THE EFFECTS OF PROLONGED TRAINING ON THE RESISTANCE TO RADIATION-INDUCED CHANGES IN MALE ALBINO RATS

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Robert Kertzer
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This is to certify that the

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THE EFFECTS OF PROLONGED TRAINING ON THE RESISTANCE TO RADIATION-INDUCED CHANGES IN MALE ALBINO RATS

presented by

Robert Kertzer

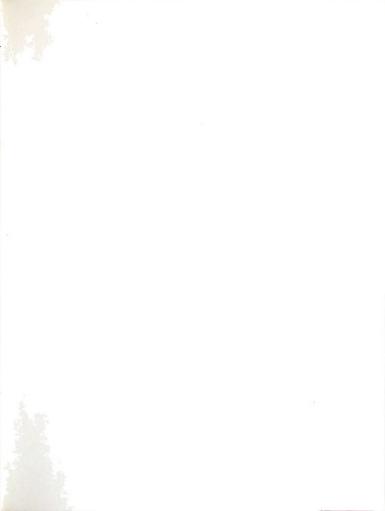
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ABSTRACT

THE EFFECTS OF PROLONGED TRAINING ON THE RESISTANCE TO RADIATION-INDUCED CHANGES IN MALE ALBINO RATS

by Robert Kertzer

The purpose of this investigation was to study the effects of various levels of preirradiation physical activity, from weanling age to adulthood, upon the radiation resistance of mature rats.

Two-hundred and fifty 26-day old male albino rats

(Sprague-Dawley strain) were randomly assigned to one of five treatments. Group 1 (sedentary control) received no special treatment, other than radiation, and was confined to individual sedentary cages both prior to and after being irradiated. Group 2 (spontaneous control) received no special treatment, other than radiation, and was housed in individual spontaneous exercise cages until irradiated and then confined to individual sedentary cages. Group 3 (sedentary forced) was housed in individual sedentary cages both prior to and after being irradiated. During the training period prior to irradiation, these animals were forced to swim daily for one-half hour with two per cent body weight attached to the

base of the tail. Group 4 (spontaneous forced) was housed in individual spontaneous exercise cages until irradiated and then confined to individual sedentary cages. Prior to being irradiated these animals also were forced to swim daily for one-half hour with two per cent body weight attached to the base of the tail. Group 5 (spontaneous effect) was housed in individual spontaneous exercise cages both prior to and after being irradiated. These animals were not subjected to the preirradiation forced training regimen.

The preirradiation treatments were begun at 27 days of age and were carried on throughout puberty and early adult-hood. On the 83rd day of the preirradiation treatments, 20 per cent of the animals, randomly selected with stratification by groups were placed in sedentary cages for an approximate 64-hour rest period prior to irradiation. The forced swimming regimen was terminated for these animals at this time. On the 84th, 85th and 86th days, a similar procedure was followed with 20, 30 and 30 percent of the animals respectively. Following the 64-hour rest period, each animal was exposed to 650 r while confined in a three-inch by nine-inch lucite chamber.

Nine days before and five days following irradiation, a blood sample was drawn from the orbital sinus of each animal

to determine the WBC and eosinophil count. During the 30 days immediately following irradiation, mortality and survival time in hours were recorded for all groups of animals. At the end of the 30-day period, the surviving animals in all groups were sacrificed. Upon death or sacrifice, body weight as well as the weights of the spleen and adrenals were determined.

Statistical analysis of the experimental data has prompted the following conclusions:

- 1. Forced swimming for one-half hour daily with two per cent body weight attached significantly increases spontaneous activity.
- Forced swimming and/or spontaneous activity for a prolonged period reduce body weight.
- 3. Illumination of animal quarters 24 hours daily significantly reduces volitional activity as compared to 12-hour per day illumination.
 - 4. Irradiation decreases spontaneous activity.
- 5. Prolonged training does not alter WBC or eosinophil levels either prior to or following irradiation.
- 6. Prolonged training has no effect on either adrenal weight per body weight or gross splenic weight following irradiation.

- 7. Level of preirradiation physical activity has no effect on postirradiation mortality and survival time.
- 8. Body weight appears to be the most significant factor influencing survival time following irradiation with the heavier animals in all treatment groups having significantly increased survival times.

THE EFFECTS OF PROLONGED TRAINING ON THE RESISTANCE TO RADIATION-INDUCED CHANGES IN MALE ALBINO RATS

Ву

Robert Kertzer

A THESIS

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BARRE

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1966

DEDICATION

To my wife Joyce, for maintaining an intact family unit.

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The author owes an untold debt of gratitude to Dr. W. D. Van Huss, for being scholar, friend and chaplain, each at the appropriate time, and to Dr. W. W. Heusner for demonstrating unequivocably that all of the skills necessary for outstanding teaching, creative research and scientific coaching can be mastered by one man.

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CHAPTER I THE PROBLEM

Introduction

In recent years, the rapid development of nuclear armaments, combined with conflicting international ideologies, has contributed to the constant possibility of a world catastrophe. Furthermore, automation has reduced the amount of physical activity necessary to carry on the tasks of daily living. It would be well to know the interrelationships and possible physiological consequences of these socially superimposed phenomena.

Statement of the Problem

The purpose of this investigation was to study the effects of various levels of preirradiation physical activity, from weanling age to adulthood, upon the radiation resistance of mature rats. The information gained should aid in evaluating the influence of physical conditioning upon the mortality and selected physiological and anatomical parameters of animals exposed to lethal doses of radiation.

Importance of the Problem

Considerable work has been done already on (a) the effects upon mortality of fatigue produced by exhaustive exercise immediately prior to and/or immediately following irradiation

(7, 8, 36, 38); (b) the effects upon mortality of daily postirradiation exercise combined with various radiation doses (19, 20); and (c) the effects of radiation upon recovery from fatigue (8), the ability to perform an exhaustive exercise test (6, 21, 35, 40) and volitional activity (18, 22). Data are incomplete in regard to the effects of radiation upon animals subjected to physical training over a long period of time prior to being irradiated.

There is substantial evidence to indicate that extended programs of relatively vigorous daily activity result in significant alterations in a number of physiological and anatomical parameters which are also affected by irradiation (5, 9, 10, 11, 12, 16, 25, 26, 28, 29, 32, 33, 44). Some of these changes are similar to those produced by irradiation, whereas others are distinctly opposite (2, 4, 7, 8, 19, 20, 30, 31, 35, 36, 37, 40, 41). This raises the question as to whether or not various types of prolonged physical training will influence resistance to damage caused by lethal doses of radiation.

Limitations of the Study

1. Small laboratory animals may be investigated in numbers sufficient for generalization within the chosen population; however, the physiological results of

animal studies cannot be translated directly to human subjects.

- 2. The strong psychosomatic response which may be expected in man when he is aware of the fact that he has been exposed to a lethal dose of radiation limits extrapolation from the rat to the human.
- 3. No attempt was made either to measure or control food intake.
- 4. The physiological changes produced by 650 roentgens of radiation may be vastly different than those produced by other doses.
- 5. Exercise regimens, other than those employed in the present investigation, might produce dissimilar results.

 Definition of Terms
- 1. Roentgen. One roentgen is that quantity of X-or gamma radiation such that the associated corpuscular emission (electrons and ions) per 0.001293 gm. of air produces, in air, ions carrying 1 electrostatic unit of charge of either sign (2).
- Mode of Irradiation. 250 k v p x-rays; 15 M.A.;
 5 mm. Cu (HVL 1.5 mm Cu) 78 inches TSD; 3.6 r/minute
 (air dose).

3. \underline{LD} 50/30. - That dosage of radiation estimated to eliminate 50% of the population within a 30-day period.

CHAPTER II REVIEW OF RELATED LITERATURE

In making a study of the effects of prolonged training on the resistance to radiation-induced changes it seems wise to have some knowledge of the effects of pre- and post-irradiation exercise and the associated changes in both mortality and related physiological and anatomical parameters.

American Investigations

Postirradiation Exercise

Smith and Smith (35) forced mice to exercise in a revolving cage following irradiation. Animals receiving 325 r tolerated 12 hours of continuous activity immediately after or at any time up to 13 days postirradiation.

Animals receiving 400 r tolerated eight hours of continuous activity on three consecutive days beginning immediately after or at any time up to 13 days postirradiation with little, if any, effect upon survival time. All animals receiving 600 r and then forced to exercise for eight continuous hours on three consecutive days died. When the radiation effects in exercised animals were compared with those observed in nonexercised irradiated control animals, it was concluded that there were no marked consequences

either of irradiation upon exercise tolerance or of postirradiation exercise upon mortality.

Smith and Smith (36) subjected mice to various levels and durations of exercise following whole-body irradiation. Three days of moderate exercise of eight consecutive hours a day in equally spaced sessions of three hours, decreased slightly, if any, the tolerance of mice to prior irradiation. Following a radiation dose which was 100 per cent lethal, seven of 30 mice could not tolerate three successive days of exercise for eight hours a day. No differences in survival time were noted between those mice surviving the exercise period and irradiated controls. The radiation tolerance of mice was not increased by phenobarbital sedation following irradiation. It was concluded that radiation lethality doses not parallel the rate of O₂ utilization under the experimental conditions employed.

Kimeldorf and Jones (20) studied the relationship of radiation dose to lethality in exercised animals exposed to x-rays. Male Sprague-Dawley rats were forced to swim until fatigued daily for four weeks following irradiation. As a result, these animals showed a greater mortality, with increased deaths at lower doses, than similar animals receiving only radiation. The nonexercised rats displayed

a calculated median lethal dose which was 28 per cent higher than that computed for exercised animals. It was concluded that exercise increases the level of mortality when performed postirradiation.

Kimeldorf, Jones and Castanara (21) studied the effect of irradiation upon the performance of daily exhaustive exercise by the rat. For periods as long as nine weeks postirradiation, rats were forced to perform a standardized exhaustive swimming test five times weekly. The ability to perform this test was decreased by exposure to x-rays in the 300-1000 r range. The extent of the decrease in performance was dependent upon dosage. Those rats surviving the test period recovered sufficiently to attain their preirradiation exercise levels by the ninth week. However, these animals were not able to perform as well as nonirradiated exercised control animals. The rats dying within a short period following irradiation were almost normal in performance, whereas those animals dying later displayed a lower level of performance which varied with the duration of the survival period.

Kimeldorf et al. (22) studied the effect of repeated exposures to x-rays on the volitional activity of adult male rats. Under controlled conditions of light, sound and

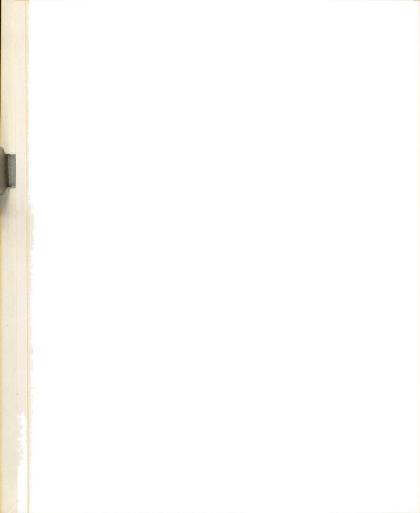
temperature, the daily volitional activity of each animal was recorded for 15 consecutive weeks. Dose increment effects were investigated by subjecting animals to 50 r, 100 r and 150 r at weekly intervals. The resulting cumulative doses were 600 r, 1200 r and 1350 r, respectively. By spacing 150 r doses at seven, 14 and 28 day intervals, the effect of changing the interval between exposures was studied. Irrespective of increment size or interval between exposures, a decrease in activity was noted after each irradiation. Statistically significant differences were observed between experimental and nonirradiated control groups immediately following each 150 r exposure, after six of 12 exposures to 100 r and following three of 12 exposures to 50 r. The decrease in activity was a function of the increment size rather than the cumulative dose. With the exception of weekly 150 r exposures, recovery occurred within a week following each exposure. After six weekly exposures to 150 r, recovery in activity was less than normal. The responses to each 150 r dose were comparable regardless of the intervals between exposures.

Jones et al. (18) also studied the effect of irradiation on voluntary activity of the adult male rats

utilizing single doses of x-rays, ranging from 200-1000 r. A prompt significant reduction was noted at all doses. period of increased activity immediately followed the initial decrease. Within five days postirradiation, all animals exposed to 200 r and 300 r were completely recovered. No further detectable effects of irradiation upon voluntary activity at these levels were noted. animals were exposed to x-rays of 400 r or more, some animals died. In the animals which survived, there was an initial period of depressed activity, followed by a recovery period, and then a second depression. This subsequent reduction in activity reached a low value during the third week postirradiation. The amount of time required for surviving animals to completely recover from the second depression in activity seemed to be proportional to the x-ray dose. Those rats which died within the first nine days postirradiation displayed voluntary activity levels which continuously decreased from the day of irradiation until death. In animals dying after nine days postirradiation, the first depression was followed by some recovery. However, there was a second decrease in activity which persisted until death.

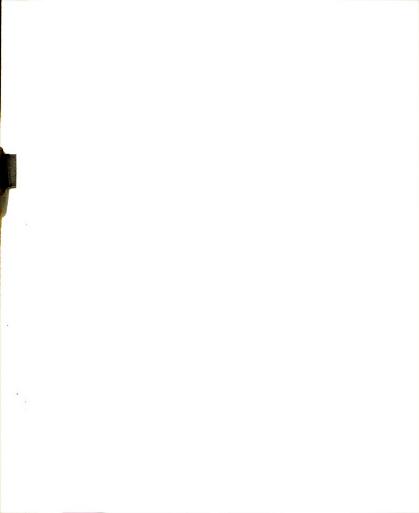
Kimeldorf and Baum (19) investigated the changes in

organ and body growth following exhaustive exercise, xirradiation and postirradiation exercise. Eight hundred and sixty-four male Sprague-Dawley rats were used in the investigation. Animals were subjected to no stress, to repeated swims to exhaustion, to various single doses of irradiation, or to irradiation plus various numbers of bouts of postirradiation exhaustive swimming. The animals were 55 days old when the experimental treatments were begun, and sacrifices were conducted 3, 9, 18 and 30 days follow-Body weight was reduced in the experimental animals by both exhaustive exercise and exposure to irradiation. Relative to body weight: (a) either exercise or irradiation produced a decrease in thymus weight, an increase in adrenal weight, and no change in kidney weight; (b) exercise produced an increase and irradiation a decrease in the weights of the gluteus maximus, heart, spleen and testes; (c) exercise had no effect upon the pituitary weight whereas irradiation reduced the weight of this gland; and (d) exercise increased thyroid weight while irradiation failed to alter it. In general, changes following irradiation were found to be immediate and to be related to dosage, whereas exercise-induced changes were accumulative and related to the number of repetitions. When animals were subjected to



irradiation plus exhaustive fatigue, the responses were predominately those of irradiation and were not markedly increased by exercise. Postirradiation exercise did tend to prevent recovery from radiation damage.

Smith and Smith (39) studied the effects of thyroid and radiation on sensitivity to hypoxia, basal rate of 0, consumption and tolerance to exercise. Mice treated with thyroid were found to have increased basal O consumption, increased sensitivity to hypoxia and a depressed ability to tolerate exercise. These three parameters followed the same course of development with time. Within the limits imposed by the experiment, animals exposed to 325 r exhibited no decrease in exercise tolerance and no observable changes in basal O2 consumption. These irradiated mice did show a decrease in sensitivity to progressive hypoxia. In mice receiving both thyroid and irradiation there were no increases in basal O_2 consumption or decreases in tolerance to exercise beyond those caused by thyroid alone. However, the doubly treated animals had a greater resistance to hypoxia than animals receiving only thyroid. It was concluded that early failures in an exercise test and deaths of thyroid-administered animals during exercise were indicative of impaired functional capacity



of the heart rather than of general muscular fatigue.

Preirradiation Exercise

Brown and White (7) studied preirradiation fatigue as a factor in the prevention of irradiation deaths in rats. Ten female Sprague-Dawley rats were swum to exhaustion on ten successive days. Five of these animals were irradiated on the eleventh day with 1200 r of cobalt 60 immediately after an exhaustive swim. The other five animals received the same dose of radiation but without immediately prior exercise. All animals which swam before being irradiated were alive one month after irradiation, whereas all of the other animals died within ten days following the radiation exposure. It was concluded that fatigue-induced anoxia serves as a protective mechanism against lethal doses of radiation.

Preirradiation Training

Kimeldorf and Jones (20) demonstrated that a short training program prior to irradiation (for a period of ten days) has no significant effect upon mortality.

Pre- and Postirradiation Exercise

Brown and White (8) forced sixteen adult Sprague-Dawley rats to swim to exhaustion on ten successive days. The animals then were matched on mean swimming time and assigned



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Preirradiation Exercise

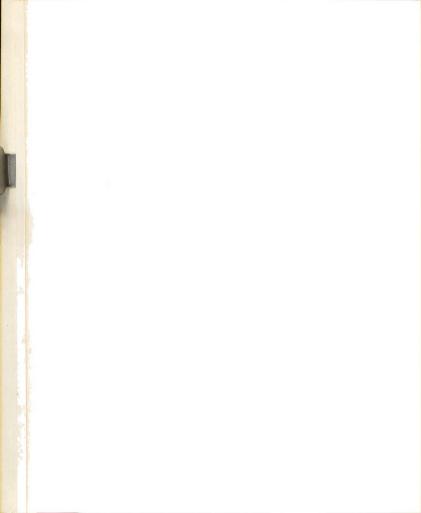
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Preirradiation Training

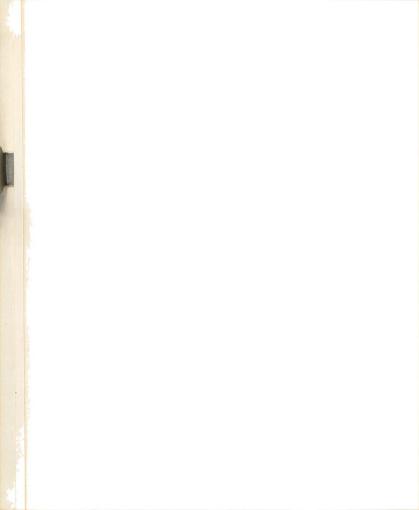
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Pre- and Postirradiation Exercise

Brown and White (8) forced sixteen adult Sprague-Dawley rats to swim to exhaustion on ten successive days. The animals then were matched on mean swimming time and assigned



to two treatments. On the eleventh day, the animals in Group I were swum to exhaustion, immediately irradiated with 1200 r of cobalt 60, and two hours later again swum to exhaustion. Group II was irradiated first, immediately swum to exhaustion, and two hours later again fatigued by a swim to exhaustion. The groups had similar swimming times during the first swim on the day of irradiation, but Group II swam significantly longer during the second session. It was concluded that irradiation immediately following exhaustive fatigue retards the biological processes involved in recovery from fatigue more than irradiation immediately prior to fatigue. Subsequently, both groups were forced to swim to exhaustion once a day until death or for a period of seven days after irradiation. The animals in Group II were able to do significantly more work, as measured by total swimming time, during this postirradiation period but died significantly earlier. All animals in Group II died within six days after irradiation; only two animals in Group I died within six days and two lived more than 30 days. Statistical analysis revealed that the difference in postirradiation work was not responsible for the difference observed in mortality rate. Both differences were shown to be the result of the relative states of fatigue of the two



groups at the time of irradiation. It was concluded that

(a) anoxia associated with fatigue protected the animals

in Group I from radiation injury, (b) preirradiation anoxia

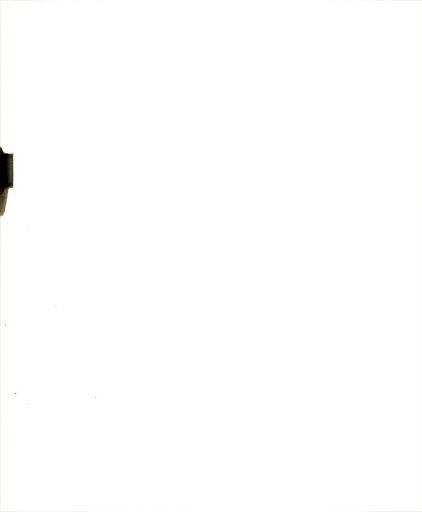
could not explain the lack of recovery from postirradiation

fatigue in Group I, and (c) a condition which increased

radiation injury in Group II also increased their relative

ability to do work postirradiation.

Kimeldorf, Jones and Fishler (23) studied male Sprague-Dawley rats in an effort to ascertain the role of metabolic level in determining radiosensitivity. The experimental animals performed a standardized exhaustive exercise, consisting of swimming in individual tanks. These animals were exercised once a day for ten days prior to irradiation. Following irradiation they were exercised daily, five times per week. After irradiation with 600 r, 50% of the exercised rats died and all nonexercised irradiated controls survived. At a dose (700 r) that was lethal to 44% of the nonexercised animals, mortality was 92% among exercised rats. At a highly lethal dose (860 r), exercised animals displayed symptoms of roughened coat, diarrhea and crusted nares much sooner following irradiation than did the nonexercised controls. The exercised rats had a much shorter postirradiation survival time in addition to a higher mortality



rate. The authors conclude that the results provide evidence of the relation between radiosensitivity and metabolic level.

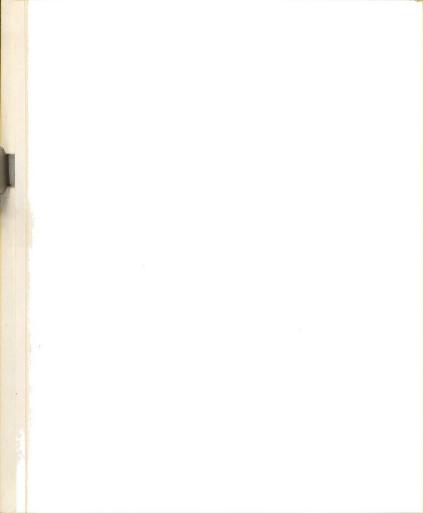
Russian Investigations

Zimkin and Korobkov, two Russian investigators, have reviewed the studies of their co-workers in the area of exercise and radiation (50).

Postirradiation Exercise

Sergeyev, working with rabbits, demonstrated a rise in mortality in animals exercised following a radiation dose of 1000 r. Intensity of radiation sickness was increased in the exercised animals. In the investigations of Popov, all dogs died who were forced to execute daily hourly runs on a treadmill at a speed of 6 km./hr. following irradiation. Markelov also demonstrated that following an intravenous injection of 1 millicure/kg. of radioactive Sr₈₉, physical exercise intensified radiation sickness in rats.

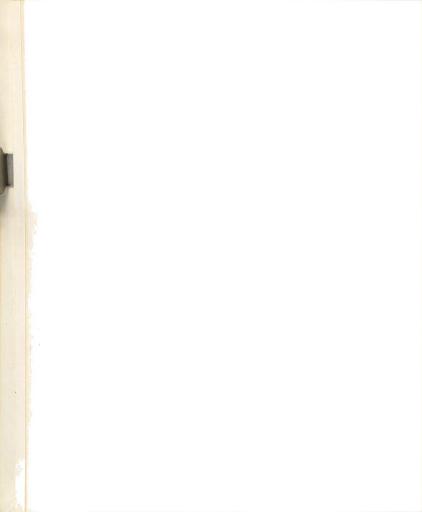
On the other hand, Trifonov showed that daily moderate exercise following irradiation both reduces and postpones the onset of mortality. Mortality of 24 control rats subjected to irradiation of 1150 r was 54 per cent after 25 days with the average length of life of those dying being 3.77 days. Animals which were swum without weights for 15 minutes daily over a ten-day period following irradiation



with the same dose had a 35 per cent mortality with the average life span being 6.57 days. More severe exercise after irradiation (1 hour and 20 minutes daily for ten days) produced no further decrease in mortality but did prolong the life of those who eventually perished. Pinchook and Scherban irradiated mice with either 800 or 1200 r before forcing them to swim for 30 minutes in water at 25-30° C. After a dose of 1200 r all mice died. However, mice who were only irradiated lived, on the average, less (4-12 days) than those irradiated and swum (4-75 days). 80 mice exposed only to irradiation with 800 r 15 (18.7 per cent) survived, but 20 (25 per cent) of those irradiated and swum survived. For the mice who died after being subjected only to irradiation the average length of life was less (8.87 days) than for those subjected to irradiation and subsequent swimming (10.35 days).

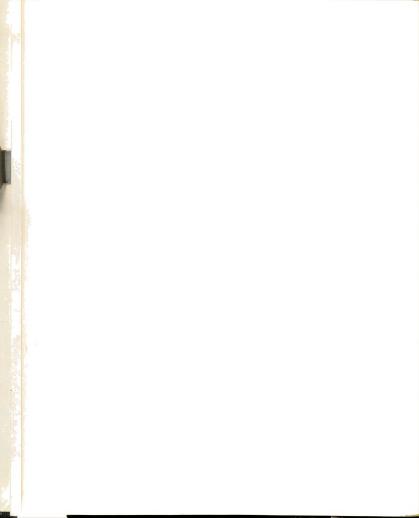
Preirradiation Exercise

Oogodskaya and Yondin forced rats to swim for 8-10 minutes with a ten-gram weight on their tails at 15-20 minutes before or immediately before irradiation. Mortality for 40 control rats was 35 per cent, while mortality for 40 exercised rats was only 22 per cent. In one experiment of Trifonov, 25 rats were swum to exhaustion

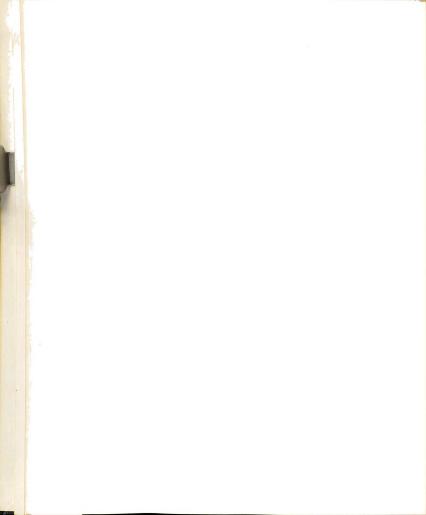


immediately prior to irradiation with 1150 r. Mortality in the experimental group was approximately the same (56 per cent) as in a group of nonexercised control rats (54 per cent). However, average length of life in the exercised rats was greater (7.36 days) than in the controls (3.77 days). Preirradiation Training

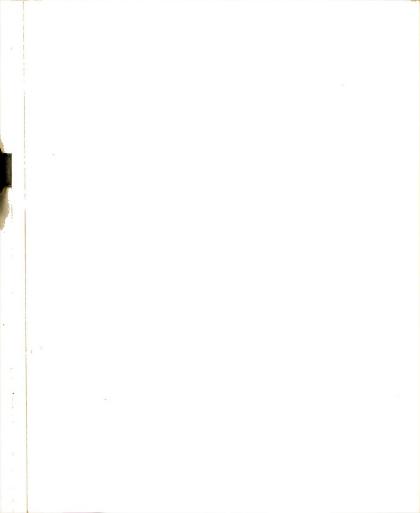
The experiments of Sergeyev demonstrated that preliminary physical training decreases the mortality of irradiated animals. Using rabbits, he showed that systematic physical exertion for 10-25 days prior to irradiation with 1000 r reduces radiation sickness. In this study, radiation sickness was slight in the trained rabbits, even when they were subjected to daily physical exertion following irradiation. Tovbin, using three groups of 12 mice each, found that after a dose of 726-800 r control group mortality was 75 per cent; in one group trained for 50 days in dynamic work, mortality was 42 per cent; and, in a group trained during the same time in static efforts (hanging on a slender pole), mortality was 25 per cent. also investigated the effects of pretraining on mortality following irradiation. Rats, which were trained by swimming and hanging from a pole for 1 1/2 months (35-38 training periods), died from radiation sickness in a



smaller percentage and on later dates than control animals. Trifonov emphasizes the importance of the exercise intensity. Longer sessions of training in swimming (up to 3 1/2 hours per day) showed a smaller prophylactic effect than shorter periods (30-60 minutes). Zimkin conducted experiments on 44 male rats of which 22 were subjected to training. Seven rats were exercised by running in a wheel which revolved at a rate of 13 revolutions per minute, and 14 rats were trained by hanging from a vertically suspended rope. The duration of exercise was increased by two minutes daily for 15 days. subsequent exercise bouts for 30 days (with interruptions for vacations) the duration was held to 30 minutes. Animals were irradiated with 600 r. All rats surviving on the 28th day after irradiation were sacrificed. Four control and four experimental animals were sacrificed immediately following irradiation in order to study histological changes in various tissues. Therefore, the analyses of mortality, body weight changes, food consumption for one hour, number of leucocytes and hemoglobin content were carried out on data obtained from 18 control and 18 experimental animals. The results indicate that the experimental rats were more resistant to radiation than the



controls. In the group of trained animals 15 survived (81.1%) while only 10 (55.5%) of the untrained controls lived. Six of the control animals died in the period from the 6th to the 10th day following irradiation. One control animal died on the 13th day and one on the 19th day after irradiation. The average length of life for the control rats who died postirradiation was 10 days while the experimental animals lived, on the average, 15 days. Food consumption and body weight were decreased in all rats, but more so in the control group. Histological changes in the heart muscle of trained and untrained animals indicated a marked protein "dystrophy"; however, Zimkin and Korobkov report it was less widespread in the trained animals.

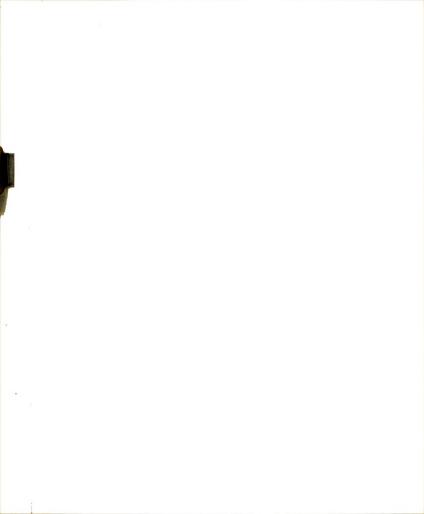


CHAPTER III EXPERIMENTAL METHOD

Design of Experiment

Sample

Two hundred and fifty weanling (26-day-old) male Sprague-Dawley rats were randomly assigned to one of five treatment groups. A sample size of 50 for each group was chosen because previous experience with animal training studies in this laboratory (15, 25, 27) indicated that the variability of the parameters studied is such that it would be desirable to be able to detect, as significant, differences at least as small as two-thirds of one standard deviation, while holding the probability of making a type I statistical error to the .05 level and that of making a type II error to the .20 level. According to these specifications a sample size of 36 in each group was calculated as sufficient to distinquish between the effects of the various training programs Assuming, however, that concurrent irradiawhich were used. tion would increase the within group variances to some unknown extent and that a few animals might be lost by drowning in the forced training period, by confinement during the radiation procedure or by the anesthetic during blood sampling, a sample size of 50 animals in each group was chosen arbitrarily.



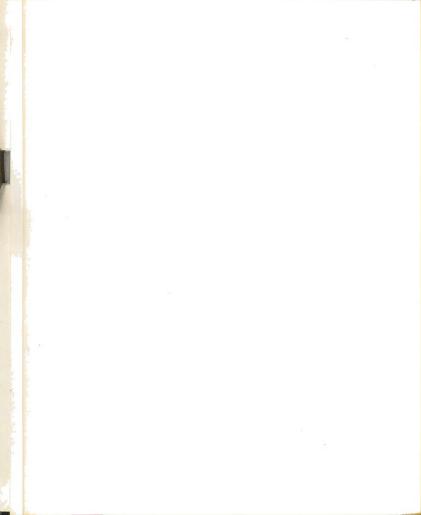
In fact, three animals in one of the forced activity groups and two in the other did drown in training. One animal in one of the other groups died while under anesthesia during preirradiation blood sampling. Consequently, animals were eliminated randomly, and 47 rats in each group were irradiated. No animals were lost as a result of confinement during irradiation. Postirradiation blood sampling resulted in the death of one additional animal. Once again, equal groups were maintained by random elimination. Therefore, 46 animals per group comprised the final sample. This yielded a minimum statistical power of .90 for the several analysis of variance calculations made.

Treatment Groups

The following five treatment groups of animals were utilized in this investigation:

Group 1: A sedentary control group which received no special treatment, other than radiation. These animals were confined to individual sedentary cages both prior to and after being irradiated. (Each sedentary cage is 24 cm. long by 18 cm. wide by 18 cm. tall.)

Group 2: A spontaneous control group which received no special treatment, other than radiation. They were housed in individual spontaneous exercise cages until irradiated



and then confined to individual sedentary cages. (Each spontaneous exercise cage consists of an individual sedentary cage plus a freely revolving drum of 35 cm. diameter and 13 cm. width. These cages permit the animals to rest or exercise at will.)

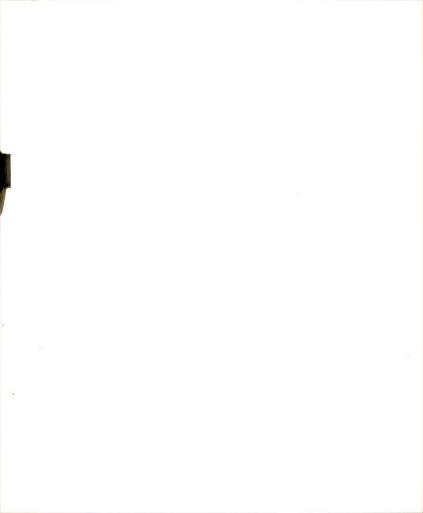
Group 3: A sedentary forced exercise group which was housed in individual sedentary cages both prior to and after being irradiated. During the training period prior to irradiation, these animals were forced to swim daily for one-half hour with two per cent body weight attached to the base of the tail.

Group 4: A spontaneous forced exercise group which was housed in individual spontaneous exercise cages until irradiated and then confined to individual sedentary cages.

Prior to being irradiated these animals also were forced to swim daily for one-half hour with two per cent body weight attached to the base of the tail.

Group 5: A spontaneous effect group which was housed in individual spontaneous exercise cages both prior to and after being irradiated. These animals were not subjected to the preirradiation forced training regimen.

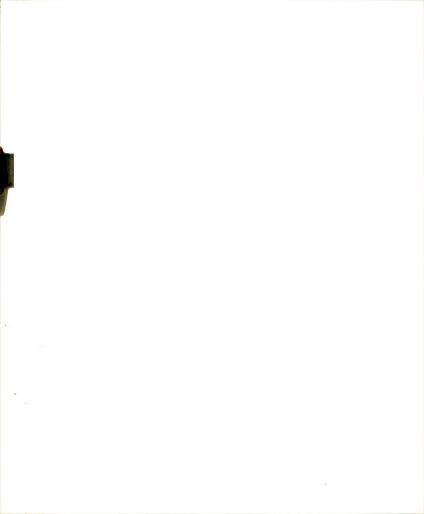
From the five treatment groups, the following were determined:



- 1. The effects of sedentary cage existence upon resistance to radiation-induced changes.
- 2. The effects of spontaneous activity upon resistance to radiation-induced changes.
- 3. The effects of prolonged forced exercise upon resistance to radiation-induced changes.
- 4. The interaction between the effects produced by spontaneous and forced exercise.
- 5. The effects of radiation upon spontaneous activity.

 <u>Preirradiation Forced Training Procedures</u>

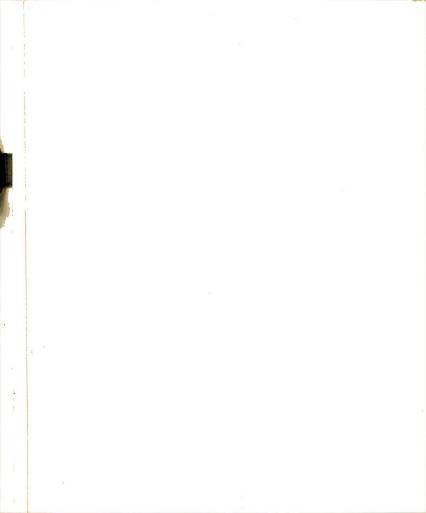
Those animals which were subjected to the swimming regimen (Groups 3 and 4) were swum in individual cylindrical tanks measuring 11 inches in diameter and 30 inches in depth. Animals were always swum between 8:00 A.M. and 11:30 A.M. Beginning on the 50th day of the preirradiation treatments, a few animals were unable to complete the required one-half hour swim with two per cent body weight attached to the base of the tail. On the 53rd day two rats died while swimming. On the 56th day another died. Swimming was omitted on the 61st day as a one-day rest period seemed advisable. A fourth animal died on the 68th day. Consequently, a second rest period was inserted on the 69th and 70th days. Beginning with the 71st day, whenever an



animal was unable to complete the one-half hour swim with weight attached, he was pulled from the tank, the weight was removed, the animal was given a one-minute rest, and he was replaced in the tank without the weight attached for the remainder of the one-half hour swim. Approximately five animals required this procedure daily with only one additional rat drowning during the remainder of the pre-irradiation period. Water temperature was maintained between 36° and 38° C. during swimming. After each swim period the animals were dried with a towel and replaced in their respective cages.

Duration of Preirradiation Treatments

The preirradiation treatments were begun at 27 days of age and were carried on throughout puberty and early adult-hood. On the 83rd day of the preirradiation treatments, 20 per cent of the animals, randomly selected with stratification by groups were placed in sedentary cages for an approximate 64-hour rest period prior to irradiation. The forced swimming regimen was terminated for these animals at this time. On the 84th, 85th, and 86th days, a similar procedure was followed with 20, 30 and 30 per cent of the animals respectively. This practice was employed since Brown and White (7) found that irradiation with 1200 r of cobalt 60



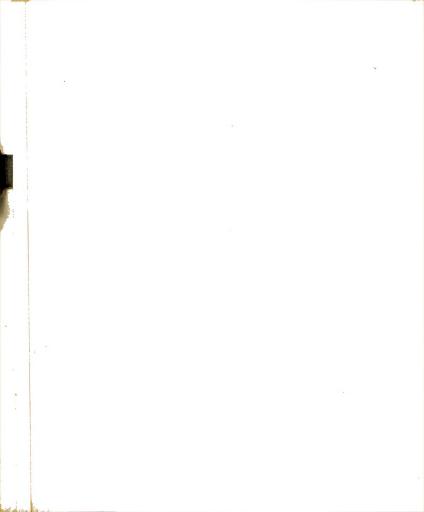
immediately following exhaustive fatigue produced no deaths within one month while all animals not exhausted by swimming died within ten days. It was assumed that exhaustive fatigue functioned as a protective mechanism. The present investigation was concerned with the long-term effects of physical training upon resistance to radiation rather than the immediate effects of fatigue. Therefore, the 64-hour rest period between the end of training and irradiation was incorporated into the experimental design.

Radiation

Following the 64-hour rest period, each animal was exposed to 650 r while confined in a three-inch by nine-inch lucite chamber. Twenty-four animals were irradiated simultaneously. The total time required for irradiation was 180.5 minutes. Animal positions were rotated every 36.1 minutes to provide equal exposures for all. The radiation dose was set at 650 r because Andrews (2) has reported that the LD 50/30 for the rat is between 600 and 700 r.

Blood Measures

Nine days before and five days following irradiation a blood sample was drawn from the orbital sinus of each animal to determine the WBC and eosinophil count. A 24-hour period of confinement in sedentary cages was provided for



all animals, regularly in spontaneous cages, prior to the drawing of each blood sample.

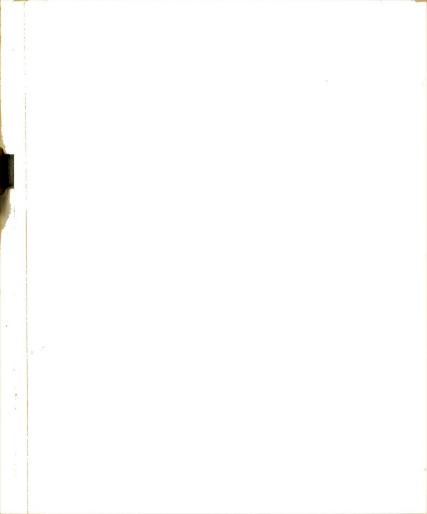
Postirradiation Period

During the 30 days immediately following irradiation, a laboratory technician was with the animals twenty-four hours a day. Mortality and survival time in hours for all groups of animals were recorded during this period. At the end of the thirty-day period, the surviving animals in all groups were sacrificed.

Upon death or sacrifice, body weight as well as the weights of the spleen and adrenals were determined. The thymus was observed subjectively, but not weighed, since its postirradiation condition prohibited proper extraction and trimming. These organs were selected for study since Andrews (2) has reported that lymphoid tissue is highly sensitive to irradiation with sufficient consistency to warrant the use of such tissues as biological radiation dosimeters.

General Procedures

Throughout the entire investigation, all animals received water and a commercial ground animal diet, ad libitum. The temperature in the housing quarters was maintained between 70° and 78° F. Body weight for each animal was determined once a week throughout the preirradiation period,

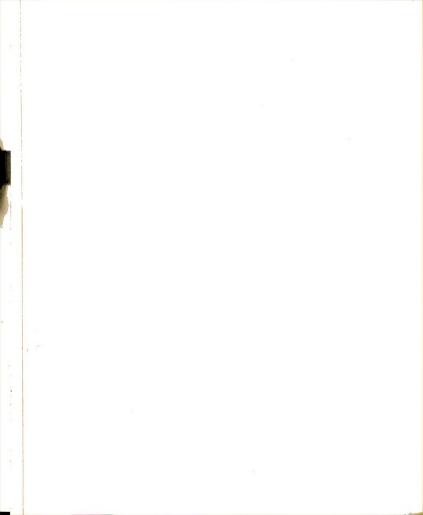


and the weight to be attached to the base of the tail during swimming was changed on the following day. Daily voluntary exercise data for each animal housed in a spontaneous exercise cage was recorded at 7:45 A.M. daily.

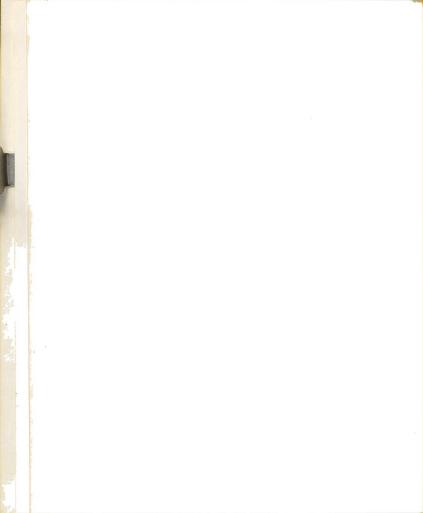
For the first 71 days of the preirradiation period, an automatic timer illuminated the animal quarters 12 hours each day. Since it was necessary for the technician to observe each animal hourly following irradiation, lights were kept on 24 hours a day beginning on the 72nd day. The 24-hour illumination was started 12 days prior to irradiation in order to provide an adjustment period for the animals. Statistical Methods

The differences in mortality between the five treatment groups were analyzed using the chi-square test for multiple independent samples (34).

A Pearson product-moment coefficient of correlation was calculated between the pre- and postirradiation spontaneous activity values for the spontaneous effect group to determine the consistency of the effect of radiation on voluntary activity of rats. The difference between the pre- and post-irradiation spontaneous activity levels in group 5 was evaluated by the standard one-way analysis of variance technique (14).



Standard one- and two-way fixed effects analysis of variance techniques were employed where appropriate to analyze the data on preirradiation spontaneous activity levels, body weights, eosinophil and white blood cell counts, organ weights and survival times (14). The Tukey method for multiple comparisons between means was used whenever significant F-values were obtained (14).



CHAPTER IV RESULTS AND DISCUSSION

Results

Daily spontaneous activity was evaluated in order to determine the effects of (a) forced swimming on voluntary exercise (b) voluntary activity on resistance to mortality following irradiation and (c) irradiation on level of spontaneous activity.

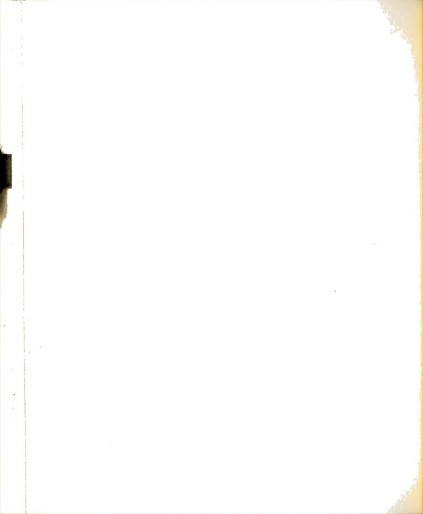
Preirradiation Spontaneous Activity

Figure 1 compares the daily voluntary activity of the spontaneous control animals (Group 2) with the spontaneous forced (Group 4) for the 84-day preirradiation training period. A one-way fixed effects analysis of variance was calculated where Groups 2 and 4 were factor A and the criterion variable was 84-day spontaneous activity. This analysis enabled one to determine the effects of forced swimming on spontaneous activity. Table 1 shows the results. Figure 2 indicates mean spontaneous activity values preirradiation.

Table 1

Analysis of Variance for Preirradiation Spontaneous Activity

Source of Variance	SS	DF	MS	F
Among Groups	9342244	1	9342244	3.89
Within Groups	216031102	90	2400345	
Total	225373346	91		



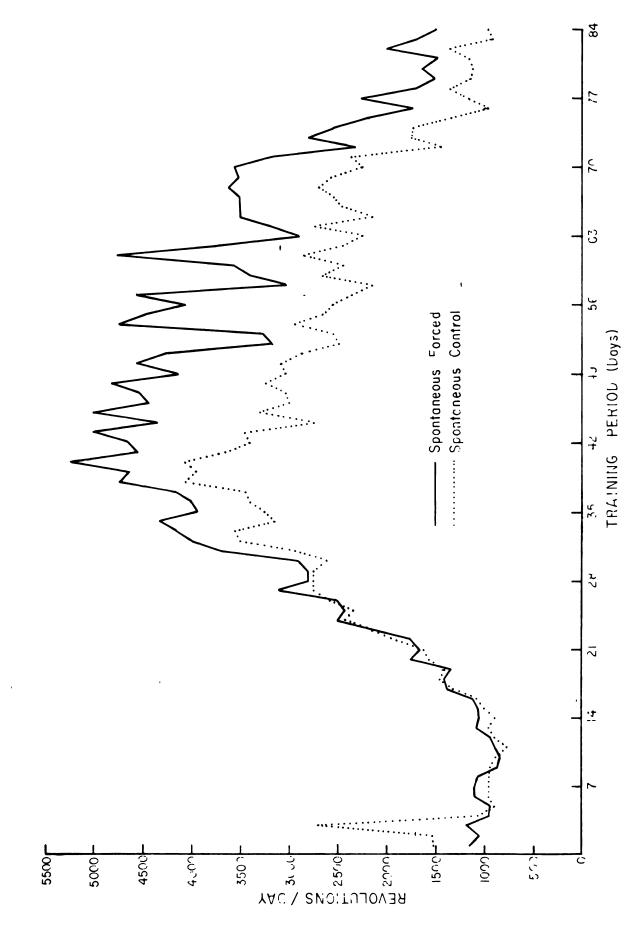


Figure 1 Daily Preirradiation Spontaneous Activity



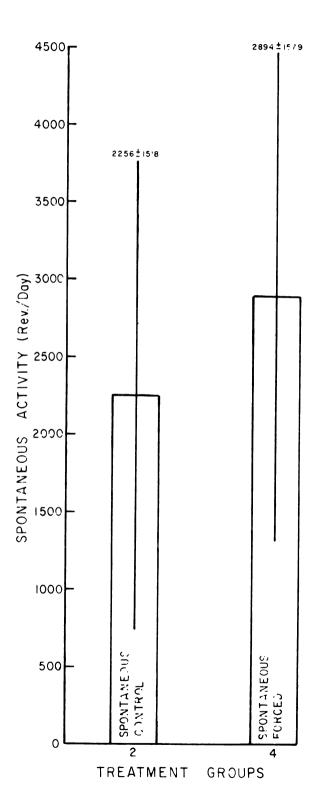
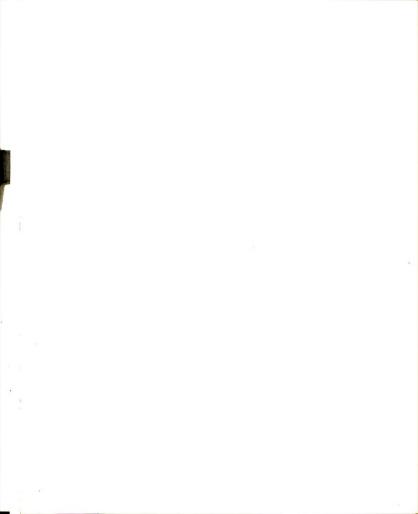


Figure 2: Mean Daily Spontaneous Activity Preirradiation



The computed F value was not significant indicating that, at the 5% level of confidence, there was no difference in preirradiation spontaneous activity between the two groups. The power of the test was .90. It should be noted, however, that the analysis of variance is not a completely satisfactory technique in interpreting longitudinal data of the sort that we are dealing with here. Consequently, a sign test was employed utilizing the same data. The sign test showed that, at the 5 per cent level, the spontaneous forced animals (Group 4) were significantly more active than the spontaneous controls (Group 2) for the preirradiation training period.

A two-way fixed effects analysis of variance was calculated where the spontaneous control (Group 2), spontaneous forced (Group 4) and spontaneous effect (Group 5) treatments were factor A; the upper and lower halves of the 84-day preirradiation spontaneous activity relative to groups was factor B; and the criterion variable was survival time in hours. This analysis permits consideration of both treatment and level of preirradiation spontaneous activity as factors in determining survival time following irradiation.

Figure 3 shows the mean values for the three groups evaluated. Table 2 shows the results of the analysis of variance test.

Table 2

Analysis of Variance for Level of Preirradiation Activity and Survival Time

		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		
Source of Variance	SS	DF	MS	F
Treatment	16168	2	8084	
Level	18342	1	18342	.595
Interaction	82299	2	41149	1.334
Error	4070745	132	30838	
Total	4187555	137		

The computed F values indicate that, at the specified level of confidence, there were no significant differences between upper and lower halves of preirradiation spontaneous activity relative to groups and survival time. For this test the probability of making a Type II statistical error was .10.

Lighting, Irradiation and Spontaneous Activity

For the first 71 days of the treatment period the lights in the animal room were kept on 12 hours per day. For the remainder of the experiment lights were kept on 24 hours a day in order to facilitate hourly checks on animals following irradiation. Three 11-day periods were selected: (a) the last 11 days prior to 24-hour lighting, (b) the 11-day period between the first day of 24-hour lighting and the first day of irradiation and, (c) the first 11 days following irradiation with 24-hour lighting. A two-way mixed



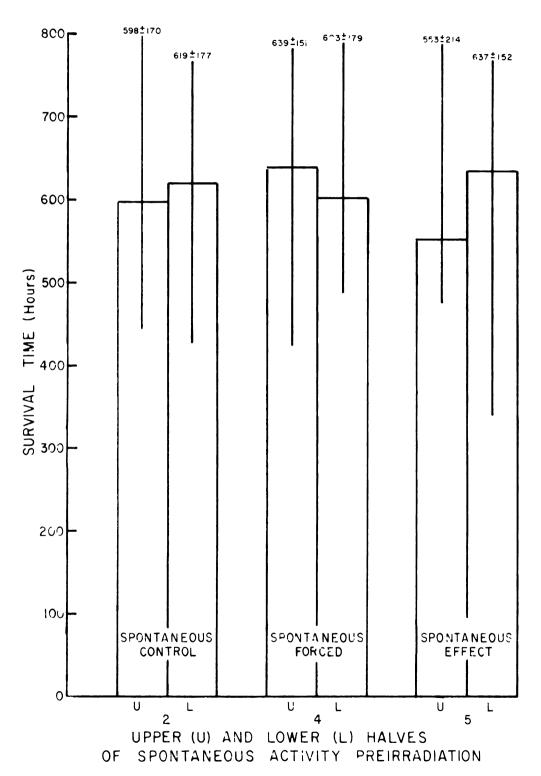
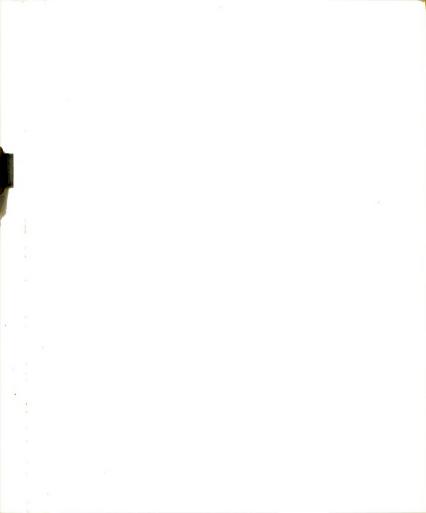


Figure 3: Upper and Lower Halves of Spontaneous Activity and Survival Time



model analysis of variance was calculated where the three 11-day periods were fixed factor A, the 46 spontaneous effect (Group 5) animals were random factor B, and the criterion variable was mean 11-day spontaneous activity. This analysis permits one to determine the effects of both 24-hour illumination and irradiation on spontaneous activity. Figure 4 shows the effects of 24-hour lighting and irradiation on spontaneous activity from the 60th day of training until sacrifice. Table 3 indicates the results of the analysis of variance test. Figure 5 shows mean activity levels for the three periods.

Table 3

Analysis of Variance for Effects of Lighting and Radiation on Activity

Source of Variance	SS	DF	MS	F
Periods	246284790	2	123142395	55.35*
Animals	211791112	45	4706469	
Interaction	200228515	90	2224761	
Total	658304418	137		

^{*} indicates that F value is significant at 5% level.

Since the computed F value was significant at the specified level of confidence a Tukey test for multiple comparisons between means was calculated. Table 4 shows the results.



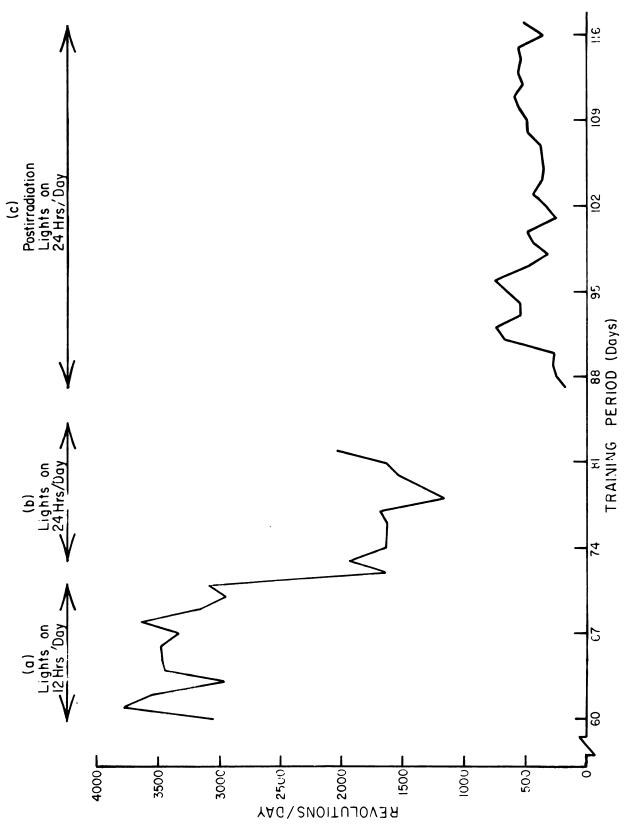


Figure 4: Lighting and Radiation Effects on Vetraity



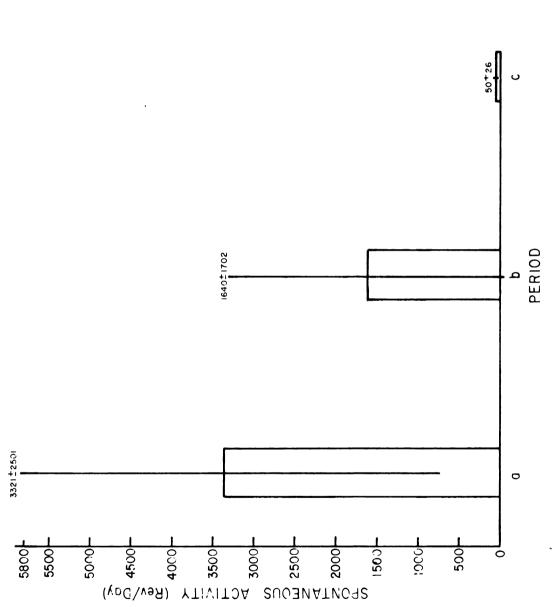


Figure st. Lighting and Radiation Effects on Activity (Mean values)

Table 4

Tukey Test for Effects of Lighting and Radiation on Activity

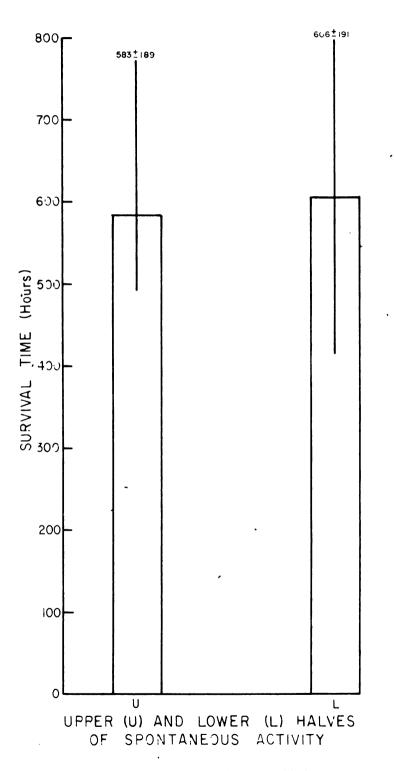
Mean Compar	isons	Significance at 5%
Period 1 >	Period 2	Significant
Period 1 >	Period 3	Significant
Period 2 >	Period 3	Significant

The results of the Tukey test indicate that mean activity was significantly higher during 12-hour lighting than during both 24-hour lighting preirradiation and 24-hour lighting post-irradiation. Furthermore, mean activity level for the 24-hour lights on period preirradiation was significantly higher than the 24-hour lights on period postirradiation.

Postirradiation Spontaneous Activity

A one-way fixed effects analysis of variance was calculated where the upper and lower halves of 3-day postirradiation spontaneous activity for the spontaneous effect (Group 5) treatment was factor A and the criterion variable was survival time in hours. This type of analysis permits one to determine the effects of level of postirradiation activity on survival time. Figure 6 shows mean survival times for the upper and lower levels of activity. Table 5 indicates the results of the analysis of variance test. The computed F value indicates that there was no difference, at the specified level of confidence, between upper and lower halves of





Floure : Upper and Lover Halves of 5-Day restirradiation Spontaneous West its and Survival Fine.

Table 5

Analysis of Variance for Postirradiation Activity Level and Survival Time

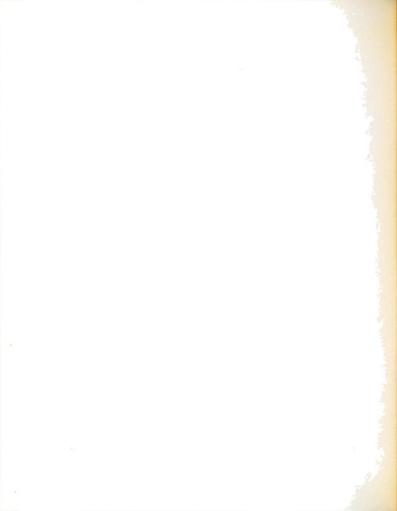
Source of Variance	SS	DF	MS	F
Among Levels	6362	1	6362	.175
Within Levels	1596980	44	36295	
<u>Total</u>	1603343	45		

postirradiation spontaneous activity and survival time. The power of the test was .90.

A Pearson product-moment correlation coefficient was calculated between 11-day preirradiation spontaneous activity and 3-day postirradiation spontaneous activity for the spontaneous effect (Group 5) treatment. The resulting r value (.344), which was significantly different from zero at the 5 per cent level, indicated that both high and low level activity animals were affected in the same way by radiation.

Body Weight

Figure 7 shows weekly body weight changes for the five treatment groups. Final body weights prior to irradiation are shown in Figure 8. A one-way analysis of variance was calculated where Groups 1, 2, 3 and 4 were factor A and the criterion variable was body weight during the last week prior to irradiation. This procedure enables one to determine the effects of the four treatments on body weight prior to



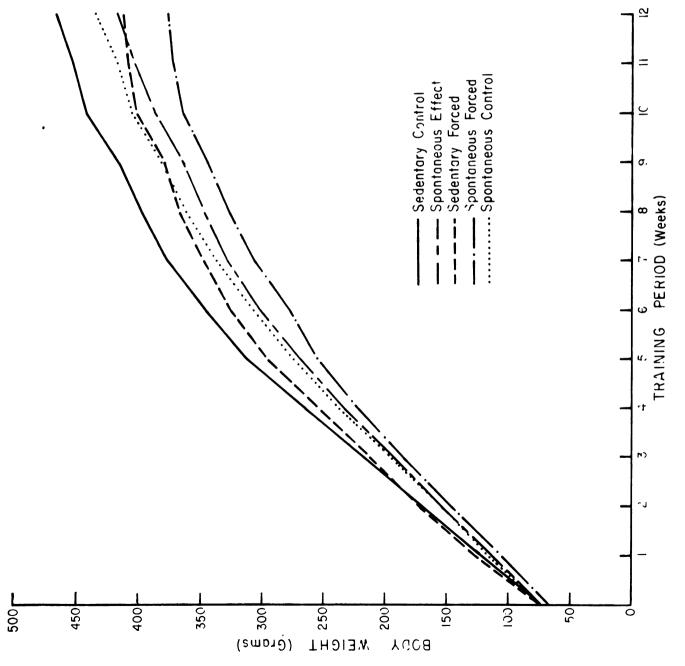


Figure 7. Treat out Effects on Body Weight



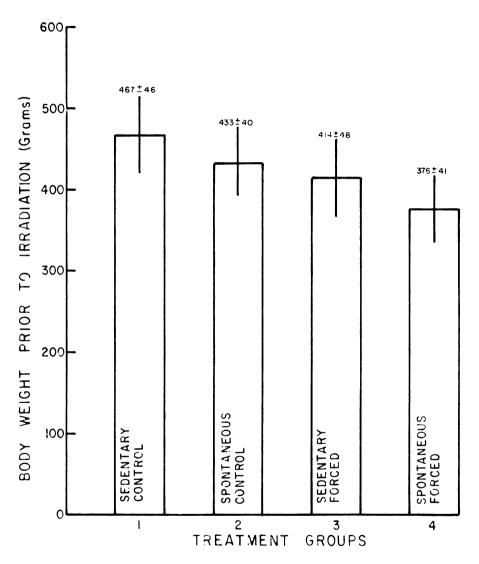


Figure 8: Mean Body Well ht Prior to Irradiation

irradiation. The results of the analysis of variance are shown in Table 6.

Table 6

Analysis of Variance for Body Weights Prior to Irradiation

Source of Variance	SS	DF	MS	F
Among Groups	195872	3	65290	32.843*
Within Groups	357836	180	1987	
Total	553709	183		

^{*} indicates that the F value is significant at the 5% level.

Since the computed F value was significant at the specified level of confidence the Tukey test for multiple comparisons between means was employed. Table 7 indicates the results.

Table 7

Tukey Test for Body Weights Prior to Irradiation

Mean Compa	rison	Significance at 5%
Group 1 >	Group 2	Significant
Group $1 >$	Group 3	Significant
Group 1 $>$	Group 4	Significant
Group 2 >	Group 3	Significant
Group 2 >	Group 4	Significant
Group 3 >	Group 4	Significant

The results of the Tukey test show that the sedentary controls (Group 1) were significantly heavier than the spontaneous controls (Group 2), the sedentary forced (Group 3)
and the spontaneous forced (Group 4) during the final week
prior to irradiation. Furthermore, Group 2 was significantly

heavier than either Group 3 or Group 4 and Group 3 was significantly heavier than Group 4.

A two-way fixed effects analysis of variance was calculated where the five treatments were factor A; the upper and lower halves of body weight relative to groups during the last week prior to irradiation were factor B; and the criterion variable was survival time in hours. This analysis permits consideration of both treatment and level of pre-irradiation body weight as factors in determining survival time following irradiation. Figure 9 shows the upper and lower halves of body weight relative to groups with respect to survival time. The results of the analysis of variance are shown in Table 8.

Table 8

Analysis of Variance for Level of Body Weight and Survival Time

Source of Variance	SS	DF	MS	F
Treatment	54857	4	13714	
Level	196925	1	196925	6.566*
Interaction	244238	4	61059	2.036
Error	6597728	220	29989	
Total	7093749	229		

The results of Table 8 indicate that the level effects are significant. The mean survival time of all animals who were in

* indicates that the F value is significant at the 5% level.

the upper half of their group was 636 hours. This was



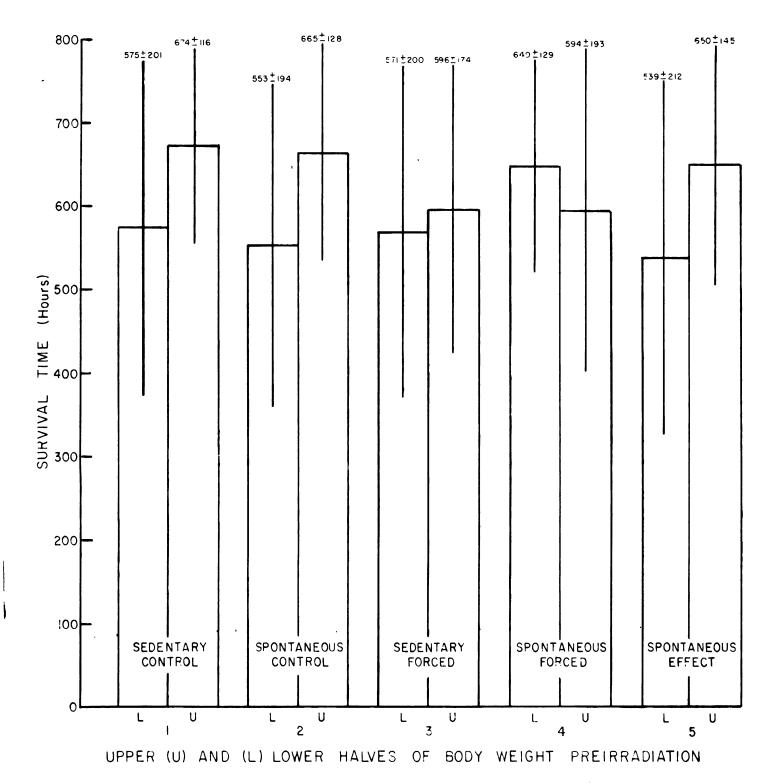


Figure 9: Upper and Lower Halves of Body Weight Preirrad. tion and Survival Time

significantly greater than the mean survival time of all the animals in the lower half of their group, which was 578 hours.

White Blood Cells

Figure 10 shows mean WBC values 9 days prior to irradiation. A one-way analysis of variance was calculated where Groups 1, 2, 3 and 4 were factor A and the criterion variable was WBC 9 days prior to irradiation. This procedure enables one to determine the effects of the four treatments on WBC count prior to irradiation. The results are shown in Table 9.

Table 9

Analysis of Variance for WBC Preirradiation

Source of Varian	nce SS	DF	MS	F
Among Groups	36375149	3	12125049	1.919
Within Groups	1137549185	180	6319717	
Total	1173924335	183		

The computed F value shows that, at the specified level of confidence, there were no significant differences between groups with regard to WBC 9 days prior to irradiation. The power of the test was .90.

A two-way fixed effects analysis of variance was calculated where the five treatments were factor A; the upper

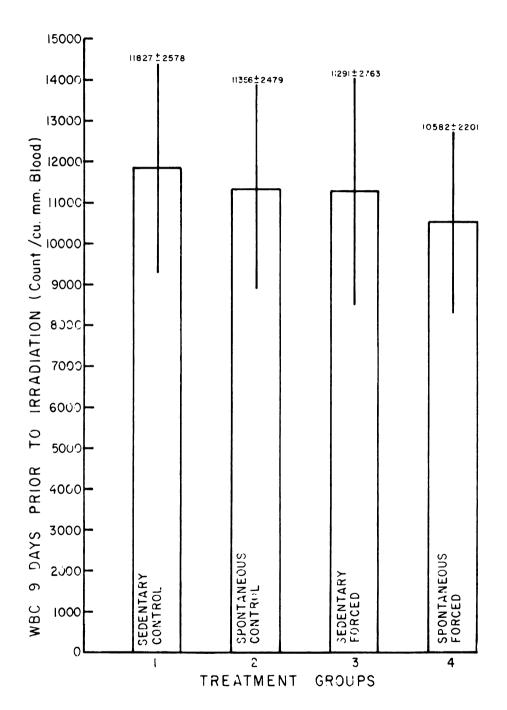


Figure 10: WBC 9 Days Prior to Irradiation

and lower halves of WBC relative to groups 9 days prior to irradiation were factor B; and the criterion variable was survival time in hours. This analysis permits consideration of both treatment and level of WBC preirradiation as factors in determining survival time after irradiation. Figure 11 shows the relationship between the upper and lower halves of WBC preirradiation and survival time. The results of the analysis of variance are shown in Table 10.

Table 10

Analysis of Variance for Levels of WBC Preirradiation and Survival Time

Source of Variance	SS	DF	MS	F
Treatment	54857	4	13714	
Level	60166	1	60166	2.065
Interaction	569954	4	142488	4.891*
Error	6408771	220	2913 0	
Total	7093749	229		

^{*} indicates that F value is significant at 5% level.

The results of Table 10 indicate that the interaction effects were significant. The Tukey test for multiple comparisons between means was employed. Those comparisons which were significant at 5% level are shown in Table 11.

Figure 12 shows mean WBC level five days postirradiation for the five treatment groups. A one-way fixed effects analysis of variance was calculated where the five treatments



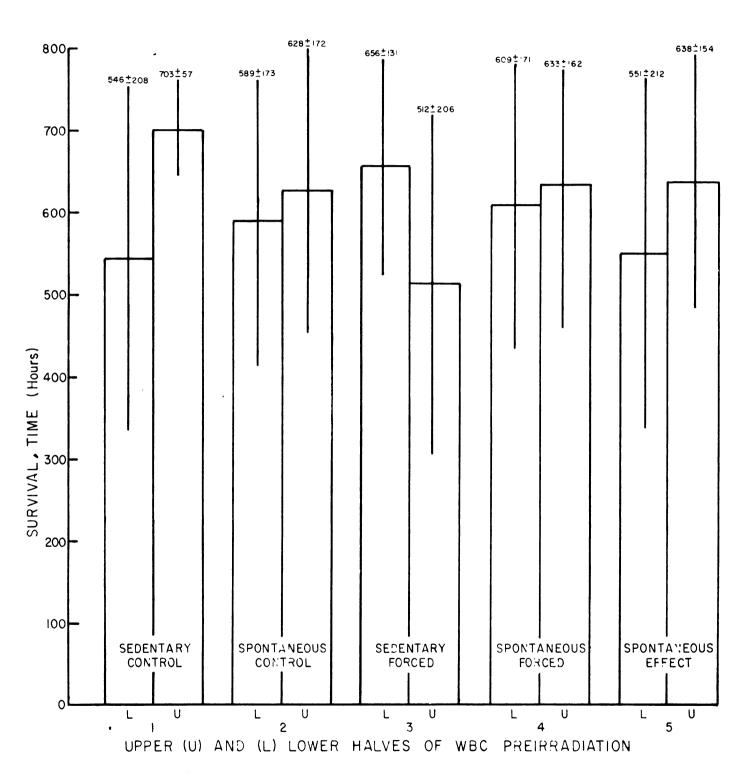
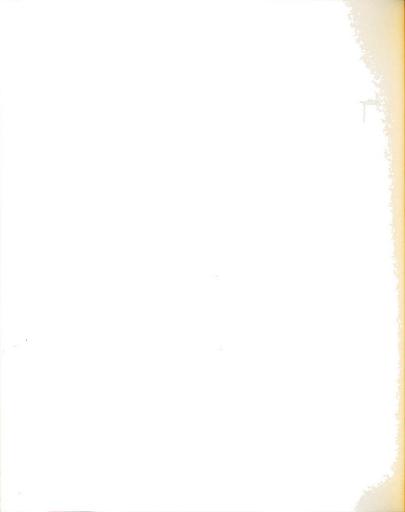


Figure II: Upper and Lower Halves of WBC Preirradiction and Survival Filme



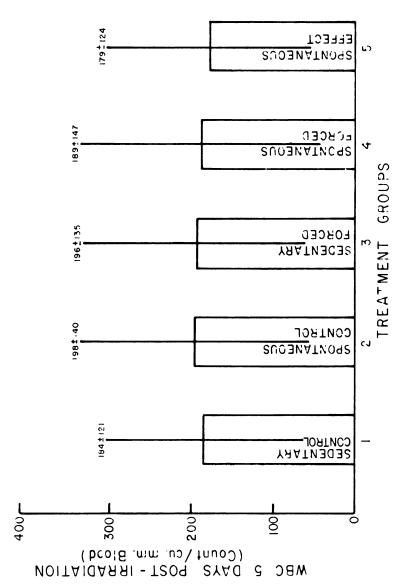


Figure Lit. W.BC & Days Posturradiotion

Table 11

Tukey Test for Levels of WBC and Survival Time

	upper > 2						3	upper
3	lower > 5	lower,	1	lower,	3	upper		
5	upper > 3	upper						
4	upper > 3	upper						
2	upper > 3	upper						

were factor A and the criterion variable was WBC five days postirradiation. This analysis permits one to evaluate the effects of the treatments on WBC postirradiation. The results are shown in Table 12.

Table 12

Analysis of Variance for WBC Five Days Postirradiation

Source of Variance	SS	DF	MS	F
Among Groups	12239	4	3059	.170
Within Groups	4061250	225	18049	
<u>Total</u>	4073489	229		

The results, as indicated in Table 12, show that there were no significant differences in WBC postirradiation between groups. The probability of making a Type II statistical error was .10.

A two-way fixed effects analysis of variance was calculated where the five treatments were factor A; the upper and lower halves of WBC five days postirradiation relative to groups were factor B; and the criterion variable was survival time in hours. The above procedure permits consideration of both treatment and level of WBC postirradiation as factors in determining survival time following irradiation. Figure 13 shows the relationship between upper and lower halves of WBC postirradiation and survival time. The analysis of variance is shown in Table 13.

Table 13

Analysis of Variance for WBC Level Postirradiation and Survival Time

Source of Variance	SS	DF	MS	F
Treatment	54857	4	13714	
Level	7123	1	7123	.227
Interaction	140011	4	35002	1.117
Error	6891757	220	31326	
Total	7093749	229		

The F values, as indicated in Table 13, show that there were no differences between level of WBC postirradiation relative to groups and survival time.

Eosinophils

Figure 14 shows mean eosinophil levels nine days prior to irradiation for Groups 1, 2, 3 and 4. A one-way fixed effects analysis of variance was calculated where Groups 1, 2, 3 and 4 were factor A and the criterion variable was eosinophil count nine days prior to irradiation. The



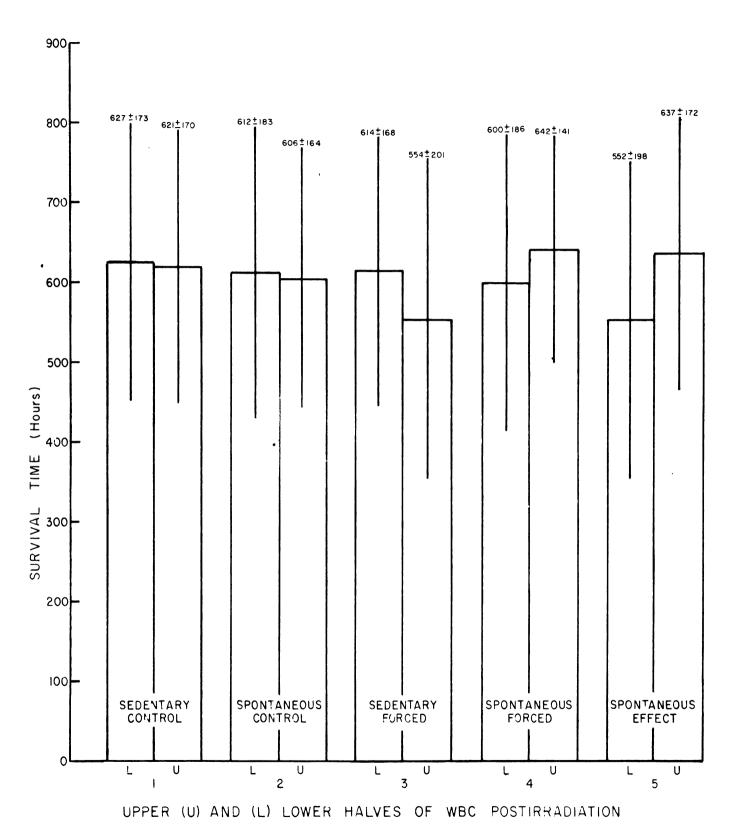


Figure 13: Upper and Lower Halves of WBC Postirradiation and Survival Fire



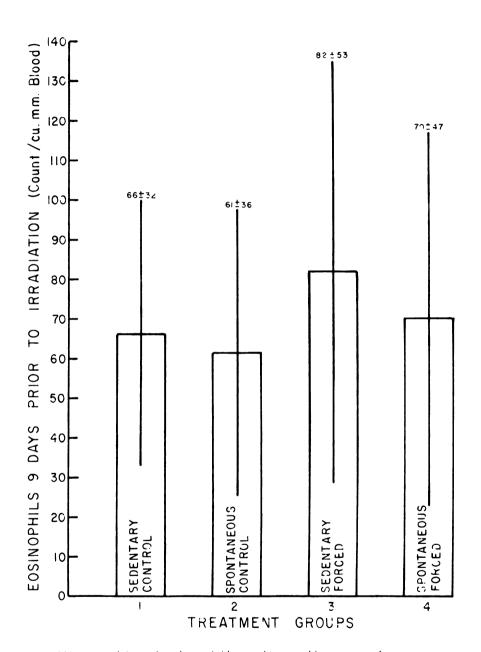


Figure 14: No. inophils + Days Prior to Irred tion

analysis permits one to determine treatment effects on eosinophil level prior to irradiation. The results are shown in Table 14.

Table 14

Analysis of Variance for Eosinophil Count Nine
Days Preirradiation

Source of Variance	SS	DF	MS	F
Among Groups	10455	3	3485	1.868
Within Groups	355815	180	1865	
Total	346271	183		

The results of Table 14 indicate that, at the specified level of confidence, there were no differences in preirradiation eosinophil level between groups. The power of the test was .90.

A two-way fixed effects analysis of variance was calculated where the five treatments were factor A; the upper and lower halves of eosinophil count relative to groups nine days preirradiation was factor B; and the criterion variable was survival time in hours. This procedure allows one to consider both treatment and level of preirradiation eosinophil count as factors in determining survival time following irradiation. Figure 15 shows the relationship between upper and lower halves of eosinophil count and survival time. The results of the analysis of variance are shown in Table 15.



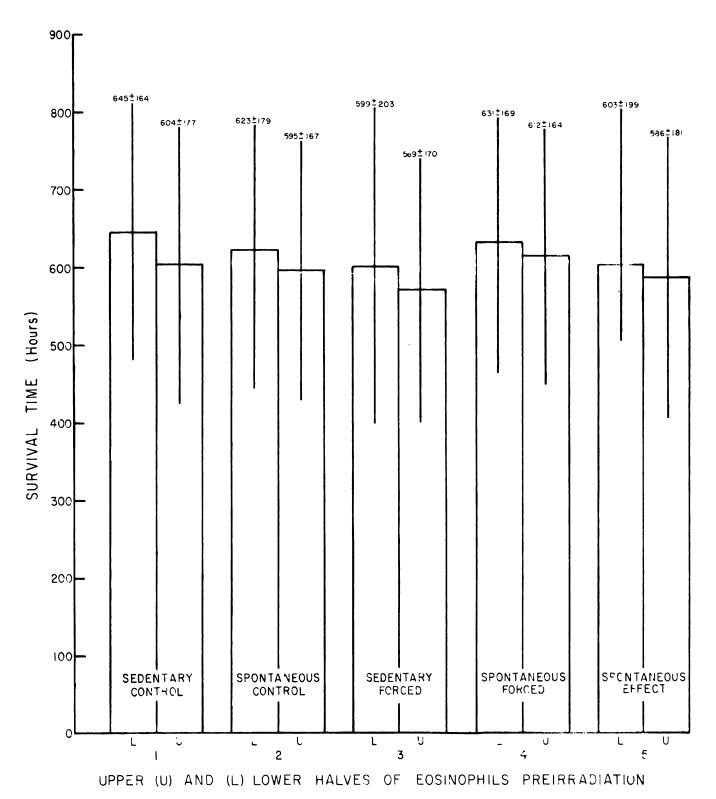


Figure 1s: Upper and L. ver Halves of Eeslmophills Preirradiation and Survival Line

Table 15

Analysis of Variance for Preirradiation Eosinophil
Level and Survival Time

Source of Variance	SS	DF	MS	F
Treatment	54857	4	13714	
Level	42540	1	42541	1.339
Interaction	4394	4	1099	.035
Error	6991957	220	31782	
Total	7093749	230		

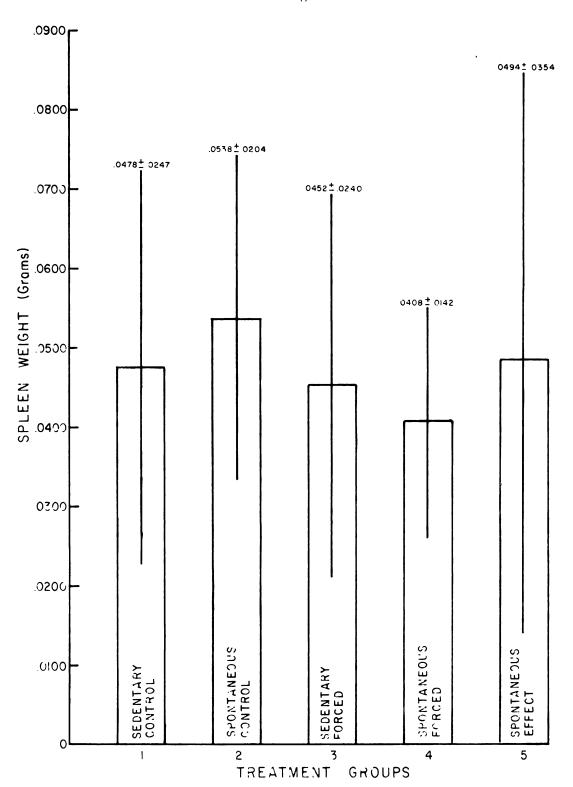
The F values, as shown in Table 15, indicate there was no significant differences between upper and lower halves of pre-irradiation eosinophil level relative to groups and survival time in hours. The probability of making a Type II statistical error was .10.

Blood sampling five-days postirradiation indicated that all animals, except six had eosinophil counts of zero. The six exceptions were animals 164 and 176 of Group 2, animal 27 of Group 3, animal 97 of Group 4 and animal 211 of Group 1.

Spleen Weight

Figure 16 shows the treatment effects on spleen weight at death. A one-way fixed effects analysis of variance was calculated where the five treatments were factor A and the criterion variable was spleen weight at death. This analysis permits one to determine the treatment effects on spleen weight at death. The results are shown in Table 16.





Floure for Treatment Effects in Spleen Weight at De th

Table 16

Analysis of Variance for Treatment Effects on Spleen Weight at Death

Source of Variance	SS	DF	MS	F
Among Groups	.00126681	4	.00031670	.50358
Within Groups	.04087826	65	.00062890	
<u>Total</u>	.04214507	69		

The results, as shown in Table 16, indicate that there were no significant treatment effects on spleen weight at death. The power of the test was .90.

Figure 17 shows the treatment effects on spleen weight at sacrifice. A one-way fixed effects analysis of variance was calculated where the five treatments were factor A and the criterion variable was spleen weight at sacrifice. The results are shown in Table 17.

Table 17

Analysis of Variance for Treatment Effects on Spleen Weight at Sacrifice

Source of Variance	SS	DF	MS	F
Among Groups	.00071695	4	.00017924	.328
Within Groups	.08475746	155	.00054682	
Total	.08547441	159		

The results, as shown in Table 17, indicate that there were no significant differences in spleen weight at sacrifice.

The probability of making a Type II statistical error was .10.



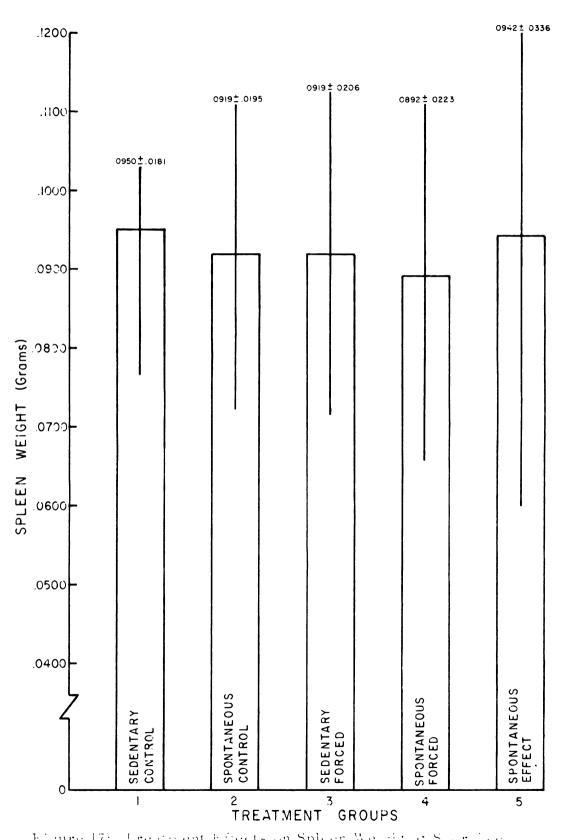


Figure 17: Treatment Effects on Spleen Weight at Sourchee

Adrenal Weight

Previous work in this laboratory (24) has indicated that adrenal weight and body weight are not correlated. Therefore, adrenal weight was expressed as a percentage of body weight for the statistical analyses that follow.

Adrenal weight per body weight at death for the five treatment groups are shown in Figure 18. A one-way fixed analysis of variance was calculated where the five treatments were factor A and the criterion variable was adrenal weight per body weight at death. This analysis permits one to determine treatment effects on adrenal weight per body weight at death. The results are shown in Table 18.

Table 18

Analysis of Variance for Treatment Effects on Adrenal
Weight Per Body Weight at Death

Source of Variance	SS	DF	MS	F
Among Groups	.00000496	4	.00000124	.639
Within Groups	.00012627	65	.00000194	
Total	.00013123	69		

The results, as shown in Table 18, indicate that there were no significant treatment effects on adrenal weight per body weight at death. The power of the test was .90.

The treatment effects on adrenal weight per body weight at sacrifice are shown in Figure 19. A one-way fixed



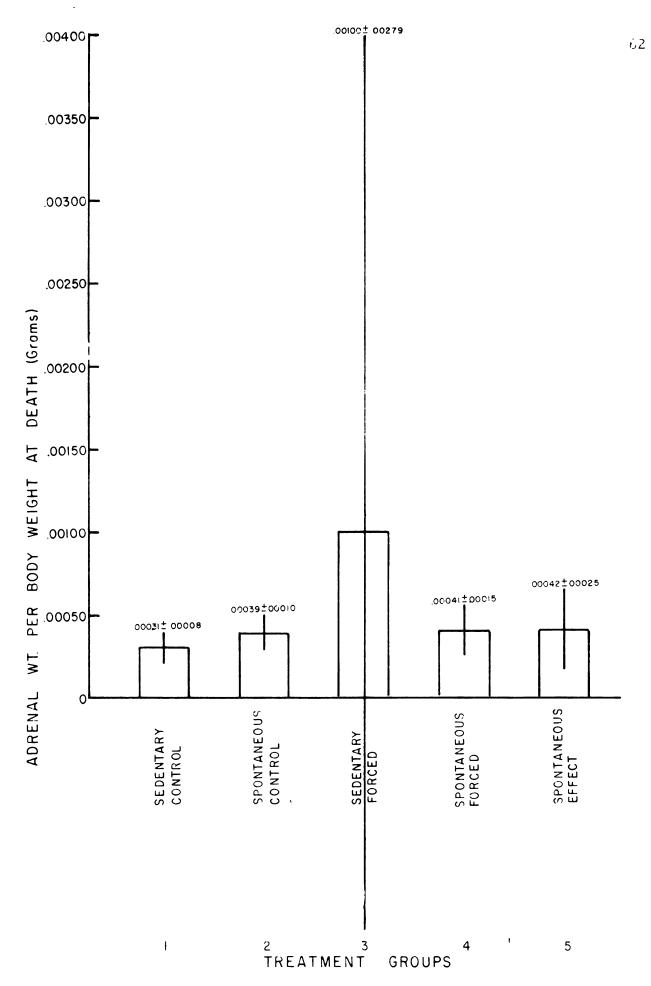


Figure 18: Adrenal Weight Per Body Weight at Death



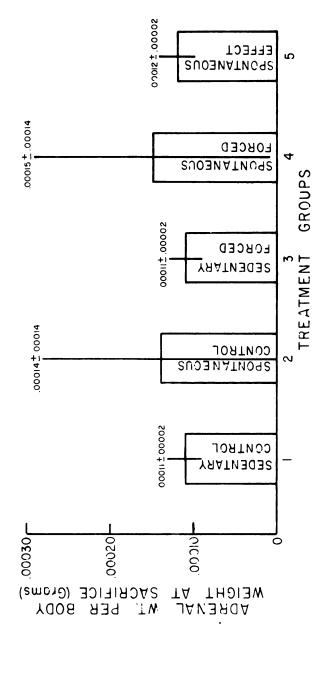


Figure 19: Adrenal Weight Per Back Weight at Sacrafice

effects analysis of variance was calculated where the five treatments were factor A and the criterion variable was adrenal weight per body weight at sacrifice. The results are shown in Table 19.

Table 19

Analysis of Variance for Treatment Effects on Adrenal
Weight Per Body Weight at Sacrifice

Source of Variance	SS	DF	MS	F
Among Groups	.0000004	4	.0000001	1.073
Within Groups	.00000132	155	.0000001	
Total	.00000136	159		

The results, as shown in Table 19, indicate that there were no significant treatment effects on adrenal weight per body weight at sacrifice. The probability of making a Type II statistical error was .10.

Survival Time

The effects of the five treatments on survival time of all animals are shown in Figure 20. It should be noted that if an animal lived until sacrifice he was assigned a survival time of 715 hours. A one-way fixed effects analysis of variance was calculated where the five treatments were factor A and the criterion variable was survival time in hours. This procedure permits one to determine the treatment



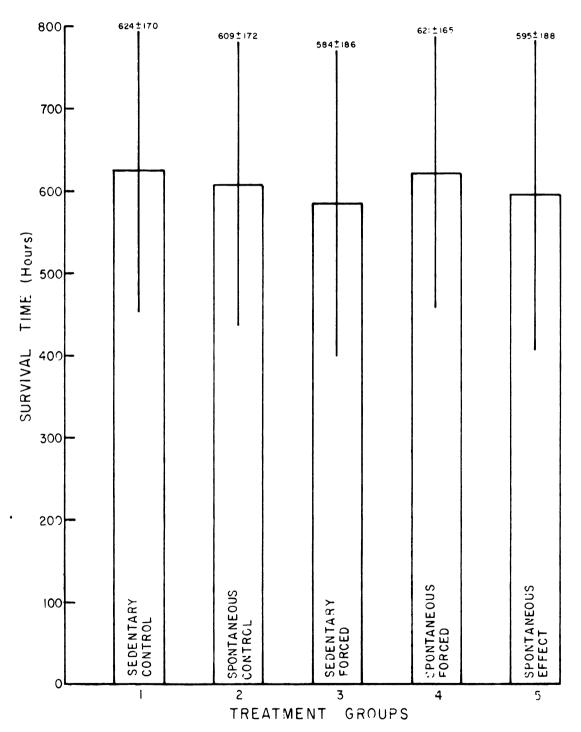


Figure 20: Survival Time of all Art als

effects on survival time following irradiation. The results are shown in Table 20.

Table 20

Analysis of Variance for Treatment Effects on Survival
Time of All Animals

Source of Variance	SS	DF	MS	F
Among Groups	54857	4	13714	.438
Within Groups	7038892	225	31282	
Total	7093749	229		

The results, as shown in Table 20, indicate that there was no significant treatment effect on survival time of all animals. The power of the test was .90.

Figure 21 shows treatment effects on survival time of only those animals which died during the 30-day postirradiation mortality period. A one-way fixed effects analysis of variance was calculated where the five treatments were factor A and the criterion variable was survival time. This procedure allows one to determine treatment effects on survival time of only those animals which died. The results are shown in Table 21. The results, as shown in Table 21, indicate that there were no significant treatment effects on survival time of those animals which died. The probability of making a Type II statistical error was .10.



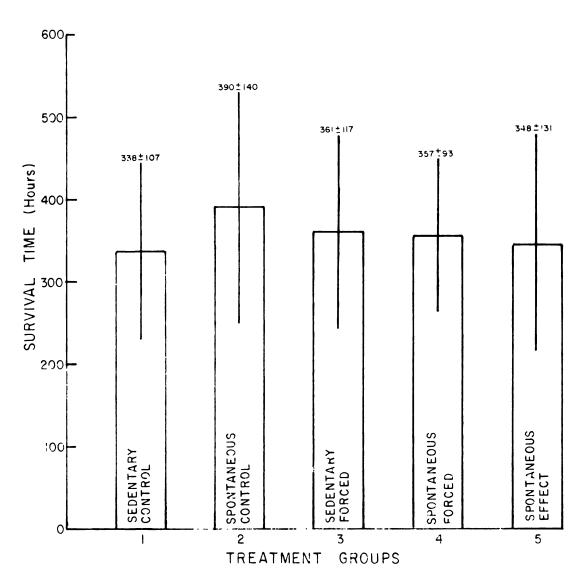


Figure 31: threleaf filme of Animal, Willen Died

Table 21

Analysis of Variance for Treatment Effects on Survival
Time of Only Animals which Died

Source of Variance	SS	DF	MS	F
Among Groups	21839	4	5459	.377
Within Groups	941953	65	14491	
Total	963793	69	· · · · · · · · · · · · · · · · · · ·	

Mortality

A Chi-square test for k independent samples was calculated where the five treatments were the k=5 samples, "die" and "live" were the r=2 rows, and the criterion variable was observed frequency in each cell. This analysis allows one to determine the treatment effects on mortality following irradiation. The results are shown in Table 22.

Table 22
Chi-square Test for Treatment Effects on Mortality

Group	1	2	3	4	5
Die	17	12	15	15	11
Live	29	34	31	31	35

The computed Chi-square was 2.46 which was insignificant at the 5% level. Figure 22 shows the cell frequencies for the Chi-square test.



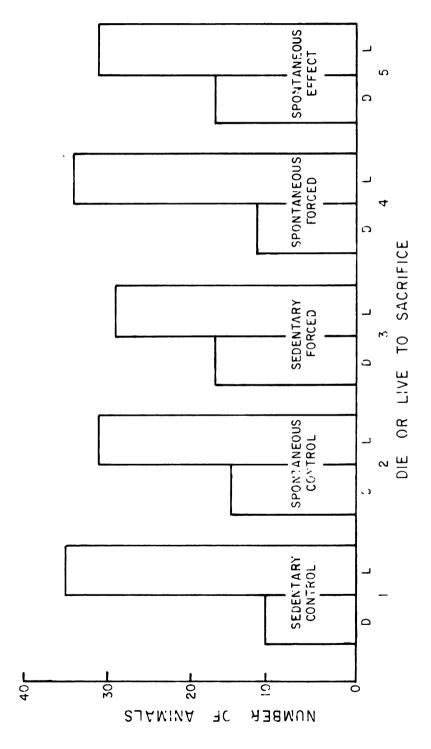


Figure 22: Freetment Group, and Mortality

Discussion

Spontaneous Activity

Previous work in this laboratory by Hanson and Van Huss (15) and Van Huss, Mickelsen and Heusner (49) have shown that animals which were forced to swim for one-half hour daily for 35 days had a significantly lower voluntary activity level than their spontaneous controls. Reference to Figure 1 will indicate that in the present investigation there were no differences between the two groups for the first 30 days of training. However, after 30 days and for the remainder of the preirradiation training period those animals which were forced to swim daily had consistently higher activity levels than the control animals. Apparently after 30 days the forced swimming, in some way, acted as an incentive for voluntary running. It should be noted that these differences were not significant at the specified level of confidence (Table 1) when the analysis of variance test was employed, but were highly significant when the sign test was utilized.

No previous work has been done relating level of preirradiation spontaneous activity and survival time following irradiation. Table 2 and Figure 3 show that level of voluntary activity does not significantly alter survival time. Jones et al (18) and Kimeldorf et al (22) have shown that irradiation produces a rather dramatic decrease in voluntary activity of rats. These results have been substantiated in the present investigation (Tables 3 and 4 and Figure 4). Furthermore it would be wise for future investigators to carefully regulate the amount of time that the animal rooms are to be illuminated if spontaneous activity is to be a measured parameter. Figure 4 clearly demonstrates that 24-hour per day illumination results in substantially decreased spontaneous activity when compared with 12-hour per day illumination.

Published results on the effects of postirradiation exercise on mortality are conflicting. Trifonov (50) and Pinchook and Scherban (50) have demonstrated decreased mortality and increased survival time in animals subjected to exercise following irradiation while Kimeldorf and Jones (20), Kimeldorf and Baum (19), Sergeyev (50), Popov (50) and Markelov (50) have shown increased mortality and decreased survival time. Smith and Smith (35), (36) report no differences between rats exercised following irradiation and control animals. It should be noted that all of the above investigations were concerned with <u>forced</u> exercise following irradiation while the present study involved

postirradiation <u>spontaneous</u> activity. Figure 6 and Table 5 indicate that there were no significant effects of post-irradiation voluntary activity level on survival time.

Body Weight

The results of the four treatments produced significant differences in body weight prior to irradiation (Figure 8 and Tables 6 and 7). The most heavily exercised group (treatment 4) had a mean body weight significantly lower than Groups 1, 2 and 3. The sedentary control group (treatment 1) had a mean body weight significantly higher than Groups 2, 3 and 4. The results indicate that body weight was a function of the exercise regimen.

Table 8 and Figure 9 show that, regardless of treatment, the animals in the upper half of their group with respect to body weight had significantly longer survival times than animals in the lower half. Mean survival time for animals in the upper half was 636 hours as opposed to 578 hours for animals in the lower half. A plausible explanation may be that the heavier animals did not receive as high a dose as the lighter animals. Andrews states (2) "In general, decrease in dose with depth results from attenuation by absorption." An interesting question, however, does arise. Why, if the sedentary animals (Group 1) were significantly

heavier and, if being in the upper half of one's treatment group significantly improved survival time, didn't Group 1 have significantly better survival times? This investigation cannot shed any light on the proposed question, however, if one employed similar types of treatments while attempting to maintain equal body weights between groups, conclusive evidence could be obtained.

Blood Parameters

Garrey and Bryan (13) and Sturgis and Bethell (46) in their reviews of literature, have concluded that a marked leucocytosis is to be expected in circulating blood immediately following muscular exercise. Conclusive evidence has not been found regarding the longitudinal effects of training on the white blood cells. Thörner (47) and Andersen, Heusner and Pohndorf (1) have reported increases in the WBC; whereas, Hawkins (17) found no such changes. results of the present study are in agreement with Hawkins. Analysis of the preirradiation WBC count indicates that there were no significant differences in WBC between the five treatment groups (Figure 10 and Table 9). Table 10 indicates that the interaction effects of upper and lower halves of WBC relative to groups and the five treatments were significant with respect to survival time following

irradiation. Table 11 indicates the existing significant differences. Although there are significant differences no pattern with regard to either treatment or level exists and interpretation is impossible. Within the next year statistical procedures will be available that will enable one to consider the combined effects of level of WBC pre-irradiation and body weight preirradiation on survival time.

Table 12 and Figure 12 indicate that following irradiation there were dramatic decreases in WBC levels in all groups, however, no significant differences between the five treatments were detected. Bacq and Alexander (4) have reported that a large dose of radiation causes rapid damage to the bone marrow and lymphoid tissue, thus greatly suppressing the mitosis of leucocytes for eight to ten days. These observations have been substantiated in this investigation.

Figure 13 and Table 13 show that there were no significant differences between the five treatment groups regarding the level of WBC postirradiation relative to groups and survival time in hours.

Figure 14 and Table 14 indicate that there were no significant differences in eosinophil level prior to irradiation between the five treatment groups. Irradiation

virtually eliminated circulating eosinophils in all animals except six. These six showed eosinophil levels of 5.5/cu.mm blood. Similarly, there were no significant differences between the five treatment groups concerning level of eosinophils relative to groups preirradiation and survival time in hours. (Figure 15 and Table 15)

Organ Weights

It will be recalled from Chapter III that the thymus was not weighed, since its postirradiation condition prohibited proper extraction and trimming.

There is conflicting evidence in regard to the effects of exercise upon organ weights. Donaldson (11, 12) and Kimeldorf and Baum (19) found increases in splenic weight after exercise; Donaldson (9, 10), Hatai (16); and Montoye et al. (25) reported decreases; and, Hanson and Van Huss (15) and Montoye et al. (26) found no changes. Borovansky (5), Donaldson (9, 10, 11, 12), Hanson and Van Huss (15), Kimeldorf and Baum (19), and Montoye et al. (25, 27) cite increases in adrenal weights following physical training; whereas Hatai (16) and Montoye et al (26) report no effects. Asahina et al. (3) have shown that excessive physical training can produce histological deterioration and hypofunction of the thymus.

Kimeldorf and Baum (19) found that in the rat the weights of both the thymus and the spleen are reduced following irradiation. They also reported increases in adrenal weights with exposure to x-rays. Patt et al. (31) observed similar splenic and adrenal responses in rats. Such adrenal changes were not found in mice by Smith and Smith (39) following irradiation. In a subsequent study, however, Smith (37) found significant fluctuations in adrenal weights which apparently were dependent upon the amount of time elapsing between irradiation and sacrifice.

Since splenic and adrenal weights were not made prior to irradiation, it was not possible to evaluate the effects of irradiation on the weights of these organs.

Figure 16 and Table 16 show that there were no significant differences between the five treatments with respect to spleen weight at death. Similar results were found with spleen weight at sacrifice (Figure 17 and Table 17).

The five treatments produced no differences in adrenal weight per body weight at death (Figure 18 and Table 18).

Likewise, Figure 19 and Table 19 reveal no treatment effects on adrenal weight per body weight at sacrifice.

In summary, the five treatments had no effects on splenic and adrenal weights either at death or at sacrifice.

Mortality and Survival

Sergeyev (50), Tovbin (50), Trifonov (50) and Zimkin (50) found that pre-training increases survival time and decreased mortality following irradiation. Kimeldorf and Jones (20) found no differences in mortality between trained and untrained animals. The results of the present investigation are in direct contrast to the results of Sergeyev, Tovbin, Trifonov and Zimkin. Figure 20 and Table 20 show no significant differences between treatments with respect to survival time for all animals. Similar results were found with treatment effects on survival time of only those animals which died during the 30-day mortality period (Figure 21 and Table 21).

The Chi-square test showed no treatment effects on mortality (Figure 22 and Table 22). It should be pointed out that the four authors who found increased survival time with pre-training did not see fit to subject their data to statistical analysis. The resultant differences may well have been chance, rather than treatment, effects. However, it would be well to keep in mind that both the intensity and duration of training employed in this investigation was different than that employed by the authors who conclude that there were treatment differences in mortality and survival time.

CHAPTER V SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

Summary

The purpose of this investigation was to study the effects of various levels of preirradiation physical activity, from weanling age to adulthood, upon the radiation resistance of mature rats.

Two-hundred and fifty 26-day old male albino rats (Sprague-Dawley strain) were randomly assigned to one of five treatments. Group 1 (sedentary control) received no special treatment, other than radiation, and was confined to individual sedentary cages both prior to and after being irradiated. Group 2 (spontaneous control) received no special treatment, other than radiation, and was housed in individual spontaneous exercise cages until irradiated and then confined to individual sedentary cages. (sedentary forced) was housed in individual sedentary cages both prior to and after being irradiated. the training period prior to irradiation, these animals were forced to swim daily for one-half hour with two per cent body weight attached to the base of the tail. Group 4 (spontaneous forced) was housed in individual spontaneous exercise cages until irradiated and then confined to

individual sedentary cages. Prior to being irradiated these animals also were forced to swim daily for one-half hour with two per cent body weight attached to the base of the tail. Group 5 (spontaneous effect) was housed in individual spontaneous exercise cages both prior to and after being irradiated. These animals were not subjected to the preirradiation forced training regimen.

Three animals in one of the forced activity groups and two in the other drowned in training. One animal in one of the other groups died while under anesthesia during preirradiation blood sampling. Consequently, animals were eliminated randomly, and 47 rats in each group were irradiated. Postirradiation blood sampling resulted in the death of one additional animal. Once again, equal groups were maintained by random elimination. Therefore, 46 animals per group comprised the final sample.

Those animals which were subjected to the swimming regimen (Group 3 and 4) were swum in individual cylindrical tanks measuring 11 inches in diameter and 30 inches in depth. Water temperature was maintained between 36 and 38 C. during swimming. After each swim period, the animals were dried with a towel and replaced in their respective cages.

The preirradiation treatments were begun at 27 days of age and were carried on throughout puberty and early adult-hood. On the 83rd day of the preirradiation treatments, 20 per cent of the animals, randomly selected with stratification by groups were placed in sedentary cages for an approximate 64-hour rest period prior to irradiation. The forced swimming regimen was terminated for these animals at this time. On the 84th, 85th and 86th days, a similar procedure was followed with 20, 30 and 30 per cent of the animals respectively.

Following the 64-hour rest period, each animal was exposed to 650 r while confined in a three-inch by nine-inch lucite chamber. Twenty-four animals were irradiated simultaneously. The total time required for irradiation was 180.5 minutes. Animal positions were rotated every 36.1 minutes to provide equal exposures for all.

Nine days before and five days following irradiation, a blood sample was drawn from the orbital sinus of each animal to determine the WBC and eosinophil counts. A 24-hour period of confinement in sedentary cages was provided for all animals, regularly in spontaneous cages, prior to the drawing of each blood sample.

During the 30 days immediately following irradiation, a

laboratory technician was with the animals twenty-four hours a day. Mortality and survival time in hours for all groups of animals were recorded during this period. At the end of the thirty-day period, the surviving animals in all groups were sacrificed. Upon death or sacrifice, body weight as well as the weights of the spleen and adrenals were determined. The thymus was observed subjectively, but not weighed, since its posirradiation condition prohibited proper extraction and trimming.

Throughout the entire investigation, all animals received water and a commercial ground animal diet, ad libitum. Body weight for each animal was determined once a week throughout the preirradiation period, and the weight to be attached to the base of the tail during swimming was changed on the following day. The temperature in the housing quarters was maintained between 70° and 78° F. Daily voluntary exercise data for each animal housed in a spontaneous exercise cage was recorded at 7:45 A.M. daily.

For the first 71 days of the preirradiation period, an automatic timer illuminated the animal quarters 12 hours a day. Since it was necessary for the technician to observe each animal hourly following irradiation, lights were kept on 24 hours a day beginning on the 72nd day. The 24-hour

illumination was started 12 days prior to irradiation in order to provide an adjustment period for the animals.

Statistical analysis (sign test) showed that the spontaneous forced animals (Group 4) were significantly more active than the spontaneous controls (Group 2). Both preirradiation and postirradiation activity level had no effect on survival time following irradiation. Twentyfour hour lighting significantly reduced activity levels when compared with 12 hour lighting. Irradiation significantly reduced activity levels. Body weight differences between groups prior to irradiation were observed with the most heavily exercised (Group 4) being lighter than Groups 1, 2 and 3. Preirradiation WBC and eosinophil counts showed no differences between groups. Similar results were found with postirradiation blood sampling. differences between groups were noted with respect to spleen weight at death and sacrifice and adrenal weight per body weight at death and sacrifice. The comparison of both mortality and survival time in hours between the treatment groups showed no differences. Those animals which were in the upper half of their group with respect to body weight had longer survival times than those animals in the lower half.

Conclusions

Analysis of the results of this investigation has led to the following conclusions:

- 1. Forced swimming for one-half hour daily with two per cent body weight attached significantly increases spontaneous activity.
- Forced swimming and/or spontaneous activity for a prolonged period reduce body weight.
- 3. Illumination of animal quarters 24-hours daily significantly reduces volitional activity as compared to 12-hour per day illumination.
 - 4. Irradiation decreases spontaneous activity.
- 5. Prolonged training does not alter WBC or eosinophil levels either prior to or following irradiation.
- 6. Prolonged training has no effect on either adrenal weight per body weight or gross splenic weight following irradiation.
- 7. Level of preirradiation physical activity has no effect on postirradiation mortality and survival time.
- 8. Body weight appears to be the most significant factor influencing survival time following irradiation.

Recommendations

1. Unless histological or pathological investigations

are to be conducted, further research should dispense with the weighing of organs.

- 2. If spontaneous activity is to be measured, careful attention should be given to the amount of time daily that the animal quarters are to be illuminated.
- 3. A study should be undertaken in which spontaneous activity is measured for 50 days prior to irradiation with 650 r. Spontaneous activity will be measured for three days postirradiation. Use 12 hours of light and 12 hours of darkness throughout investigation. This will enable one to quantitate the effect of irradiation on voluntary activity.
- 4. It is recommended that the adrenals of all animals be subjected to histological examination (volume of three cortical zones) and plotted against survival time. This procedure will provide evidence of radiation damage and recovery trends.
- 5. It is recommended that the basic study be redone utilizing a radiation dose of 700-900 r.

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APPENDIX A

Raw Data

Legend for Raw Data

- A = Animal Number
- B = Treatment
- C = Mean Daily Voluntary Activity During Total Preirradiation Period.
- D = Level of Mean Daily Voluntary Activity Relative to Groups During Total Preirradiation Period.
- E = Mean Daily Voluntary Activity During 11 Days Preirradiation Prior to Lights On.
- F = Mean Daily Voluntary Activity Last 11 Days Preirradiation with Lights On.
- G = Mean Daily Voluntary Activity During First 11 Days
 Postirradiation.
- H = Mean Daily Voluntary Activity First 3 Days Postirradiation.
- I = Level of Mean Daily Voluntary Activity Relative to Group During First 3 Days Postirradiation.
- J = Body Weight Last Week Prior to Irradiation.
- K = Level of Body Weight Relative to Groups Last Week Prior to Irradiation.
- L = WBC 9 Days Prior to Irradiation.
- M = Level of WBC Relative to Groups 9 Days Prior to Irradiation.
- N = WBC 5 Days Postirradiation.
- O = Level of WBC Relative to Groups 5 Days Postirradiation.
- P = Eosinophils 9 Days Prior to Irradiation.
- Q = Level of Eosinophils Relative to Groups 9 Days Prior to Irradiation.
- R = Spleen Weight at Death or Sacrifice.
- S = Adrenal Weight Per Body Weight at Death or Sacrifice.
- T = Survival Time in Hours.*
- * Those animals with survival times of 715 lived to sacrifice.

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	4/14	156	171	177	177	167	167	185	167	160	146	162	167	180	174	159	181	180	179	170	152	174	162	134	137
	4/7	\vdash	\vdash	3	\sim	$^{\circ}$	126	\sim	2	\vdash	\vdash	\sim	\vdash	\sim	\sim	\vdash	\sim	\sim	3	\vdash	\vdash	2	Н	108	100
	3/31	67	69	81	81	71	74	78	72	99	99	75	29	80	80	81	29	79	79	99	70	71	73	09	99
Animal	Number	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	45	46	48	49	20	51	53

APPENDIX B (continued)

	6/22	7	2	4	5	3	Н	390	Н	3	∞	4	2	0	∞	2	0	9	7	9	2	4	m	9	∞
	91/9	\circ	Ŋ	4	\sim	\sim	Н	394	Н	Н	7	4	S	0	ω	\sim	ω	2	9	α	4	\sim	m	σ	7
	6/9	6	4	4	\sim	Η	Н	393	0	0	9	7	4	σ	\mathbf{c}	Н	7	\mathbf{c}	9	9	\sim	\sim	\sim	∞	7
	6/2	9	$^{\circ}$	$^{\circ}$	0	ω	9	362	∞	σ	3	9	\vdash	ω	4	9	2	3	4	\mathbf{C}	0	\vdash	\vdash	9	9
	5/26	4	σ	0	0	9	ω	336	7	9	\vdash	∞	0	7	7	9	\sim	2	3	7	9	σ	0	4	3
	5/19	\sim	7	9	7	3	7	337	2	ω	9	9	ω	9	Н	2	7	0	\vdash	0	∞	7	6	3	Ч
ורא	5/12	302	336	275	310	333	255	317	247	262	230	332	267	241	284	316	299	239	295	269	254	238	259	224	596
body weights	5/2	7	0	\mathbf{c}	7	0	4	299	\vdash	3	4	9	4	2	S	ω	7	3	9	9	3	3	0	3	9
ם מ	4/28	4	2	Н	ω	3	\vdash	257	Н	6	0	\mathbf{c}	Н	6	Н	4	3	7	3	4	Н	0	ω	0	П
	4/21	6	Н	ω	3	9	7	212	7	9	- α	2	7	9	7	0	9	2	9	9	7	/	2	9	7
	4/14	149	163	135	184	160	135	164	147	138	142	171	140	140	141	167	151	120	156	152	140	140	128	130	140
	4/7	108	113	92	140	114	94	111	106	26	101	120	66	66	101	113	110	91	112	117	106	101	96	94	104
	3/31	73	72	62	84	74	65	73	64	29	89	92	61	70	69	74	71	62	92	77	89	99	62	19	63
Animal	Number	55	56	57	58	59	09	61	62	63	64	65	99	89	69	70	72	73	74	75	9/	77	78	79	80

APPENDIX B (continued)

	6/22	0	\sim	3	\sim	3	S	9	9	4	\vdash	2	7	4	\vdash	S	Н	9	∞	9	2	9	9	519	\sim
	/16 6	7	9	2	2	7	5	4	9	œ	7	4.	2	7	4.	0	2	ω	9	6	7	7	7	က	4
	/9	0	0	2	3	2	7	9	σ	4	\vdash	4	9	7	Ó	9	0	2	7	9	0	3	2	20	H
	6/9	0	0	7	\sim	2	2	σ	7	3	0	4	9	7	0	2	0	4	7	4	0	0	\sim	472	0
	6/2	∞	ω	0	\vdash	0	6	7	5	2	7	Н	4	2	∞	3	ω	\sim	4	2	9	ω	Ō	448	7
	5/26	9	\mathbf{c}	6	0	∞	ω	2	3	0	9	9	2	3	9	7	2	0	7	H	9	9	7		355
	5/19	7	3	9	∞	∞	9	Ò	\vdash	4	\sim	ω	0	\vdash	4	9	\sim	∞	0	9	\sim	S	2	395	326
2	5/12	٦	\vdash	\mathbf{c}	9	9	7	6	7	9	\vdash	4	7	9	2	7	0	9	∞	7	Ч	3	3	347	ω
20116-011-7	5/2	7	ω	2	3	4	\vdash	7	2	\sim	∞	2	2	2	ω	2	9	4	2	4	7	0	6	303	2
I non	4/28	4	4	0	\vdash	0	ω	3	2	Н	4	9	\sim	Н	4	2	\sim	Н	0	2	4	9	Ω	246	\vdash
	4/21	6	0	ω	∞	7	9	9	∞	7	σ	9	9	7	Н	σ	9	7	9	σ	ω	Н	0	191	7
	4/14	9	S	\mathcal{C}	4	4	3	S	\sim	4	9	\sim	9	3	9	4	2	4	3	S	2	9	171	142	134
	4/7	119	118	104	109	102	97	108	108	94	117	103	115	102	117	108	117	102	101	112	113	111	127	84	88
	3/31																							70	
Animal	Number	81	82	83	84	85	86	87	88	89	06	91	92	93	94	92	96	97	86	66	0	0	102		104

APPENDIX B (continued)

Animal					•	1							
Number	3/31	4/7	4/14	4/21	4/28	2/2	5/12	5/19	5/26	6/2	6/9	6/16	6/22
105	72	106	4	∞	\vdash	4	∞	0	3	355	7	\circ	0
106	63	83	3	7	\vdash	4	∞	\vdash	4	372	ത	~~	$\overline{}$
107	71	110	S	0	2	7	2	4	9	387	-	\sim	₹
108	80	120	9	9	7	9	Н	2	0	420	w	9	α
109	69	103	140	175	207	244	273	310	334	357	381	399	414
110	99	104	4	ω	2	9	ω	Н	3	346	S	7	0
111	80	121	9	0	4	7	\vdash	2	Ø	400	\sim	\sim	/
112	80	116	9	0	4	7	0	2	2	370	ത	\vdash	2
114	75	108	Ŋ	9	4	9	\vdash	\sim	Ŋ	369	ന	0	-
115	29	109	2	0	4	∞	\vdash	2	7	394	Н	\sim	4
116	74	971	S	0	\mathbf{c}	0	4	ω	0	434	2	α	9
117	9/	91	3	7	\vdash	9	ω	\vdash	\sim	350	o	ത	9
119	29	104	4	7	\vdash	4	7	Н	3	354	7	α	0
120	65	82	2	7	\sim	7	٦	3	2	354	/	0	\sim
121	78	116	2	ω	7	S	9	7	4	371	ത	0	0
122	99	82	3	9	\mathbf{c}	0	9	0	3	466	ത	$\overline{}$	3
124	77	116	S	0	\sim	7	0	7	4	377	ത	\vdash	3
125	70	109	2	ω	\sim	9	σ	3	7	387	$\overline{}$	~	4
126	71	118	9	0	S	9	Ò	7	σ	422	S	9	ന
127	71	103	4	∞	\vdash	9	0	\sim	\mathbf{c}	367	ത	0	\sim
128	74	113	9	0	4	ω	0	2	∞	409	3	S	S
129	77	117	9	9	3	2	~	σ	9	311	3	4	₹
130	73	116	9	σ	4	/	\vdash	4	9	378	\circ	2	Ň
131	80	126	9	\sim	9	\vdash	m	7	6	426	Ω	7	ന

APPENDIX B (continued)

	6/22	9	4	2	491	0	2	2	9	\vdash	Ч	7	0	7	Н	7	S	7	4	∞	7	Н	2	9	7	428
	91/9	4	Н	\sim	483	ω	0	\sim	2	σ	\vdash	S	ω	0	0	2	\sim	0	Н	ω	\vdash	6	Н	S	\vdash	\vdash
	6/9	\mathcal{C}	Н	Ч	454	2	∞	3	4	ω	9	\sim	7	∞	ω	\sim	Н	9	0	7	∞	ω	2	3	0	0
	6/2	0	σ	σ	425	\sim	ω	\vdash	\sim	9	7	\vdash	9	9	9	0	0	7	ω	9	9	9	9	7	ω	7
	5/26	7	7	7	404	Н	9	0	\vdash	S	2	0	2	4	4	9	9	2	7	2	4	4	2	\vdash	9	365
	5/19	2	Ŋ	4		9	4	∞	0	2	2	7	4	2	Н	9	1	3	Ω	\sim	2	\sim	\sim	9	4	350
91112	5/12	0	7	0	329	7	\vdash	7	ω	9	9	3	0	9	ω	7	\mathbf{c}	9	7	\vdash	9	0	0	ω	\vdash	
TOM ACT	2/2	9	ω	/	301	4	7	9	7	4	ω	\vdash	9	9	S	9	3	9	9	ω	9	7	2	2	7	ω
3	4/28	٦	7	3	252	\vdash	\sim	4	\mathcal{C}	Н	4	9	7	7	\vdash	2	0	7	2	7	0	4	2	Н	\sim	\sim
	4/21	7	0	0	214	7	9	0	9	ω	σ	Н	ω	∞	ω	Н	7	ω	0	ω	∞	Н	ω	ω	0	σ
	4/14	\sim	2	2	166	4	Ω	9	S	4	9	9	4	\sim	4	7	4	4	9	4	2	9	4	4	S	2
	4/7	107	110	106	112	92	113	119	111	109	120	122	111	83	100	122	103	112	122	100	118	108	117	109	98	107
	3/31	69	73	89	8,	73	78	80	73	73	92	80	92	80	65	78	69	80	92	29	82	29	81	71	89	29
Animal	Number	\mathcal{C}	3	\mathcal{C}	135	3	\sim	\sim	\mathcal{C}	4	4	4	4	4	4	4	4	4	\mathbf{c}	\mathbf{c}	5	2	2	155	156	157

APPENDIX B (continued)

Animal						ı	ŀ						
Number	3/31	4/7	4/14	4/21	4/28	5/2	5/12	5/19	5/26	6/2	6/9	6/16	6/22
2	77	120	161	9	4	9	7	352	ω	0	Н	4	9
2	71	111	152	ω	Ñ	4	ω	315	3	4	9	7	∞
9	70	116	165	0	Ŋ	9	0	334	2	7	9	\vdash	S
9	77	119	168	0	4	2	Н	346	9	ω	\vdash	3	\mathcal{C}
9	89	80	123	7	0	4	9	289	0	\vdash	3	9	∞
9	70	112	143	9	9	4	7	298	7	3	4	9	7
9	71	122	168	2	/	3	2	370	4	7	ω	7	Н
9	70	109	154	9	3	9	9	318	3	9	7	9	П
9	73	107	136	9	9	$^{\circ}$	7	310	3	9	7	9	$\overline{\mathbf{H}}$
9	9/	128	168	\vdash	2	9	Ŕ	355	ω	9	Н	2	9
7	82	125	159	9	3	7	\vdash	344	7	ω	\vdash	\mathcal{C}	$^{\circ}$
7	71	111	155	9	3	2	7	300	3	2	7	0	Ñ
7	74	130	174	Н	/	Н	4	381	\vdash	3	Ŋ	7	Н
7	73	121	167	0	4	∞	\vdash	343	9	ω	0	Н	m
7	29	100	137	7	$\overline{\mathbf{H}}$	4	/	304	Н	4	9	1	9
7	75	120	168	\vdash	S	9	\sim	3 2 6	∞	0	3	4	Ŋ
7	73	112	150	ω	2	9	6	323	4	S	/	9	9
7	77	122	156	σ	3	2	0	324	4	2	ω	σ	Ō
7	77	119	159	6	3	7	0	326	2	9	9	9	$\overline{}$
/	20	107	147	ω	\vdash	S	7	299	\vdash	2	3	4	2
ω	64	66	135	7	0	Ò	9	272	\vdash	0	4	4	~
ω	81	116	147	7	\vdash	3	9	284	0	2	S	9	ω
182	79	118	157	193	235	278	292	313	332	347	362	374	375
ω	75	128	173	7	_	7	7	402	7	2	7	0	

APPENDIX B (continued)

	6/22	∞	2	9	7	3	2	0	9	Н	2	9	9	\vdash	ω	ω	Н	452	7	9	4	4	Н	Н	481
	6/16	9	2	3	0	Н	0	7	Ŋ	0	0	7	9	ω	7	7	9	441	7	σ	3	3	0	0	7
	6/9	2	3	9	9	0	0	9	3	ω	ω	4	\sim	7	2	2	9	421	9	9	\vdash	\vdash	σ	0	2
	6/2	4	S	7	9	7	9	3	σ	7	\mathcal{L}	0	2	4	2	\sim	Ø	394	ω	4	σ	σ	7	ω	7
	5/26	\sim	7	4	4	\mathbf{c}	\mathbf{c}	\sim	7	\mathbf{c}	Ŋ	2	\vdash	3	\vdash	0	9	381	7	Н	9	ω	2		0
	5/19	7	4	\sim	\vdash	3	2	σ	2	\vdash	3	0	0	Н	9	0	9	360	S	9	2	9	3	2	ω
ı	5/12	9	\vdash	9	9	0	0	2	0	9	0	∞	9	9	9	ω	3	322	Н	2	2	3	0	2	5
ı	5/2	9	∞	5	\vdash	7	7	6	1	9	7	4	4	7	2	2	0	315	ω	Н	7	9	7	0	317
	4/28	Ö	3	2	9	3	Ŕ	7	4	Ò	4	2	Η	3	0	3	2	270	9	9	2	2	3	9	9
	4/21	177	199	183	205	190	193	220	196	183	204	185	184	195	173	190	210	223	214	216	197	209	202	214	220
	4/14	≺⁺	2	ܡ✝	Q	Ω	Ω	7	Ω	ゼ	o	ゼ	LO	S	3	ဖ	/	175	w	/	マ	o	7	ဖ	o
	4/7	0	Н	\vdash	\sim	\vdash	Н	7	Н	0	$^{\circ}$	0	Н	2	7	Н	$^{\circ}$	127	\vdash	$^{\circ}$	ω	107	125	117	116
	3/31	99	71	99	82	73	72	72	71	72	9/	74	7.5	80	97	89	89	75	80	72	64	80	9/	69	73
Animal	Number	184	185	186	187	188	189	190	191	192	193	195	197	198	199	200	201	202	203	204	205	206	207	208	209

APPENDIX B (continued

	6/22	9	573	0	2	0	Н	3	2	3	3	2	0	0	Н	0	9	\vdash	7	2	0	2	S	9	2
	6/16	2	563	9	2	0	9	\vdash	9	П	3	4	∞	2	9	7	2	\vdash	9	4	9	\vdash	3	7	4
	6/9	442	547	386	433	486	484	411	483	515	516	432	478	480	390	487	440	394	396	435	379	413	434	462	424
	6/2	417	512	365	406	450	460	391	450	479	480	405	441	464	373	447	390	368	400	409	357	384	416	441	390
	5/26	ω	489	2	7	2	7	/	\sim	9	2	9	2	4	9	\sim	σ	\mathbf{c}	\vdash	∞	3	ω	9	\vdash	9
	5/19	380	451	333	371	396	416	355	401	433	426	376	394	410	338	404	366	340	390	368	316	371	376	393	375
1	5/12	4	409	\vdash	വ	7	α	\sim	9	0	α	4	9	7	\vdash	9	\sim	$\overline{}$	Ω	4	ത	\sim	Ŋ	വ	337
1	5/2	\vdash	360	ω	\vdash	\sim	5	9	0	Ω	4	0	2	4	9	3	0	σ	2	\vdash	9	9	2	2	9
	4/28	268	289	238	267	279	299	262	276	285	280	257	280	285	264	280	258	259	275	270	223	263	268	566	245
	4/21	2	230	9	\sim	2	2	\vdash	7	2	7	0	7	\sim	\vdash	\sim	\vdash	\vdash	2	\vdash	∞	0	\vdash	0	7
	4/14	182	179	152	167	274	184	170	176	176	178	163	178	180	169	171	169	167	172	176	156	157	170	177	173
	4/7	3	130	0	7	7	3	$^{\circ}$	$^{\circ}$	$^{\circ}$	$^{\circ}$	Н	2	7	7	\vdash	2	7	3	3	\vdash	0	7	\sim	\sim
	3/31	79	72	65	70	70	81	69	72	64	74	64	79	71	73	78	75	75	80	72	64	89	9/	77	75
Animal	Number	Н	211	\vdash	\vdash	\dashv	\vdash	Н	\vdash	Н	Н	2	7	2	7	7	7	2	2	7	7	3	3	\sim	\mathcal{C}

APPENDIX C
Starting Positions for Irradiation of Animals

Nos. 1-50 Nos. 51-100 Time Sed. Forced Spont. Forced Day Finished Box Pos. An. Pos. Box An. Ι Α 48 В 86 Ι II R С 33 II 98 1:00 III С 16 D III 55 P.M. IV D 23 IV Е 73 Thurs. v Е 41 Α V --24 Ι В 40 C June I 63 С II 35 II D 6:00 III D 24 III Е 93 P.M. IV Е 27 IV Α 83 А V --V В 58 т C 1 Ι D 96 II Е D 9 II 75 12:00 III Е 32 III Α 89 IV Α 38 IV Noon В 7.2 Fri. V В 13 V С 80 25 Ι 8 100 June D Ι Ε II Α 77 E 43 II 4:00 III Α 18 III В 61 P.M. IV В 30 IV C 85 V C 6 V D 84 Ι Е 20 I Α 69 II Α 3 II В 90 12:00 III В 45 III С 53 IV C D Noon 25 IV 65 Sat. V D 5 V E 88 26 June Ι Α 11 Ι В 99 II II С В 19 71 3:00 III C 10 III D 76 D Е P.M. IV 34 IV 79

V E 14

V A

Nos. Spont.	101-1 Con		Nos. Spont.	151-	200 fect	N Se		201- Con	250 trol
Box	Pos.	An.	Box	Pos.	An.	Во	x]	Pos.	An.
I	С	124	I	D	188		I	E	237
II	D	112	II	E	153	I	I	A.	201
III	E	113	III	Α	180	II	I	В	244
IV	A	123	IV	В	190	I	V	С	240
V	В	128	V	С	184		V	D	238
I	D	142	I	E	156		I	А	236
II	E	119	II	Α	198	I	I	В	235
III	А	107	III	В	163	II	I	С	232
IV	В	115	IV	С	166	I	V	D	223
V	С	127	V	D	200		V	E	222
I	E	134	I	А	189		I	В	208
II	А	141	II	В	181	I	I	С	205
III	В	133	III	С	177	II	I	D	228
IV	С	138	IV	D	169	I.	V	E	215
V	Ď	114	V	E	168	•	V	A	
I	Α	139	I	В	173		I	С	212
II	В	104	II	С	162	I	I	D	202
III	С	150	III	D	155	II	I	\mathbf{E}	217
IV	D	109	IV	\mathbf{E}	178	I.	V	A	218
V	E	140	V	Α		•	V	В	209
I	В	145	I	С	161		I	D	233
II	С	130	II	D	171	I	I	\mathbf{E}	239
III	D	120	III	\mathbf{E}	170	II	I	A	211
IV	E	129	IV	A	158	I.	V	В	214
V	Α		' V	В	197	•	V	С	249
I	С	122	I	D	154		I	E	234
II	D	135	II	\mathbf{E}	183	I		A.	247
III	E	106	III	Α	191	II	I	В	225
IV	A	105	IV	В	151		V	С	210
V	В	101	V	С	152		V	D	220

110

APPENDIX C (continued)

Starting Positions for Irradiation of Animals

		No	s. 1-5	0	Nos	. 51-1	.00
	Time	Sed.	Ford	ced	Spont.	Ford	ed
Day	Finished	Box	Pos.	An.	Box	Pos.	An.
		I	В	12	I	С	64
		II	C	39	II	D	59
Sat.	7:00	III	D	15	III	E	87
26	P.M.	IV	E	49	IV	A.	57
June		V	A		V	В	70
		I	C	17	I	D	56
		II	D	36	II	E	66
	12:00	III	E	22	III	A	74
	Noon	IV	A	37	IV	B	97
		V	В	46	V	С	51
		I	D	29	I	E	91
	3:00	II	E	4	II	A	82
	P.M.	III	A	42	III	В	81
		IV	В	2	IV	C	68
Sun. 27		V	С	26	V	D	60
June		I	E	50	I	A	62
		II	A	7	II	В	92
	7:00	III	В	31	III	C	95
	P.M.	IV	C	21	IV	D	94
		V	D	28	V	E	78

Nos.	101-1	-50	Nos.	. 151-	-200	Nos	. 201	-250
Spont.	Cont	rol	Spont.	. Eff	ect	Sed.	Co	ntrol
Box	Pos.	An.	Box	Pos.	An.	Box	Pos	. An.
I	D	121	I	E	185	I	A	204
II	E	146	II	A	192	II	В	207
III	A	116	III	В	199	III	С	241
IV	В	149	IV	С	182	IV	D	245
V	С	102	V	D	165	V	E	224
I	E	111	I	A	174	I	В	227
II	А	143	II	В	160	II	С	213
III	В	125	III	С	196	III	D	243
IV	С	147	IV	D	193	IV	\mathbf{E}	226
V	D	144	V	${f E}$	157	V	A	
I	Α	108	I	В	186	I	C	203
II	В	110	II	С	164	II	D	206
III	С	137	III	D	176	III	E	219
IV	D	126	IV	E	195	IV	A	229
V	E	117	V	Α		V	В	248
I	В	136	I	С	172	I	D	231
II	С	132	II	D	179	II	E	216
III	D	103	III	D	159	III	Α	221
IV	E	131	IV	A	187	IV	В	250
V	А		V	В	175	V	С	242





