would be the development of delayed hypersensitivity to thyroglobulin and thyroiditis would appear only subsequently. The finding of a relatively high incidence of delayed type of hypersensitivity in animals without thyroiditis is, therefore, consistent with the hypothesis. This raises the question whether a critical level of sensitivity or some additional factor is necessary to elicit the immunologically mediated tissue damage.

Summary. 1. Among each of 2 groups of guinea pigs immunized with 50 μg and 500 μg of picrylated thyroglobulin in Freund's adjuvant respectively, 57.2% (63 of 110 animals) developed thyroiditis 17 days following the initial dose of antigen. Delayed skin reactivity to intradermal thyroglobulin was observed in 72.7% of the animals. There was no significant difference in incidence of thyroiditis and delayed skin reactivity in the 2 groups of animals. However, circulating antithyroglobulin antibody as determined by passive hemagglutination, was found in 4.6% (2 of 43 animals) in the low antigen group and 30% (18 of 60 animals) in the high antigen group.

2. The incidence of thyroiditis and delayed skin thyroglobulin reaction were positively correlated, while no such correlation between thyroiditis and circulating antithyroglobulin antibody was apparent.

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Radiosensitivity of Swine from Irradiated Parentage. (26520)

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Various parameters have been studied in the progeny of irradiated humans(1,2), dogs (3), and rodents(4.5), but we are not aware of any studies on the radiation sensitivity of progeny from irradiated large mammals. Some change in radio-sensitivity might be expected for life shortening effects have been reported in offspring of irradiated mice(6) and rats (7). The present report concerns the radiation response of offspring from parent swine exposed to the mixed gamma-neutron flux from a nuclear detonation.

Material and methods. Offspring from 3 parent categories of predominantly Landrace swine were studied. The *Progeny of Irradiated Parents* group was composed of 89 pigs sired by a boar surviving exposure to 268 rads (55% LD 50/30). The sows had received doses from 268 rads to 515 rads (mean dose 351 rads, 72% LD 50/30). Conditions of exposure for the parent swine have been described(8,9). *Progeny of an Irradiated Male* consisted of 44 offspring resulting from mating an irradiated boar (268 rads) with sows which had been placed as controls during field studies on the effects of a nuclear detonation (8,9). Dosimetric data indicated that these sows received less than 1 rad during the field

TABLE I. Litter Size.

Parentage	Avg No. pigs: Per litter	Farrowed alive	Surviving to weaning
Non-irradiated	10.3	9.7	8.0
Irrad. ♂, non-irrad. ♀	11.0	10.5	7.2
Irradiated	10.6	10.4	9.1

test. *Progeny of Non-Irradiated Swine* were 73 pigs produced by non-irradiated parents. Of these, 49 resulted from breeding a mixed breed boar with sows which had served as controls during the field studies mentioned previously. The remainder of the control group (24 pigs) was of similar breed, but from other stock.

The boars were housed separately and first mated with the sows approximately 8 months after irradiation. The first litters were then farrowed about one year after irradiation of the parent animals.

These pigs comprised first and second litters of the sows used. Average litter sizes, number of pigs farrowed/litter, and number of pigs/litter surviving to weaning age based on about 75% of the pigs used (unfortunately some litter size data was lost) is contained in Table I.

The pigs were allowed to eat a 20% protein hog food (without antibiotics) and were well adapted to this food when weaned at 8 weeks of age. The animals were vaccinated against hog cholera and swine erysipelas and were maintained under conditions of accepted swine management. At 11 weeks of age, pigs from each category of parent irradiation were grouped according to the irradiation dose to be received, using a table of random numbers. Physical examinations were performed on all pigs, and weights and hemograms were obtained.

The pigs were irradiated at 84 (±1) days of age with X-rays produced by a 3.5 mev Van de Graaff generator operated at a constant potential with a dose rate of approximately 150 r/min. The radiation source and calibration procedures used have been described(10). After irradiation the swine were fed commercial hog food (without antibiotics) and water was available *ad libitum*.

TABLE II. Mortality in Offspring.

Dose, r	Parentage: Non-irrad. swine	Irrad. swine (both parents)	Irrad. boar, non-irrad. sow
175	0/8 *	0/14	1/6
225	1/14	0/18	0/9
280	4/14	3/19	5/12
360	8/14	9/18	5/10
450	12/14	14/17	6/7
570	5/5	3/3	—
720	4/4	—	—
LD 50/30	335r	361r	332r
95% confidence limits	303-370r	333-391r	282-390r

* No. dead within 30 days/No. irradiated.

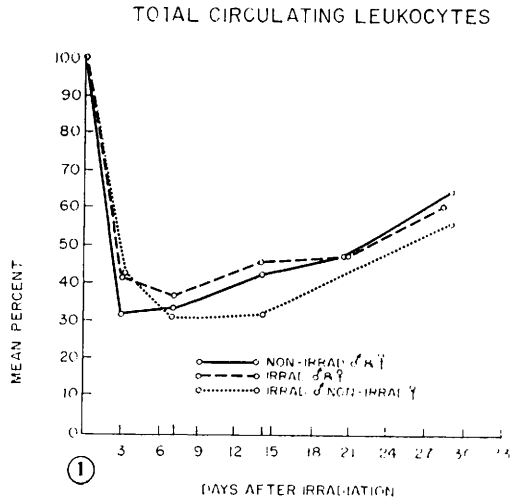
TABLE III. Survival Time, Days.

Dose, r	Parentage: Non-irradiated Mean	Non-irradiated Range	Irradiated Mean	Irradiated Range	Irrad. ♂, non-irrad. ♀ Mean	Irrad. ♂, non-irrad. ♀ Range
175	—	—	—	—	21	21
225	21	21	—	—	—	—
280	19	17–21	17	14–20	15	15–17
360	17	11–22	14	6–19	18	12–27
450	14	9–21	14	9–26	14	10–15
570	11	9–15	8	7– 9	—	—
720	9	7–10	—	—	—	—

Results. The number of pigs used and mortality in each group is contained in Table II for various experimental doses. By probit analysis(11) an LD 50/30 of 335r for offspring of non-irradiated swine was obtained. For progeny of irradiated parents LD 50/30 was 361r, and for pigs from the irradiated boar and non-irradiated sows LD 50/30 was 332r. Ninety-five per cent confidence limits were similar for all groups. The radiation response of offspring from the most heavily irradiated parents (mean dose to sows 460 rads, 95% LD 50/30, dose to boar, 268 rads) did not differ from that of the control population.

Mean survival times (Table III) did not differ significantly for the 3 categories of parent irradiation at different dose levels, or when all decedents in each parent category were combined. These survival times are dose dependent and are comparable to those usually reported for midlethal range irradiation.

Mean circulating leukocyte response and



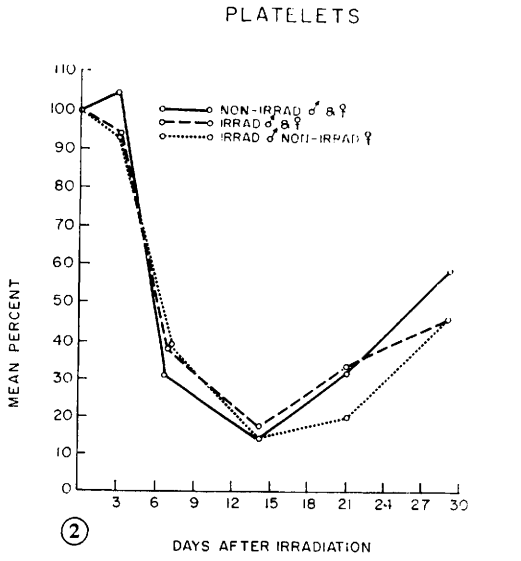


FIG. 1. Circulating leukocyte response for all swine. Plotted points are mean % of mean pre-irradiation values.

FIG. 2. Blood platelet response for all swine. Points are mean % of pre-irradiation values.

mean platelet response for all swine in each category of parent irradiation are presented in Fig. 1 and Fig. 2, respectively.

Times of onset and signs and symptoms of the radiation syndrome, as well as weight response for each group were as expected for midlethal range irradiation. Gross pathological changes seen at autopsy were typical of radiation damage and related to survival time.

Discussion. The failure to observe a change in radiation sensitivity could have resulted from our inability to optimize experimental conditions. Mouse data(6) indicate that for genetic effects neutrons are more effective than photons, and that maximal effects are to be expected from matings 19-23 days after irradiation. Both the delayed breeding time of 8 months and the fact that the radiation of the parents was about 50% gamma radiation and 50% neutrons operate to reduce the expected effect. Comparative data are not available on radiation effects of offspring of irradiated females. If effects on male and female are additive an enhanced effect would be expected in our irradiated parent group.

The decrease in life span following sublethal irradiation has been related to a decrease in radiation resistance(12,13,14). Other workers have failed to show such a decrease in resistance to radiation after recovery from an acute radiation exposure(15,16). From our data it appears that the point estimate of 0.077% life shortening for each rep received by the paternal parent(6) cannot be directly applied to a decrease in the LD 50/30 in progeny produced some time after irradiation of large mammals.

A brief comment on litter size shown in Table I is worthwhile. Generalizations cannot be made from these particular matings. However, there was no indication that irradiation produced a reduction in litter size or in viability of the offspring. Litter sizes were similar for all groups and number of pigs surviving to weaning age is consistent with the experimental facilities. Our data agree with that reported for X-irradiated dogs(17). The relatively low average for pigs surviving to weaning age in the irradiated boar—normal sow group is due to one litter in which a sow having insufficient milk saved only 3 of 15 live pigs farrowed.

Demonstration of a decrease in litter size from irradiation of the paternal parent to this dose would not be expected from the number of matings reported herein. However, the continued fertility of these sows with no decrease in litter size after surviving approxi-

mately 55-106% LD 50/30 acute dose and the similar results in dogs(17) are in distinct contrast to the results in mice in which similar doses have produced drastic effects on fertility.

Two hundred and six 12-week-old swine from non-irradiated parents, from irradiated parents, and from an irradiated boar and non-irradiated sows showed no significant difference in sensitivity to X-rays as measured by 30-day lethality. Lethality was essentially identical for each group as was survival time, hematological response, weight change, clinical signs of radiation sickness and gross changes at autopsy.

Summary. LD 50/30 values for 12-week-old offspring from non-irradiated swine, from irradiated swine, and from an irradiated boar and non-irradiated sows were not significantly different. Survival times for progeny of the different parent categories were not significantly different and were within the usual range for midlethal irradiation. Other responses were similar in each group.

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Interaction of Histamine, Serotonin and Heparin with Hexadimethrine Bromide, a Mast Cell Fragmentor. (26521)

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We reported(1,2) that hexadimethrine bromide (Polybrene*), an anti-heparin agent, caused disruption of tissue mast cells in the rat both *in vitro* and *in vivo*. It was suggested that histamine, serotonin and heparin, presumably released from these fragmented tissue mast cells, might perhaps be factors contributing to the symptomatology of this polymer following its injection in large doses.

* 1,5-dimethyl-1,5-diazaundecamethylene polymethobromide, Abbott.

This present study was undertaken to explore further the possible role of these mast cell components as they affect the toxicologic response to this anti-heparin agent in mice, rats and guinea pigs. To this end, experiments were run to ascertain whether depletion or accumulation of either or both of these amines by prior pretreatment with suitable agents could alter the subsequent response of the animals to a lethal dose of this polymer.

Methods. To deplete most of the tissues of the rat of their histamine, 5 injections of