TABLE 2

FREQUENCY OF CHROMOSOMAL ABERRATIONS AFTER REMOVING PLANTS FROM 2 MONTHS' EXPOSURE TO 1.7 r OF γ RADIATION. RECOVERY PERIODS, 1 WEEK TO 4 MONTHS

Recovery time	No. chromosomes	Chromatid breaks	Chromosome breaks	Total % breaks
1 week	3,150	7	3	.32
2 weeks	4,320	4	0	.09
3 "	5,760	4	4	.14
4 "	2,910	1	0	.03
6 "	1,800	0	0	.00
4 months	6,180	3	0	.05

Counts from control plants were made at the same time. The normal sterility varies considerably, presumably in response to environmental conditions of temperature and light, and ranged from 5 to 14%. The percentage of sterility in the controls was deducted from the sterility of the exposed plants to give the net sterility due to radiation effects. The data are shown in Table 3.

TABLE 3

POLLEN STERILITY INDUCED BY CONTINUOUS RADIATION AND THE RECOVERY OF POLLEN FERTILITY SUBSEQUENT TO 5 WEEKS OF EXPOSURE

No. weeks exposure	Net pollen sterility			
	During exposure		After exposure	
	1.7 r/day	8 r/day	1.7 r/day	8 r/day
1	6	−1	28	42
2	11	4	28	42
3	29	3	18	48
4	37	14	18	56
5	24	35	4	37
6	35	37	3	33
7	31	50		50
8	42	53		53
9	25	48		18
10	27	43		9
11	21	55		9
12				2
13				0

At an intensity of 1.7 r/day the pollen sterility increased during the first 3 weeks and then leveled off at about 30%, although there was considerable variability from week to week. At 8 r/day the maximum sterility was not reached until about the sixth or seventh week, presumably in consequence of the retarding effect of the greater amount of radiation; but after 6 weeks' exposure, the pollen sterility remained at about 50% during the subsequent weeks. At this intensity there was considerable inhibition of floral development, and very few flowers were produced after 2 months of exposure.

After 5 weeks of exposure some of the plants were removed from the field of radiation in order to see how long the pollen sterility would continue. At 1.7 r/day the pollen fertility at 5 weeks after exposure was practically normal. At 8 r/day the plants did not recover normal fertility until about 12 weeks after removing them from the beam of γ rays. This greater delay in recovery is attributed to the greater retardation of growth of the plants at the higher intensity.

The lack of a cumulative effect in the production of microspore chromosome aberrations and pollen fertility after several weeks' exposure to low intensities of γ rays, and the recovery of normal microspore chromosomes and pollen fertlity after the plants are removed from the radiation field, indicate that cells containing chromosome aberrations do not continue to divide or are outgrown by the normal cells. Earlier work (*1*) has shown that, if sufficient radiation is given to produce chromosomal aberrations in nearly all cells, the plant dies. At low intensities of radiation many cells are not permanently affected, and presumably these cells are the ones that produce the normal microspore chromosome complements and the fertile pollen grains. Continuous exposure to several roentgens per day does not seriously reduce pollen fertility or seed set, although it is possible that some deleterious mutations may appear in later generations. The fact that both chromosome aberrations and pollen sterility level off after a few weeks of exposure indicates that the plants can survive and reproduce after months, or perhaps even years, of exposure.

These results indicate that Tradescantia plants, and probably most plants, can survive continuous radiation at the rate of several roentgens per day. Unfortunately, they cannot be expected to apply to the higher animals, including man. The factors of determinate growth, high sensitivity of critical tissues, the absence of haploid mitosis in gametophytic development, and the lack of rapid somatic divisions preceding egg formation, should render animals much more vulnerable to low intensities of ionizing radiation.

References

1. SAX, K. *Genetics*, 1941, **26**, 418.
2. SPENCER, W. P., and STERN, C. *Genetics*, 1948, **33**, 43.
3. UPHOFF, D. E., and STERN, C. *Science*, 1949, **109**, 609.

A Comparison of the Response of Normal and Hypothyroid Mice to Acute Whole Body Roentgen Radiation[1]

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In 1949 Blount and Smith (*1*) showed that premedication with thiouracil slightly decreased the mortality of mice subjected to acute whole body roentgen ray irradiation. This would indicate that the hypothyroid state was conducive to survival after roentgen ray irradiation. Shortly thereafter Patt *et al.* (*6*) reported significant decreases in radiation mortality in animals premedicated with cysteine. It was postulated that the beneficial effect

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observed was the result of protection of the sulfhydryl groups in the animal organism. This statement, coupled with the fact that thiouracil and its derivatives have a potential sulfhydryl group in their molecules, led us to investigate the possibility that such drugs would protect animals against the lethal effects of roentgen radiation. Furthermore, it was possible that the effect of such drugs could be enhanced by longer premedication periods than those employed by Blount and Smith (*1*).

protection was produced by these drugs. It is possible that the potential sulfhydryl group in the thiouracil compounds was unavailable, and thus combination could not take place between it and similar groups in the animal organism.

Statistical evaluation of the mortality data in Table 1 by the method of Litchfield (*5*) reveals that the slopes of the curves for a given experiment are almost identical. Furthermore, in a given experiment and between different

TABLE 1

RESPONSE OF NORMAL AND HYPOTHYROID MICE TO ROENTGEN RAY IRRADIATION

Drug	Total mortality					Approx. LD_{50}/day‡					Total drug ingested in mg (av. values)**				
	C†	1	2	3	4	C†	1	2	3	4	C†	1	2	3	4
Thiouracil	6/10*	10/10	9/10	7/10	8/10	11	8.5	13	14	12	0	65	122	174	292
Propyl thiouracil	9/10	10/10	8/10	10/10	5/7	13	8.5	9.2	12	12.5	0	39	98	132	200
	10/10	10/10	10/10	10/10	9/9	10	10	9	11	13	0	52	128	189	260
Methyl thiouracil	9/10	9/10	9/10	7/9	7/10	13	11	12	15	12.5	0	79	160	264	316

* Ratio signifies number dead over total number of mice in group.
† Control; 1, 2, 3, 4 signify number of weeks of antithyroid premedication.
‡ Day upon which 50% of the group died because of irradiation. ** Mg of drug/mouse/week.

Adult male mice, CF #1 strain, weighing 20–33 g (av. 23 g), raised in our own colony, were divided into 5 groups of 10 animals each and caged individually as described by Bratton (*2*). The control group received plain tap water, and each of the other groups received 0.1% of the antithyroid drug in their drinking water for periods varying from 1 to 4 weeks. These drugs were solubilized by the use of an equimolar quantity of sodium bicarbonate and heat. In each experiment all the mice were irradiated as a single group in a cage similar to the one previously described for guinea pigs (*4*). Upon completion of the 28-day premedication period, the animals were subjected to 550 r acute whole body roentgen ray irradiation. The technical factors were: 250 kv, 15 ma, TSD 100 cm, filters: 0.21 mm Cu inherent, 0.5 mm Cu parabolic, and 1.0 mm Al; HVl 1.85 cm Cu, size of field—total body; r/min measured in air 9.06–9.70. Uniformity of dosage was insured by rotating the radiation cage during treatment. The 250 kv Picker Industrial Unit used was calibrated before each experiment with a Victoreen Thimble r-meter. After irradiation the animals were maintained on their ordinary diet (Rockland pellets) and received no further antithyroid medication. Autopsies were performed upon all animals that died during the 30-day experimental period and upon all survivors at the end of that time. The usual signs of radiation damage (diarrhea, bloody stools, petechial hemorrhages, pale mucous membranes, etc.) were observed in all the irradiated animals. Gross examination of the thyroids of the medicated animals showed the usual signs of antithyroid medication, the over-all effect being greater with the longer premedication periods (3 and 4 weeks). Details of the results are given in Table 1.

Although Table 1 shows that large amounts of antithyroid compounds were ingested, it is evident that no experiments, there is relatively little difference in the radiation LD_{50} day (50% radiation mortality), and thus there is little difference in the susceptibility of normal and hypothyroid animals to roentgen ray irradiation damage. This indicates that the mechanism involved in both the normal and the hypothyroid animal is probably the same, and that the hypothyroid state confers no real protection on the animal. It is well known that in the hypothyroid state there is a diminished utilization of oxygen as compared to the normal. However, Zondek (*7*) has shown that there is very little difference in oxygen saturation and oxygen tension in the normal and the hypothyroid states and that the oxygen dissociation curves in both states are almost identical. Thus it is possible that the amount of free oxygen, and not its rate of utilization, determines the extent of damage produced by roentgen ray irradiation. This would be in accord with the statement of Dowdy, Bennett, and Chastain (*3*) that roentgen ray irradiation damage is the result of radiochemical reactions involving free oxygen.

References

1. BLOUNT, H. C., JR., and SMITH, W. W. *Science,* 1949, **109**, 83.
2. BRATTON, A. C., JR. *J. Pharmacol. exp. Therap.,* 1945, **85**, 111.
3. DOWDY, A. H., BENNETT, L. C., and CHASTAIN, S. M. *Study of the effects of varying oxygen tensions on the response of mammalian tissue to roentgen irradiation.* U.C.L.A. 55, Jan. 3, 1950.
4. HALEY, T. J., and HARRIS, D. H. *Science,* 1950, **111**, 88.
5. LITCHFIELD, J. T., JR. *J. Pharmacol. exp. Therap.,* 1949, **97**, 399.
6. PATT, H. M., *et al. Science,* 1949, **110**, 213.
7. ZONDEK, H. *The diseases of the endocrine glands* (trans. by C. Prausnitz), Baltimore: Wm. Wood Co., 1936, 3rd ed. P. 121.