AET Protection of Reproductive Capacity of Irradiated Mice. (27560)

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In recent years major attention has been focused on protecting mammals against acute radiation lethality by injection of chemical compounds before irradiation. Much less is known, however, about the ability of protective compounds to modify radiation injury at low dose levels, especially in mammalian germ cells. The effects of acute radiation doses on male fertility are well known(1,2). Wang *et al.*(3) found that 2-mercaptoethylamine (MEA) was capable of preventing transient sterility in male mice during the first 3 months after acute irradiation of the whole body, or the testes. In rats, treatment with MEA before 230-460 r X irradiation partially inhibited the reduction of the number of spermatogonia and resting prespermatocytes(6). Lüning *et al.*(4) demonstrated the effectiveness of MEA in protecting against radiation-induced genetic damage. They found that pretreatment of male mice with MEA reduced the postimplantation death of embryos sired shortly after irradiation to about 75% of that for males given physiological saline. These results are contrary to those of Kaplan and Lyon(5).

In female mice, irradiation causes a shortening of the reproductive period. The strong dependence of this effect on dose rate indicates that some natural repair of radiation damage to oocytes can occur(7). Rugh and Wolff(8) showed that pretreatment with MEA or cystamine delayed the onset of sterility in female mice given 50 r of X irradiation. Since AET (S,2 - aminoethylisothiourea - DiHBr) was found to be more effective than MEA in protecting the marrow and intestinal systems (J. R. Maisin and D. G. Doherty, unpublished data), we felt it worthwhile to determine the protective effect of AET on the reproductive capacity of female mice after irradiation.

Materials and methods. A previous study (9, and Ehling, unpublished data) of the variation in reproductive performance of female mice of 5 strains after 50 r X irradiation had established the relative fertility, calculated as percentage of the normal unirradiated female using total number of offspring/female as a measure, to be: SEC, 16%; A, 18%; SEA, 19%; NB, 32%; and DBA, 56%. The sensitivity of the SEC strain governed its selection for use in this experiment.

Forty SEC females with a mean age of 14 weeks were divided into 3 groups. Groups I and II received an intraperitoneal injection of 7 mg AET (as MEG in phosphate buffer, pH 7.2), Group III an equal volume of saline. Groups II and III were injected 15 to 20 minutes before whole-body X irradiation. The mice were exposed to 50 r in a Lucite wheel rotating on a 10.8-cm thick Masonite scatter block (dose rate 80 r/minute; 250 kvp; 15 ma; inherent filtration, 3 mm Al; hvl, 0.4 mm Cu; target-object distance, 84 cm). One day after exposure, each female was caged separately with a nonirradiated C3H male for the duration of the experiment. This interval between irradiation and mating was chosen to avoid the high incidence of induced dominant lethals in the first meiotic division(10). Control females (Group I) were mated in the same way, and litters were recorded and killed at birth. The experiment was limited to 36 weeks, because after that time the production of offspring in nonirradiated females decreased sharply.

Results and discussion. Irradiation with 50 r markedly reduced the reproductive capacity of both the saline-injected and the AET-pretreated mice. The results obtained are summarized in Table I along with the data (Ehling, unpublished data) from an experiment conducted under identical condi-

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TABLE I. Reproductive Capacity of SEC Females Over a Period of 252 Days.

Dose (r)	Pretreatment	No. of females	No. of offspring	No. of litters
0	None*	17	1,161	164
0	AET	10	745	106
50	AET	20	333	69
50	NaCl	10	100	17
50	None*	18	198	32

* Unpublished data from another experiment.

tions but with no chemical treatment. It can be readily seen that the dose of AET alone had no effect on the reproductive capacity of the mice, and that the irradiated saline controls were comparable to an irradiated, untreated group. The results have been pooled (Table II). The average reproductive period, calculated as time between the first mating and birth of the last litter, is materially shorter in both irradiated groups than in the unirradiated, but it is longer (110 days) for the animals pretreated with AET than for the untreated group (43 days). The mean number of offspring/female (Table II) is raised from 10.6 in the 50 r group to 16.7 in the AET-pretreated group. This difference is highly significant, yielding a t-value of 3.76, $p<0.001$. The corresponding values for the mean number of litters/female are 1.8 for the unprotected group and 3.5 for the protected group ($t = 4.93$, $p<0.001$).

These results clearly demonstrate that treatment of SEC females with AET before 50 r X irradiation affords some protection to the reproductive capacity, increasing the offspring/female ratio by a factor of 1.6 and the litter/female ratio by 1.9. In addition, the fertile period in the protected female is 2.6 times longer than in the unprotected. These findings are similar to those of Rugh and Wolff(8) for MEA, and indicate that both compounds have about the same reproductive protective efficiency at this low radiation dose level.

TABLE II. Relative Fertility and Standard Errors of SEC Females (252 Days).

Treatment	Offspring/ female	%	Litters/ female	%
0 r	70.6 ± 2.8	100	10.0 ± .2	100
50 r + AET	16.7 ± 1.6	24	3.5 ± .4	35
50 r	10.6 ± .7	15	1.8 ± .1	18

Summary. Treatment of female mice with S,2-aminoethylisothiourea-DiHBr (AET) before 50 r whole-body X irradiation gave some protection to their reproductive capacity when compared to irradiated controls, increasing the length of the reproductive period, the number of litters per female and the number of offspring per female.

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