which ranged from obvious intense injury with necrosis to no apparent inflammatory reaction and suppression of any inapparent inflammation by adrenocorticosteroids. Thus the possibility must be entertained that increased excretion was related to introduction of chelating agents. The observation warrants extension of studies to humans where use of chelators may offer an additional experimental approach to a study of factors influencing urinary levels of acid mucopolysaccharides in humans. The mechanism by which chelators may have induced an increased level of excretion in rabbits is not known. Whether the same observation of increased excretions holds in humans will be investigated.

Summary. (1) Introduction of chondroitin sulfate into the blood stream of rabbits was followed by elevated excretion of acid mucopolysaccharides in urine totalling 5-10% of injected amount over 2-4 days thereafter. Repeated injections were followed by excretions which were still 5-fold greater than baseline levels one week after third and last injection. (2) Repeated subcutaneous injection of disodium EDTA and disodium calcium EDTA into rabbits was followed by a brief and frequently mild rise in urinary excretion of acid mucopolysaccharides; onset, degree and duration of rise varied widely from animal to animal.

The authors are indebted to Harry T. Tully and W. J. K. Rockwell for management of daily urine collections and injection of rabbits and to Sadie Taylor for skillful technical assistance; also to Philip Pickett for preparation and special staining of histologic sections.

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Received October 13, 1959. P.S.E.B.M., 1960, v103.

Radiation Avoidance in the Mouse. (25597)

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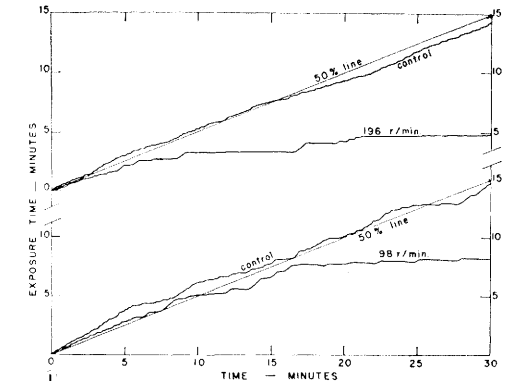
It is commonly stated that animals are incapable of detecting high energy radiation with the unaided senses but there is some evidence that it can be sensed under certain circumstances. Two individuals who received a substantial beta particle dose to the hands reported a local "tingling sensation" during exposure. Another individual receiving several thousand rads from an electron beam experienced a burning sensation although there was probably no temperature rise greater than 0.05°C. In animals relatively small doses of penetrating radiation have produced later avoidance behavior(1) in cats, rats, and mice. A direct radiation avoidance has been reported(2) in albino rats at dose rates of 1-4 r/minute after a total dose of 360 r had been delivered. Our experiments were designed to determine whether mice were capable of sensing the presence of an X-ray beam, and if so, whether it was recognized as something sufficiently unpleasant to be avoided.

Methods. During each run the test animal was in a plastic cage 25 x 9 x 6 cm pierced with many small holes to permit free air circulation. This cage was mounted on a knife

edge so that it could tilt freely through a small angle as the mouse moved past the center line. An aluminum box surrounded the cage to provide uniform enclosure conditions. Fresh air was supplied to the enclosure through 2 symmetrically placed manifolds with many small ports so that an adequate flow could be maintained without a strong blast. One-half of the enclosure was under 8 inches of lead which reduced radiation to less than 10^{-3} of that in the unshielded half. Shield and exposure cage were enclosed in a light-tight box to eliminate external visual clues to the test animal. An electrical contact closed when the mouse was in the exposure half of the cage. This contact actuated a linear potentiometer driven by a synchronous motor to put a steadily increasing signal onto a strip chart recorder. In a symmetrical environment the normal expectation would be for 50% occupancy in either half of the exposure cage. When the animal was in position voltage supplied to the potentiometer was made twice the calibration voltage. Fifty per cent occupancy would then produce a record having segments with twice the calibration slope interspersed with segments of zero slope. Thus a 50% occupancy record would follow in staircase fashion the smooth calibration line. Adult mice of NIH strain were used. Before each run a calibration was made to establish the 50% occupancy slope. Then a mouse was put in the test situation for a run without radiation. Recording started 5 minutes after the light-tight box was closed and continued 30 minutes. During this control all machinery capable of providing auditory clues was put in operation. A random orientation around the center line of the vertical beam was used to randomize unsuspected auditory clues. After each run the plastic box was thoroughly washed in detergent. If this step was omitted the next occupant would not divide his time equally between the two halves of the box. Five days after the control run each mouse was run with radiation at one of the nominal dose rates of 50, 100, 170 or 200 r/minute with 10 animals in each dose rate group. All radiations were done with X-rays produced at 3 Mev with a Van de Graaff generator, at one meter TSD.



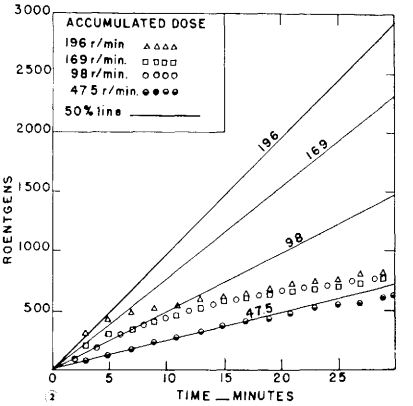


FIG. 1. Records of occupancy of test cage, with and without radiation. Coordinate lines on recording paper have been lost in reproduction.

FIG. 2. Mean dose accumulation at the 4 dose rates.

Results. Although there were individual differences each animal was sufficiently active to sample each half of his environment a good many times during a 30 minute run. The records shown in Fig. 1 are typical. With no radiation each animal followed the 50% line quite closely, indicating a lack of bias in the test environment.

With radiation the 50% line was followed for a few minutes and then each animal began to show a preference for the shielded section. Each venture outside was short, hence the total stay outside was below normal expectancy. Although the number of in-out cycles was reduced in the presence of radiation there were enough trials in each case to suggest that the animal recognized the outside environment and found it unpleasant.

By the time an animal had established a preference for the shielded environment he

had received a substantial dose of radiation, and this may have been a factor in reducing the activity(3). Thus in Fig. 1 the 98 r/minute animal showed a definite deviation from normal expectancy at 9 minutes and 440 r while the 200 r/minute animal made a choice at 2 minutes and 200 r.

Fig. 2 shows mean normal expectancy, control occupancy, and accumulated radiation dose for the 4 dose rates. There was, of course, no actual dose accumulation for controls, the values showing what would have been received if the beam had been on. In each group there is a definite radiation avoidance, starting after a dose of 300-400 r has been received.

During the last 10 minutes each group accumulated radiation at the rate of about 15 r/minute, independent of dose rate available. The 30 minute dose accumulations are surprisingly similar, being 625, 810, 780 and 830 r respectively.

Discussion. Relatively large variations might be anticipated in experiments involving animal behavior and in general the present data are surprisingly consistent. With no radiation, occupancy of the test cage was essentially symmetrical indicating a nearly clueless environment. At an available dose rate of 47.5 r/minute there was increased variability in individual responses, some animals spending more than expected time in the beam. Response patterns suggest an awareness of a new environmental element without recognizing it as unpleasant or threatening.

At 98 r/minute and above the new element is increasingly recognized as unpleasant and reaction to it becomes more uniform. At 200 r/minute the irradiated area was avoided for relatively long periods and ventures into the beam were short.

The present experiments are not adequate to establish whether avoidance arises from a direct stimulation or is the result of stimulation by radiation products such as ozone or the oxides of nitrogen. An argument against a secondary stimulation lies in the relatively constant dose, but variable time, at which avoidance becomes established. Under the experimental conditions equilibrium concentrations of gaseous radiation products should be attained very rapidly and recognition should be equally prompt.

It appears that the clue to avoidance does not lie in the emission of visible light arising from fluorescence in the irradiated plastics. Control experiments were run with the enclosure uniformly illuminated at a level high enough to mask any feeble emissions due to fluorescence. Avoidance behavior was identical with that seen in darkness.

The fact that avoidance is established at about the same dose as in the rat(2) is interesting but probably fortuitous.

Summary. Ability of mice to recognize presence of X-ray beam, and to consider it obnoxious, has been investigated. At 50 r/minute and above there is an increasing avoidance of the radiation beam. Avoidance may be due to presence of ozone and oxides of nitrogen, although this seems unlikely from results of controlled ventilation experiments. Direct visual clues from fluorescence in the plastic cage are not responsible for the avoidance.

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Received October 27, 1959. P.S.E.B.M., 1960, v103.