Study of the Synergistic Effects of Heat Exposure and Ionizing Irradiation in the Hamster (33407)

R. R. J. CHAFFEE AND X. J. MUSACCHIA
University of California, Santa Barbara, California 93106; and Department of Physiology and Space Sciences Research Center, University of Missouri, Columbia, Missouri 65201

In mammals, whole-body exposure to high levels of irradiation (circa 1000 R) results in an increased rate of mortality due to a variety of physiological (pathological) effects. Exposure to high ambient temperatures, above the thermal neutral zone, also results in some physiological changes which reflect conditions of stress. These changes are not entirely deleterious since heat-acclimated hamsters are better able to survive acute elevated heat exposure than are nonacclimated controls (1). There is very little information available concerning the combined effects of prolonged heat exposure plus ionizing radiation. Carlson and Jackson (2) found that under particular experimental conditions exposure to high temperatures and chronic intermittent low level radiation tended to increase the life expectancy of Sprague-Dawley rats. From their report one might suppose that some synergistic action of heat acclimation and exposure to low level ionizing radiation results in enhanced viability. However, there is no reason to suspect that heat-acclimated animals exposed to high levels of ionizing radiation would respond in a comparable manner. Indeed, it seems more logical to suggest that effects from the two forms of environmental insult would be additive and reflected in an increased mortality rate.

The hamster provides a number of interesting aspects in studies which combine heat exposure and radiation damage. In the hamster, both acute heat exposure and heat acclimation result in an elevation of deep body temperature (1). Thus from a consideration of Arrhenius' principles concerning temperature dependent chemical reactions, certain biological (in this case pathological) events should occur more rapidly in heat-exposed hamsters. One might hypothesize that death from radiation damage should appear sooner. On the other hand, in the hamster, heat-acclimation and acute heat exposure both result in a lower metabolic rate (3). Following prolonged heat exposure, hamsters have a lower body weight, relatively reduced liver, testis, kidney, heart and epididymal fat pad weights (1), and there is presumably a lowering of the rate of total body protein recycling (4). With this combined decrease in metabolic activity, as well as growth, one might expect that some biological events in the heat-exposed animals are slowed and the pathology and death due to radiation might be delayed. Since experimental evidence to support or contradict either of these suppositions has been lacking, the following experiments were performed to determine the effects of prolonged heat exposure and whole-body irradiation on survival time in hamsters.

Methods and Materials. Ninety-two adult male hamsters (*Mesocricetus auratus*) from the colony room were divided into two groups: (A) controls (51 animals) were retained at 24°; (B) heat acclimated (41 animals) were placed in a hot room at 34–35°. Both groups were maintained at about 40% humidity. All animals were caged singly, exposed to 12 hr of light/day, and given Wayne lab Blox pellets and water *ad libitum*. At the end of the 2-month temperature exposure period, both controls and heat-acclimated animals were weighed and given a single whole-body radiation dose of 750 rads at a rate of 170 R/min using a GR-12 gamma cell, United Nuclear of California. Details of the irradiation procedure have been described elsewhere (5). The irradiation dose of 750 rads was approximately the LD_{50} (30) for

This research was supported by United States Air Force Contract No. F29600-67-C-0009; Contract No. DADA 17-68-C-8064 from the U.S. Army Medical Research and Development Command; and NASA Grant NGR 26-004-021.

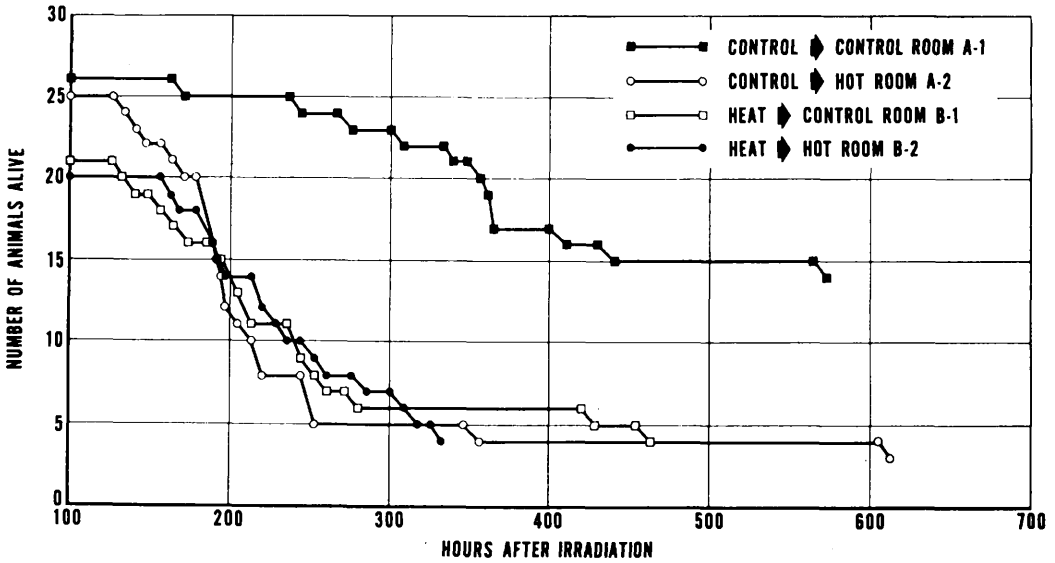

FIG. 1. Numbers of surviving animals in each experimental group at various periods of time after irradiation.

the strain of hamsters used. These animals were obtained from a commercial source (Eldridge Rabbitry, Creve Cour, Missouri).

Following irradiation, half of each group, A-1 and B-1, were placed in the 24° environment, and the other half of both groups, A-2 and B-2, respectively, were placed in the hot room. All animals were kept on the preirradiation laboratory regimen with respect to food, water, light, and caging. Animals were checked at 8-hr intervals (7 a.m., 3 and 11 p.m.) and the time of death was recorded to the nearest 1/3 day unit. Body weights were recorded at the time of death.

Results and Discussion. The survival data and weight changes following irradiation are presented in Fig. 1 and Table I. The increase in rate of mortality induced by irradiation in the heat-exposed groups, A-2, B-1, and B-2 are notable. Of particular interest is the relatively comparable lethality of heat either before, after, or both before and after irradiation. The shortest postirradiation survival time appears in the A-2 animals (Table I). This could be explained on the basis that in the A-2 group there is a double stress imposed simultaneously, i.e., postirradiation effects plus being placed in a hot environment. The possibility of a double stress in the B-1 animals must also be considered since these are heat acclimated before irradiation and then suddenly exposed to 24°. This could, in effect, be a cold stress for these animals (1). They appear to be no different with respect to postirradiation survival time from the B-2 group. In any event, the data clearly indicate that in hamsters heat and irradiation form a synergistic and highly lethal combination of factors. These results support the concept that the heat-induced

TABLE I. Effect of Thermal Treatment and Whole Body Irradiation (750 rads) on the Survival of Adult Syrian Hamsters.

Group[a]	Total no. of animals	Av wt. loss of animals that died (g)	Time after irradiation when 50% of animals were dead (hr)
A-1	26	30.3	573
A-2	25	23.3	197
B-1	21	19.5	245
B-2	20	18.8	237

[a] A-1 = hamsters acclimated to 24°, irradiated and returned to 24°; A-2 = hamsters acclimated to 24°, irradiated and then put in hot room (34–35°); B-1 = hamsters acclimated to 34–35°, irradiated and then put in room at 24°; and B-2 = hamsters acclimated to 34–35°, irradiated and returned to hot room at 34–35°.

elevation of deep body temperature acts additively with a high dose of radiation to reduce survival time.

In an earlier work, Crile (6) showed that exposure to moderate heat (circa 44°) and radiation were effective in destroying various transplantable tumors in mice. It is of interest that such synergestic, or additive, effects may be operative on a local level, e.g., tissues and organs, as well as tumors, and on the whole animal level, as demonstrated using hamsters.

The present experiment is initial in nature and caution is advised in extrapolation to possible results with other species. However, because of growing possibilities of accidental exposure (e.g. industrial or warfare) to ionizing radiation in combination with environmental heat stress this overall area warrants considerable additional effort.

Summary. Adult male hamsters were placed in a hot room, 34–35°, and heat acclimated for 2 months. Controls were maintained at 24°. Each animal was given a single whole-body exposure to ionizing radiation from a 60 cobalt source. Half of the heat-acclimated animals were then transferred to 24° and half returned to the hot room. Half of the controls were placed in the hot room after irradiation. Comparisons of survival times were made; heat exposure either before or after irradiation, or both before and after irradiation lowered the survival time to less than 50% that of the controls, i.e., hamsters which were irradiated but not heat exposed.

1. Cassuto, Y. and Chaffee, R. R. J., Am. J. Physiol. **210**, 423 (1964).

2. Carlson, L. D. and Jackson, B. H., Radiation Res. **11**, 509 (1959).

3. Cassuto, Y., Ph.D. dissertation, University of California, Riverside, California, 1964.

4. Chaffee, R. R. J., Jousef, M. K., and Johnson, H. D., Federation Proc. **27**, 633 (1968).

5. Barr, R. E. and Musacchia, X. J., Proc. Soc. Exptl. Biol. Med. **24**, 1204 (1967).

6. Crile, G., Jr., Cancer Res. **23**, 372 (1963).

Received June 20, 1968. P.S.E.B.M., 1968, Vol. 129.

Antibody Formation in Hibernating Ground Squirrels (*Citellus tridecemlineatus*)* (33408)

J. M. MCKENNA AND X. J. MUSACCHIA

Departments of Microbiology and Physiology, School of Medicine, and the Space Sciences Research Center, University of Missouri, Columbia, Missouri 65201

While the literature on various aspects of the physiology of mammalian hibernation is voluminous, surprisingly little has been published concerning the immune mechanisms of mammals in this state. Andjus *et al.* (1) injected rabbit erythrocytes intravenously into hibernating ground squirrels, and assayed the sera for agglutinins for periods up to 40 days of hibernation. They reported that, as long as the animals were hibernating, no circulating agglutinins were formed. Jaroslow and Smith (2) gave a single intraperitoneal injection of ^{131}I-labeled bovine serum albumin (BSA) *before* placing the ground squirrels at 5°, and studied antigen disappearance. They concluded that there was no net synthesis of antibody.

It is the opinion of the few workers in this field that the hibernating mammal is not capable of producing circulating antibodies while in hibernation. This opinion has been based almost exclusively on studies of the primary response to a few antigens using relatively insensitive methods for detecting antibodies. Furthermore, it has not been established whether the essential machinery to invoke an anamnestic response is operating in hibernating mammals.

* Supported in part by NASA Grant 26-004-021 S2. We wish to acknowledge use of laboratories in the Research Reactor Facility, University of Missouri, Columbia, Missouri.