Goltz(3); the latter also reported cortisone as effective in dba mice. Jacobson *et al.*(7) found spleen transplants to be protective; this work was extended by Cole *et al.*(5) who found spleen homogenates affording protection in LAF_1 mice. Bacq *et al.*(8) mention cysteine as being a protective agent in rats if the rat liver is shielded during irradiation.

The marked ability of estrogens to ameliorate radiation injury has been noted in clinical radiotherapy. Postmenopausal patients show much more drastic symptomatic reactions than do premenopausal cases. The inference has been that endogenous levels of estrogen are sufficiently high to afford protection against radiation injury in the premenopausal state but are lacking in the postmenopause period.

Summary. 1. In dba mice diethylstilbestrol and estradiol benzoate reduce the acute radiation mortality. The androgens, testosterone propionate and depotestosterone cyclopentylpropionate, afford no protection against acute lethal radiation dose. 2. The estrogens afford protection when given for 7 days before or after the irradiation. 3. No toxic effects due to estrogens or androgens were seen in the administration of the hormones for 7 days after irradiation.

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Influence of X-Irradiation on Oxygen Poisoning in Mice.* (21002)

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The initial work on this subject already reported(1) showed a synergism between x-irradiation (8800 r) and oxygen (5-6 atmospheres) in their simultaneous effects on the survival times of mice. When intervals of 2 minutes, 30 minutes, and 2 hours were allowed between X-irradiation and oxygen poisoning, the small but significant shortening of the survival times in oxygen gradually decreased and disappeared within 5 hours. These experiments gave some support to our hypothesis on a possible common mechanism between the initial effects of X-irradiation and the effects of high oxygen tensions. When an 18-hour interval was allowed, a nonsignificant, slight reversal of this phenomenon was noticed, showing now a slight tendency to protect against O_2 poisoning. It was evident that further investigations with increasing intervals might reveal some interesting influence of the secondary phenomena of X-irradiation on oxygen poisoning.

The material presented here is a study of the effects of 8800 r (which will kill these mice in about 4 days) on the survival times of mice submitted to 6 atmospheres of oxygen

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30 to 84 hours after irradiation.

Materials and methods. Chambers, made from 6-inch steel pipe which had a 3-inch window in one end and a volume of 6.2 liters, were used for testing mice. A tray of soda lime covered with a wire mesh platform with a vertical partition divided the chamber lengthwise. Transverse partitions kept the mice in the front half of the chamber, in the cone of radiation. (Two 5-volt bulbs in the chamber provided light.) In every experiment each chamber held 10 20 g female "Webster mice" of the Clara Lynch strain, 5 on each side of the central partition. A 1000 kilovolt peak General Electric Industrial X-ray Generator was used at a current of 3 milliamperes. Radiation dosages were measured with a Victoreen ionization chamber. The irradiated chamber was placed so that its center was 13½ inches from the X-ray target and the control chamber was 20 feet away, behind a lead shield. No radiation could be detected in the control chamber. Within the irradiated chamber the dose rate was 250 roentgens per minute with only slight fluctuations from day to day. The total time of exposure to irradiation was approximately 35 minutes, so that the dose of irradiation in all experiments was approximately 8780 r. The dose rate was limited by the characteristics of the X-ray apparatus. A continuous air flow was maintained in the two chambers during the irradiation. After the irradiation the mice were removed from the chambers and returned to the laboratory with food and water until they were submitted to 6 atmospheres of oxygen. The intervals in these experiments were 30, 48, 72 and 84 hours between the end of irradiation and the submission to oxygen. Each chamber held 5 irradiated mice on one side of the chamber and 5 control mice on the other side. Oxygen was supplied to the two chambers by hoses from a single cylinder of oxygen fitted with an Airco Reduction valve so that the pressure was the same in both chambers. The pressure was increased at the rate of 5 lb per minute to six atmospheres (75 psi gauge). There was a small continuous flow of oxygen through the chamber during the experiments, and the presence of soda lime kept the carbon dioxide concentration undetectable. Survival time was taken from the time 6 atmospheres of oxygen was attained until respirations ceased. In one instance the exact time of death could not be determined and the mouse was dropped from the average survival time. Observation was made of the time of onset of convulsions and exhaustion and also of the condition of the lungs at autopsy. Two experiments were done at each of the first 3 time intervals and 3 experiments were done at 84 hours, as 10 of the 30 irradiated mice had already died at that time.

Results. Fig. 1 illustrates that within five hours the synergistic effect of oxygen and radiation had disappeared, as previously reported(1). When a 30-hour interval was allowed (Table I and Fig. 1) a reverse effect was observed, showing a significant protection against oxygen poisoning by a previous irradiation. Moreover, at 84 hours when the irradiated animals had begun to die from the terminal effects of irradiation they were very markedly protected against oxygen poisoning. There was no noticeable difference in the time of onset of convulsions between

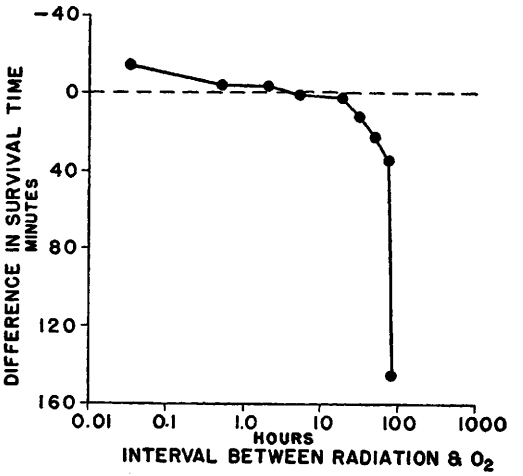

FIG. 1. Influence of initial and of secondary effects of X-irradiation on oxygen poisoning. Ordinates are differences in survival time (min.) resulting from exposure to X-irradiation compared to that from exposure to oxygen alone. Abscissae are intervals between exposure to radiation and to oxygen plotted in a logarithmic scale. Shortest interval is 2 min. Animals remained in high oxygen until death and survival times were measured from the time 6 atmospheres was attained until time of death.

TABLE I. Effect of Previous Radiation on Survival Times of Female Mice in 6 Atmospheres of Oxygen.

Interval, hr	No. of mice Control	No. of mice Radiated	% wt loss† of radiated mice	Mean survival time, min. Control	Mean survival time, min. Radiated	Increased survival due to radiation, min.	"P," %
30	19	20	10.0 ± 2.07	39.6 ± 1.77	51.7 ± 3.30	12.1 ± 3.75	.3
48	20	20	14.6 ± 2.09	34.2 ± 1.73	56.2 ± 3.73	22.0 ± 4.11	.0
72	20	20	22.7 ± 1.78	43.4 ± 1.73	77.4 ± 5.57	34.0 ± 5.83	.0
84	30	20*	29.3 ± 1.45	47.2 ± 1.41	193.0 ±24.29	145.8 ±24.33	.0

* Ten of 30 irradiated mice died between 72 and 84 hr, from the effects of radiation.
† Difference in final weight between control and irradiated mice in % of final control weight.

the previously irradiated and the control mice. Usually non-irradiated mice are in exhaustion approximately 20 minutes after the pressure has reached 6 atmospheres. With increasing intervals between irradiation and oxygen poisoning the time at which the irradiated mice were exhausted became progressively longer. In fact, at 84 hours some of the irradiated mice did not become exhausted until as much as 200 minutes elapsed. Only when the interval was 84 hours was a difference noticed in the appearance of the lungs of the irradiated and control mice. At that interval more than half of the lungs of the previously irradiated animals were in fairly good condition. It is interesting to mention here that Newsom and Kimeldorf(2) reported that there is an increased tolerance to lethal levels of hypoxia over that of controls following 500-600 r X-irradiation in rats. They concluded that this is, at least in part, a consequence of post irradiation anorexia as suggested by the comparable tolerance to hypoxia exhibited by non-irradiated rats fasted for 72 hours.

On the other hand, regarding increased oxygen tensions, Ozorio de Almeida reported (3) a striking increased resistance in rats starved for 4 to 6 days prior to the survival experiments in 6 atmospheres of oxygen. This finding was later confirmed by Campbell(4).

In our experiments there may have been starvation involved since the data in Table I indicate a significant progressive weight loss in the irradiated animals. Experiments are now in progress to determine to what extent the observed protection after irradiation is due to this factor.

Summary. The survival time of mice in 6 atmospheres of oxygen was about 40 minutes. The average survival times were prolonged 12, 22, 34, and 146 minutes, respectively, when the mice were irradiated (8800 r) 30, 48, 72 and 84 hours previously. Anorexia may have contributed to the observed protection.

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