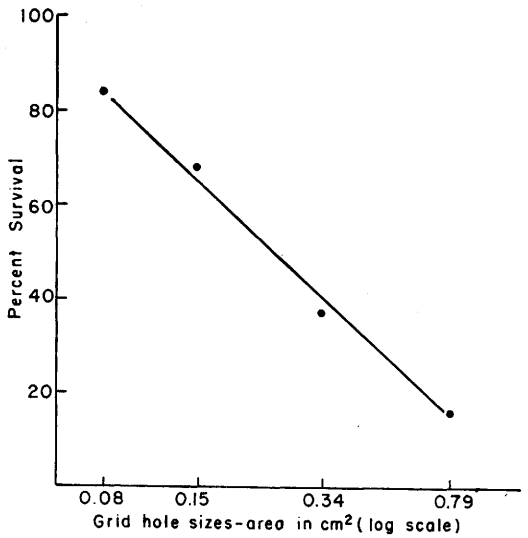

FIG. 1. Survival of rats exposed to equal volume doses of X-rays as a function of grid hole size.

tection would be related to interface area. The data obtained in the present study showed such a relationship (Table II and Fig. 1).

It should be pointed out that this theory may be further tested by changing the shape of the openings in the grids while maintaining the area of the openings constant. Circular holes should give minimum protection since the perimeter to area ratio is smaller than the perimeter to area ratio of other geometrical shapes such as the squares and rectangles that are used by clinical radiotherapists. Further study on this point is indicated.

The possibility that the protective effect obtained in the present study was exerted remotely by protection of hematopoietic and/or lymphatic tissue must be considered. Since the areas of the rat that were shielded were randomly distributed and in each case amounted to 60% of the animal, it is apparent from the laws of probability that approximately 60% of the bone marrow, spleen, lymphatic tissue, etc., were protected. If protection had been obtained by the remote effects of shielding these tissues, then no difference in survival with grid openings of various sizes would be expected. Since differences were found it must be concluded that the protective effect could not be explained on this basis.

Studies in which large single areas of animals have been shielded and the remainder exposed to radiation have shown that in general there is a fairly specific threshold of dosage which cannot be exceeded if the animal is to survive(3). This threshold presumably represents the level at which remote effects of shielding are no longer effective and direct irreversible damage to vital tissues leads to death. The present study suggests that the local effect of shielding may be effective in protecting animals at doses in excess of those at which the remote effects are operative. It seems likely, on the basis of these considerations, that shielding of a given percentage of an animal by a grid may be preferable to shielding a similar percentage of an animal by a single solid sheet of protective material.

Summary. Exposure of rats to equal volume dose of x-radiation (200 kg roentgens) through grids having various diameter hole sizes but a constant open area to closed area ratio resulted in increasingly greater survival as the grid hole sizes were decreased. Significantly greater survival was obtained in rats exposed through grids than in rats exposed to total body x-irradiation. It is suggested that these results may be explained by a beneficial local effect of partial shielding whereby normal tissue adjacent to irradiated tissue initiates repair in the irradiated areas. Degree of survival appeared to be directly related to the area of interface between normal and radiated tissue.

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Normal and Altered Thyroidal Function in Domesticated Goldfish, *Carassius auratus.** (21037)

OLGA A. BERG AND AUBREY GORBMAN.

From the Departments of Zoology, Barnard College and Columbia University, and Department of Biology, Brookhaven National Laboratory.

The ability of thyroid follicles of fishes to accumulate radioactive iodine appears to be inversely proportional to the amount of iodine in their aqueous environment(1). Thus, it has been shown that marine fishes living in an iodine-rich environment seldom concentrate thyroidally more than 2 to 3% of a tracer dose of I^{131} while freshwater fishes living in a relatively iodine-poor medium accumulate up to 30% of an injected dose of I^{131}. The radioiodine turnover of such a freshwater fish can be reduced until it resembles that of a salt water fish by the addition of iodine to the water(1,8). It also seems to be true that euryhaline fish such as *Fundulus heteroclitus* that live in water which is salty at certain times, and almost fresh at others, can rapidly change their iodine metabolism while strictly marine fish such as *Fundulus majalis* are not so adaptable(5).

In a survey of the radioiodine turnover of freshwater fishes, we have found only one species, the common goldfish *Carassius auratus*, whose thyroid gland is not a relatively avid collector of radioiodine. The thyroidal epithelium of this species is normally squamous, denoting comparative inactivity, but it is extremely sensitive to thyrotropic hormone stimulation, so much so that it has been suggested as the basis for the bioassay of TSH (3,4). We were surprised to find that untreated goldfish make almost no thyroxine within the usual time required for such biosynthesis by other species, and undertook the following series of experiments with thyrotropic hormone to try to alter their exceptionally low level of iodine metabolism.

Material and methods. Eighty-four goldfish were injected intraperitoneally with 5 Junckmann-Schoeller units of thyrotropic hormone (TSH)† per day in .05 cc of 0.9% saline solution. Twenty-four animals received a total of 20 units of thyrotropin in 4 days; 60 others, 25 units in 5 days. The day after the last injection of TSH all were injected with about 20 μc of carrier-free I^{131} and sacrificed in groups of 6 at intervals thereafter up to 170 hours. Ninety-nine fish, used as controls received the tracer dose of I^{131} at the same time as the experimental animals and were sacrificed after a similar interval. Twenty-four additional fish were each injected with 2 frog pituitaries suspended in .05 cc of 0.9% saline solution. Forty-eight hours later they received tracer doses of I^{131}. Another group of 10 fish was kept for 2 months in conditioned aquarium water at the genetics laboratory in the American Museum of Natural History. This water is known to be extremely low in iodine (0.5

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† The thyrotropic hormone was kindly supplied by Armour and Co. Their preparation number is P 589-80 and is stated to contain 10 J-S units per mg.