TECHNICAL PAPERS

The Influence of Thyroid and Thiouracil on Mice Exposed to Roentgen Radiation

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Although reports are not entirely in agreement, there is considerable evidence that heat sensitizes neoplastic tissue to high-energy electromagnetic irradiation (*1, 3, 6*). It has been postulated that temperature effects are, at least in part, referable to effects on cellular metabolism, but few studies have been reported in which metabolic rate was varied independently. The present experiments were made to determine whether or not thyroid or thiouracil feeding would alter the incidence of death among mice exposed to severely damaging whole body radiation.

Mice were of the N.I.H. strain, the first shipment consisting of 70 males about 10 weeks old, the second of 59 males and 61 females about 6 weeks old. They were divided into 3 comparable treatment groups as shown in Table 1. One group was maintained on the stock diet of powdered Purina dog chow. Desiccated thyroid was added to the stock diet for the older mice in the second group, beginning 13 days prior to irradiation (0.5% for 9 days and 0.3% thereafter), and to that of the younger mice, beginning 8 days prior to irradiation (0.5% for 5 days and 0.3% thereafter). In the third group the older mice received 0.5% thiouracil with the stock diet, beginning 13 days prior to irradiation; the younger mice, 0.5% thiouracil beginning 8 days prior to irradiation.

Irradiation was administered at the National Cancer Institute. Peak voltage of the machine was 186 kv; effective voltage, 170 kv; current, 20 ma; added filtration, 0.55 mm of aluminum and 0.25 mm of copper; and focal distance 50 cm. Eight or 9 mice, drawn at random in approximately equal numbers from the three diet groups, were irradiated simultaneously. The mice were under observation for 4 weeks following irradiation.

Evidence that the thyroid of the diet strongly affected metabolic rate is adduced from the fact that when 8 mice from each diet group of the first shipment were subjected to a 24-hour fast in preparation for the determination of oxygen consumption, 4 of those on 0.5% thyroid died, while none of those on the control diet or on thiouracil died. As a result of this experience, we reduced the thyroid content of the diet to 0.3%.

A few determinations of oxygen consumption were made after the mice had been on the experimental diets for about a week and before they were irradiated. The method described by Tabor and Rosenthal (*4*) was used, except that each determination was made with 2 or 4 mice in the chamber, and the lowest value of 2 to 6 determinations of 5-min duration at 22° C was used for each group. The average for 8 mice receiving thyroid was 40% higher than that for mice on the control diet, while the average for 6 mice on thiouracil was 6% higher than the control value. A more extensive study of the oxygen consumption of thyroid-fed mice before and after irradiation is in progress.

The incidence of death following irradiation is shown in Table 1. The difference between the 54.8 mortality of the thyroid group and the 15.6% mortality of the control group is highly significant as shown by chi-square. The difference between the 9.4% mortality of the thiouracil group and the mortality of the control group is not statistically significant.

TABLE 1

THE INFLUENCE OF THYROID AND THIOURACIL ON THE INCIDENCE OF DEATH

Shipment no.	Desiccated thyroid		Control diet		Thiouracil	
	Dead	Alive	Dead	Alive	Dead	Alive
1 (♂)	13	8	5	19	4	21
2 (♂)	12	9	3	16	2	17
2 (♀)	9	11	2	19	0	20
%	54.8		15.6		9.4	

It is of additional significance that 20 of the mice receiving thyroid had died by the 10th day following irradiation, while at that time only 3 of those on the control diet had died. Among the younger mice (shipment 2), 6 died between the 3rd and 5th days, while the first death among those on the control diet occurred on the 5th day, and no others on the control diet died until the 10th day. All of the deaths in the thiouracil group occurred after the 10th day following irradiation.

By use of an oral clinical thermometer with the bulb completely inserted into the rectum, temperatures were determined on 6 mice of each diet group at the end of the 4 weeks of observation following irradiation. Temperatures of the thyroid group averaged 38.5° C (range, 38.2°–39.1°), of the control group, 37.6° (range, 37.4°–37.8°), and of the thiouracil group, 37.2° (range 37.0°–37.6°).

Thyroid feeding resulted in a relatively small increase in rectal temperature, while, without doubt, the metabolic rate was considerably elevated. In preliminary experiments the mortality of irradiated mice, kept in an environment of 10° C, was significantly higher than that of mice at 29° C. At 10°C the rectal temperature is reduced by only about 1 degree from its value in an environment

of 29° (*5*), while according to Herrington (*2*), total heat production is approximately doubled at the lower temperature.

It seems probable that metabolic activity, rather than body temperature, is the predominant factor in increasing the mortality of mice exposed to severely damaging Roentgen radiation. Further experiments concerned with these relationships are in progress.

References

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A Method for Studying Growth in Different Groups of Arthropods

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Linear growth in arthropods is largely discontinuous and usually, but not always, most conspicuous during the molting interval (*1, 5*). Shafer (*9*) likens the linear-growth curve to a series of steps. Size increments during the successive molts are subject to pronounced variation depending, in many instances, on the food supply and on the temperature factor. Also, the final size attained following a particular molt is a function of the initial size, *i.e.* the dimensions prior to molting. Hence, the effect of variation in respect to a particular molt is likely to be cumulative to different degrees in succeeding molts. Wesenberg-Lund (*10*) refers to the rearing method and the method of population analysis for studying age and size of insects at particular instars. MacKay and Weymouth (*4*) in their classical study of *Cancer magister* Dana used population data, largely, for their estimates of per cent increase in size, number of instars, age at sexual maturity, and maximum age.

Animals that grow by molting comprise such a large group that no one method is likely to apply reasonably well to all of them. Rather it is expected that a combination of two or more methods may be needed in the study of even one restricted systematic group. From our studies of the blue crab, *Callinectes sapidus* Rathbun, a method has evolved for estimating the number of post-larval molts typical of a species, and also the size characteristics of the different instars (*2, 3, 6,* and *7*). Because of the application of this procedure to other arthropod groups and its potential value as a tool in attacking diverse practical, as well as theoretical, growth problems, the essentials of the method are related here. The technic was made possible by the large numbers of crab measurements made by Miss Ellen H. Gray and the ingenious rearing experiments carried out by Mrs. Mildred D. Sandoz while working with the writer at the Chesapeake Biological Laboratory and the Virginia Fisheries Laboratory.

The immediate antecedent of these observations was the work of Robertson (*8*) who, by great patience and effort, was able to rear postlarval crabs of this species to an advanced stage in development. Cognizance of the difficulties involved and the obvious variability in the results discouraged similar attempts by us to solve the problem of rearing blue crabs through to the last instar.

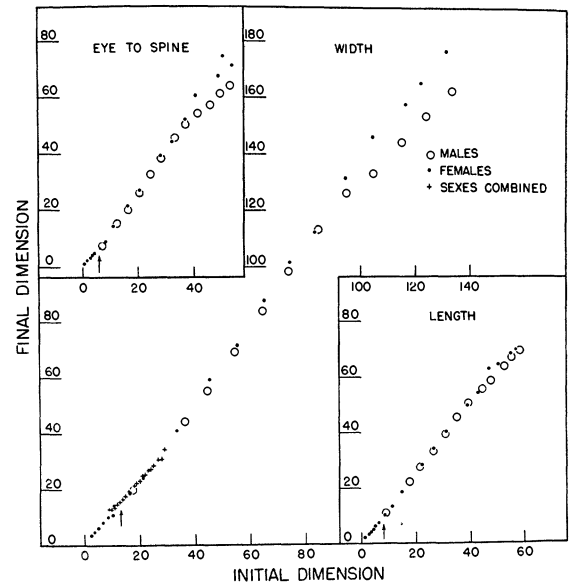

FIG. 1. Relation of initial to final size in *Callinectes sapidus* Rathbun. Sexes are combined in groups to the left of the arrows and in the plus groups.

Even if it were possible to do so, individual variation is so great that a prohibitive, and doubtless impossible, number of crabs would need to be reared in order to yield reliable size averages, representative of the species. The procedure outlined below proved to be reasonably satisfactory and is, seemingly, subject to wide application in the arthropod group.

Small crabs caught just prior to molting were kept in running salt water in the laboratory until they molted. Large crabs molted successfully in specially constructed floats kept near the shore. Hence, simulation of essentially normal conditions was accomplished. Reasonably large numbers of crabs of all sizes were measured before (initial dimension) and after (final dimension) molting. From these data a curve was constructed indicating, for example, the final width, corresponding to any initial width (Fig. 1). This growth curve proved to be a very valuable tool, because once the width of the first instar is known, we have a starting point for using the curve to estimate the theoretical number of instars characteristic of the species. Mrs. Sandoz established the mean width of the first postlarval instar to be 2.5 mm. Thus, from the chart we learn that a crab having an initial width of 2.5 mm has a final width of 3.7 after molting. But this final dimension now becomes the initial width