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Estimation of the genetic influence on growth and organ weight changes in mice following total body x-irradiation

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ESTIMATION OF THE GENETIC INFLUENCE ON GROWTH AND ORGAN WEIGHT CHANGES IN MICE FOLLOWING TOTAL BODY X-IRRADIATION

by

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INTRODUCTION

Inter-specific variation in response to irradiation has been acknowledged and, to some degree, has been quantitated. However, genetic variation within a species, although recognized, has not been put to severe test as an experimental variable in radiobiological studies.

This research has been designed to measure the possible existence of genetically determined differential responses to total body x-irradiation. Six inbred strains of mice have been used for this purpose. These strains have been previously differentiated by their resistances to mouse typhoid, caused by the organism, Salmonella typhimurium. The radiation response has been measured in terms of body weight change through a twenty-day post-irradiation period. In addition, representative radio-sensitive and radio-resistant organs, including the heart, kidneys, liver, spleen, and testes, have been weighed.

Although utilization of genetically controlled material can usually increase experimental accuracy, the degree to which this is enhanced is generally unknown. It is the purpose of this investigation to determine the contribution of the genotype to the over-all variation in biologic response to total body x-irradiation.

REVIEW OF LITERATURE

The most effective quantitation of inter-specific differences in reaction to irradiation has been in dosage-mortality studies. However, the many physiological differences in response, from one species to the next, as described by Prosser (1947), have not been fully integrated into a broad analysis of the lethal effects of irradiation.

A possible key to the understanding of the mechanisms of differential reactions to irradiation may be found in the more complete analysis of differences that may exist within a species. At this level of study, dissimilarities in the morphology and physiology are minor deviations from the species mean or normal biology.

Intra-specific Differences in Radiation Response

Apparently the first recognition of strain or genetic variation in the reaction to irradiation was made by Henshaw (1944). A comparative study of mouse strains C3H and LAF_1 at 50, 100, 200, and 400r total body exposure to x-irradiation brought out many quantitative differences. The lethal dose for C3H mice was found to be 450r, while that for the LAF_1 mice was approximately 600r. Cellular changes bore out the observed difference in resistance to the lethal effects.

With respect to the leukopenic response of the peripheral blood, Henshaw stated that 50r and 100r on a C3H mouse were equivalent to 100r and 200r, respectively, on a LAF_1 mouse. Histological changes in the hematopoietic tissues, testes, and intestinal mucosa also demonstrated a greater resistance to cellular injury in the LAF_1 mice. Henshaw stated that the changes were qualitatively similar, indicating that a higher critical-dose threshold existed in LAF_1 mice.

Further information with regard to strain differences in response to irradiation was given by Lorenz, et al. (1947) and by Henshaw, Riley, and Stapleton (1947) in a symposium on the Plutonium Project. In the work described by Lorenz, et al., four strains of mice, A, C3H, dba, and LAF_1, were chronically exposed to gamma radiation. One interesting strain difference was seen by the authors. For strains C3H and LAF_1, used previously by Henshaw (1944) to indicate strain differences, the present study confirmed Henshaw's observations on the comparative resistance of the LAF_1 mice. At 4.4r/8 hrs./day, the irreversible sterilization dose for female LAF_1 mice was between 770r and 880r, while only 450r was necessary to cause the same effect in C3H mice. C3H males were sterile at 800r, while LAF_1 males bred normally at 1100r. Strain dba apparently paralleled the C3H strain.

In addition, two different inbred families and a heterogeneous stock of guinea-pigs were entered in the experiments.

The inbreds, identified as Families 2 and 13, showed a striking difference in the lethal dose range with respect to deaths from anemia and thrombocytopenia. At a chronic exposure of 8.8r/8hrs./day, the cumulative lethal dose range for Family 2 was from 1200r to 1600r. For Family 13, it was from 1900r to 2100r. The heterogeneous stock showed a lethal dose range of 700r to 4400r. No genetic interpretations were made by the authors; however, it would seem that the heterogeneous animals presented a genetic situation wherein a broad range of genotypes was sampled. On the other hand, the inbreds not only showed a very narrow range within families, but also showed a family difference in the lethal dose range. The effective isolation of two divergent genotypes was indicated.

It is of interest to note that in the heterogeneous stock the 50 per cent death point was reached at a place where only about 20 per cent of the total dose range had been covered, that is, somewhere in the vicinity of 1400r. This indicated an extreme skewing of susceptible genotypes, and, considering that the criterion of death was anemia and thrombocytopenia, it partially confirmed the observation that the guinea-pig was highly susceptible to death from these causes. Only a small number of animals were capable of offering any resistance to this species weakness.

In this same report, a sex difference was noted by the authors. In the LAF_1 mice, the incidence of induced lymphoid leukemia was nearly twice as high in the females as in the males. Exact figures for this were not given, but it was stated that the incidence was 45 per cent in the females at its peak, with the exception of the highest dose level of 8.8r/day. At the latter dose, the incidence reached 70 per cent.

Henshaw, et al. (1947) also employed four mouse strains. These were: CF1, ABC, A, and C_{58}. The mice were exposed to either neutrons, gamma rays, or beta particles. Both single and chronic exposure methods were used. The chronic exposure results indicated that strain ABC was more resistant than strain CF1. The ABC mice required a greater total exposure to gamma rays before their life span was shortened to the same degree as that of the CF1 mice. Under a single exposure to fast neutrons, the ABC mice were more resistant to lethal effects, as well. Differential dosage relationships were not given. No sex differences were observed with respect to weight loss, hematologic change, or shortening of life span under chronic exposure to gamma irradiation. The authors concluded that the strain differences were more a matter of degree than of type.

In 1948, Evans reported a study on two strains of mice exposed to small daily doses of fast neutrons. The strains involved were CF1 and Rockland Farms Swiss mice. Balanced numbers of males and females of each strain were used at each of four levels of chronic exposure. When the response was measured as a percentage of control survival for each strain, the CF1 mice were more susceptible. At 1.4n/day, they accumulated only 162n before they were reduced to a 37 per cent survival, while the Swiss mice accumulated between 228n and 235n to be reduced to 49 per cent survival.

However, when the mean survival time (MST) was used to measure response, no true strain difference existed. The CF1 mice had a shorter MST at all dosage levels, but this included the controls. Thus, normal CF1 mice had an MST of 420 days, while at 0.07n/day it was 412 days, and 168 days at 1.4n/day. These were reductions to 98 per cent and 40 per cent of their control, respectively. The Swiss mice had a normal MST of 475 days, 55 days longer than CF1 mice. At 0.07n/day and 1.4n/day, the Swiss mice were reduced to 443 and 206 days or 94 per cent and 43 per cent of their control. These compared very closely with the values in the CF1 strain. As Evans noted, a strain difference in MST existed in the irradiated mice, but it was entirely a function of a basic strain difference in the expected life span.

In light of Evans' findings, one can question the similar type of strain difference, observed by Henshaw, et al. (1947), discussed above. The fact that the ABC mice required a greater total dosage of gamma radiation to have their life span shortened to a degree similar to CF1 mice may well be due to a basic genetic difference in life expectancies. This is indicated in data given by Sacher (1950), who gave the life span of CF1 mice as 425 days as compared to 538 days for the

ABC strain. In the reviewer's opinion, CF1 mice may have been expressing a non-specific response to irradiation in the study reported by Hensaw, et al.

Evans also observed a rather clear-cut sex difference in response. At 80r/day of x-ray, the males required 19 days and the females required 25 days of exposure to reach the 50 per cent mortality level. This was a difference of 480r on the cumulative dosage scale.

In a summarizing report of the hematologic effects of radiation, Jacobson, Marks, and Lorenz (1949) brought out many significant genetic differences. For the most part, these were inter-specific differences with respect to sensitivity to hematologic change, mortality, type of induced anemia, and rate of recovery. Unfortunately, the only intra-specific or strain difference was confounded with sex differences. CF1 females were stated as more resistant to hematologic alteration than strain A males, after internal exposure to radium.

Kohn (1950) described the genetic differentiation of four strains of rats in terms of their normal blood cholesterol levels. Two strains were classed as "high" and two as "low". The differences were stated as resulting from chance isolation during inbreeding. The strains involved were: SD (Sprague-Dawley); OM (Osborne-Mendel-Vanderbilt); TBH (Tumblebrook hooded); and H (Holtzmann).

In 1951a, Kohn reported the blood plasma changes in these rat strains following total body x-irradiation. Basically the $LD_{50/30}$ doses were; H: 770r; OM and SD: 730r; TBH: 650r. Changes in glucose, inorganic phosphorous, and non-protein nitrogen were the same for all strains. A basic strain difference in the normal glucose level was unaffected by radiation in strains SD and OM. Blood chloride response was qualitatively similar in the four strains, but definite quantitative differences appeared. All strains started at a level of 607-608 mgs. percent. After an initial drop, a rise occurred at the second or third post-irradiation day which was followed by a sustained high level or plateau until about the tenth day. The exact time of return to normal level varied, to some degree, with the strain. The precise strain differences in chloride response were measured by the height of the peak rise and the plateau level. In this respect, strain H was least affected, strains OM and SD moderately affected, and strain TBH was most affected. The degree of effect correlated well with the LD_{50} doses. Kohn considered the chloride shift an integrative mechanism that was a secondary systemic physiologic response, wherein most of the chloride passed to the plasma from intracellular sources.

Estimates of total protein on strains H, OM, and SD showed a drop after exposure while strain TBH remained unaffected. Albumin-globulin ratio changes were unreliable, while cholesterol response was the same in strains H and SD.

The latter represent "high" and "low" strains, but the basic difference was not altered by irradiation. In no instances were sex differences observed.

Kaplan and Paull (1952) reported a strain or genetic modification of response to spleen shielding in x-rayed mice. Using strains A and C57, the authors exposed three groups of mice in each strain. One group was left intact, a second was sham-shielded, and the third had lead-shielded spleens. At 550r, the mortality, in the intact group, was 60 per cent in C57 mice and 75 per cent in A mice. Deaths began about five days earlier in the C57 strain. In both strains, sham-shielding caused deaths to occur earlier, but their final mortality was the same as for the intact controls. In the lead-shielded groups, 23 per cent mortality occurred in C57 mice while no strain A mice died. Histologic changes of the thymus, lymph nodes, and bone marrow were essentially the same for both strains. The shielded spleens, however, gave indication of cellular differences in response. The more effectively protected mice, strain A, showed a proliferation of hematopoietic tissue with little response of the lymphoid tissue. The C57 mice responded with a proportionate increase in both lymphoid and hematopoietic tissues. Thus, although both strains showed an increased cellularity and splenic enlargement, there was a genetic difference in the specific response. The authors suggest that the basic difference may lie in the importance of the spleen as a hematopoietic organ for the particular strain involved.

Lorenz, Congdon, and Uphoff (1952) studied the modification of the lethal effects of x-ray on mice, utilizing four different strains. The $LD_{50/30}$ values were stated as 650r for LAF_1, 560r for A, and 600r for strain $C3H_b$. No LD_{50} value was given for strain L. The absolute lethal dose was 900r for all strains. When a homologous bone marrow suspension was injected intra-venously 10-15 minutes after exposure to 900r, the mortality was as follows; LAF_1: 20 per cent; $C3H_b$: 30 per cent; A: 0 per cent; L: 30 per cent. Intra-peritoneal injection gave these results; LAF_1: 25 per cent; $C3H_b$: 90 per cent; A: 84 per cent; L: 40 per cent. The injection pathway was unimportant in the LAF_1 and L mice, but it was definitely important in the other two strains which showed only a minor reduction from 100 per cent mortality. A comparative lag in red cell regeneration was considered basic to the greater mortality in the $C3H_b$ mice after intra-peritoneal inoculation. The authors did not consider the genetic implications, but, since the parental L and A strains were compared with the F_1 hybrid, it appears that the favorable regenerative capacity of strain L may be dominant in the F_1.

Kohn (1951a,b) discussed the theoretical implications of both inter- and intra-specific variation in response to irradiation. He considered that for a given tissue all mammalian cells may show an equivalence of sensitivity to the primary or direct effects of radiation. Genetic differences in morphologic and physiologic response may be entirely due to the differences in sensitivity to secondary effects which arise from neural, humoral, or other physiologic connections. Secondary effects may be contiguous or distant to the primary effects, may be focal or systemic in nature, and need not be considered as primarily deleterious.

In view of the discrete and consistent cellular effects of irradiation, as seen in the induction of lethal mutation in Drosophila (Lea, 1947), it is not improbable that the primary effects are very similar in a broad range of animal cells. If we assume this to be true, then it is logical to expect genetic differences in response to be of a secondary, and often systemic, nature. Thus, the individual's entire genotype can express its full potentialities in enhancing or inhibiting the expected general response pattern after total body x-irradiation.

Body Weight Response to Irradiation

The major factor studied in this investigation has been the alteration of the normal growth of mice, as measured by changes in body weight. A body weight loss is invariably seen in mammals after exposure to x-irradiation, but the degree of loss will vary with the species (Smith, W. W., *et al.*, 1952). Weight losses and growth inhibitions are not only seen after exposure to ionizing radiations, but also after exposure to ultra-violet rays (Blum, *et al.*, 1943).

The sensitivity of the weight response has rendered it an effective means of studying the protective value of glutathione in mice after exposure to x-ray (Chapman, *et al.*, 1950; Chapman and Cronkite, 1950). Furth, *et al.* (1952) also used the loss and regain of body weight in rats as one criterion to measure the effectiveness of several antibiotics in combating radiation sickness.

The severity and serious nature of losses in body weight after irradiation have also caused it to be the subject of special investigation into physiological causation. For example, Conard (1951) has examined the x-ray induced changes in intestinal motility of the rat, while Bennett, *et al.* (1951) have investigated the rate of protein absorption on the x-rayed mouse. Basal metabolism of the rat following x-ray has been investigated by Kirschner, Prosser, and Quastler (1949) and by Smith, D. E., *et al.* (1951) in an attempt to correlate basic metabolic alterations with observed weight change. Thus, body weight changes would seem a simple measurement of expression based upon a broad complex of physiologic mechanisms. If genetic differentials exist, they should be expressive in this response.

Organ Weight Response to Irradiation

Attempts to determine the effects of irradiation expressed as changes in organ weight have been sporadic. In 1946, Brues, Sacher, and France studied the organ weight changes in x-rayed rats after both single and chronic exposure. Most visceral organs appeared resistant to change, except those primarily composed of a known radio-sensitive tissue. The spleen, thymus, lymph nodes, and testes showed atrophic changes and a loss in weight after chronic irradiation. Moderate single dose exposure only caused a transient weight loss in the spleen (Brecher, et al., 1948; Ludewig and Chanutin, 1950; Carter, 1950; Cronkite, Brecher, and Chapman, 1951a) and in the testes (Eschenbrenner and Miller, 1950). The splenic weight loss occurred very rapidly, but recovery had set in by the tenth to fourteenth post-irradiation day, even in the lethal dose range. At twenty-days post-irradiation, all of the above authors noted that the spleen was near normal weight or showing some over-compensation, depending on the dosage used. Testes weight dropped off slowly and returned to normal after about 10 to 12 weeks in mice exposed to the mid-lethal dosage range. A time element is thus of prime importance in estimating weight changes in radio-sensitive organs.

The heart, kidneys, and liver are considered as resistant organs (Bloom, 1948; Ely, Ross, and Gay, 1947), but

Ellinger (1945) listed the liver as sensitive. Of these organs, the heart is probably the most resistant, as shown by histological study after local irradiation at doses up to 7500 roentgens in the rat (Leach and Sugiura, 1941, 1942).

The liver has been shown to resist direct weight change by Brecher, et al. (1948) in the mouse, but Ludewig and Chanutin (1950) demonstrated a minor weight increase four days after exposure in the rat. The weight was normal by the tenth day and beyond. A dosage near the LD_{50} level was used in these investigations.

The kidneys also are resistant to weight change following total body irradiation of the rat (Patt, et al., 1947). A 10 to 20 per cent drop in body weight may occur after exposure to 650r and 900r, but a similar drop in kidney weight resulted in its weight per unit of body weight to remain unaffected. This inanitional type of change in organ weight was brought out by Brues, et al. (1946) in chronically exposed rats. It was also pointed out in an investigation on rats given a single exposure by Bowers and Scott (1951). They noted that a depression in the weights of the visceral organs, that were otherwise considered as resistant to radiation, coincided with the post-irradiation period of anorexia. Azarnoff and Roofe (1951) have attempted to determine the degree to which organ changes after irradiation may be due to inanition in the rat. Visceral organ weight changes are apparently due to two factors; one, the direct and organ-specific indirect effects of the radiant energy, and, two, the sum total of the direct and indirect effects that bring about a loss of total body weight and an inanitional loss of organ weight.

The selection of the specific organs studied in this investigation, as well as the time or age factors involved, was largely determined by the conditions of a previous study (Grahn, 1950). In this earlier study, a detailed examination of organ and body weights was made on six inbred mouse strains at a fixed age of 60 days. Consequently, this age was chosen to obtain the organ weights for the investigation to be reported.

A twenty-day post-irradiation interval of growth was considered, on the basis of past findings in these mice, to be sufficient to permit genetic response differentials to become expressive. It was assumed that little change of major consequence would be apparent in the heart, kidneys, liver, and spleen weights, while testes weights would be depressed. Actually, the primary hope was to determine if subtle organ changes had occurred that had previously been overlooked. The earlier organ weight study by Grahn had demonstrated the use of biometrical analyses as a means of determining the less obvious organ and body weight variations.

MATERIALS AND METHODS

Biological

The mice used in this study have been taken from six inbred strains maintained at the Genetics Laboratory, Iowa State College. They all have been inbred, by brother-sister matings, for at least 25 generations.

Selection of the mice has been done in a random manner, with the exception that obviously abnormal or unthrifty animals were not included. All mice, at the outset of the experimental period, were 40 $\pm$ 3 days old. As age has been shown to be effective in varying the survival of mice after x-irradiation (Quastler, 1945), it becomes necessary to eliminate the age variable when studying genetic variation.

Body weights were taken at the ages of 40, 41, 42, 45, 50, 55, and 60 days. The 40-day weights are all pre-irradiation initial weights. The mice were irradiated within two hours after they were weighed. Between the times of weighing, the mice were kept in the general mouse stock environment, although they were set off in a semi-isolated group. Food and water were provided <u>ad libitum</u>. The body weights from 40 to 55 days of age, inclusive, are live weights. The 60-day weight was taken immediately after death. The mice were killed on the 60th day, by means of chloroform, after being fasted for 4-8 hours. This fasting interval was sufficient to cause the elimination of most of the gastric contents, as well as a large portion of the material in the small intestine. As described by Grahn (1950), this enhances the accuracy of organ:body weight relationships.

After the 60-day body weight was taken, the mice were dissected, and, in order, the testes, spleen, kidneys, liver, and heart were removed and placed in covered weighing dishes. These were then weighed in the order of removal.

All of the weighing was done on an analytical balance. Body weights were measured to the nearest tenth of a gram, organ weights to the nearest milligram.

The mice were checked for deaths at least once each day during the post-irradiation period. Necropsies were done on those animals that were not in advanced stages of post-mortem degeneration. Unfortunately, most of the deaths occurred between midnight and seven in the morning, so that little necropsy material was of any value. It is worth noting, however, that the usual time of death coincides with the period of greatest physical activity in the mouse.

When a mouse died prior to 60 days of age, the animal was replaced. Since every mouse had a litter-mate of the opposite sex which had been irradiated at the same time, the whole litter had to be replaced, in order to retain the litter-mate control. At the doses of 0, 20, 200, and 400r, deaths were either absent or negligible. At 800r, in strain L, the death rate of over 30 per cent undoubtedly created a biased picture of this strain. No significant mortality occurred in the other strains at 800r. It should be kept in mind that the results of this investigation are upon the mice that survived for twenty days after irradiation.

Physical

The dosage levels used were 0, 20, 200, 400, and 800 roentgens, as measured in air by means of a "Victoreen" dosimeter. The readings were made at a level equivalent to the central portion of the mouse's body.

For the irradiation, the mice were placed in a wooden frame, which enclosed a circular space, one inch deep and 6-1/2 inches in diameter. This was floored by a removable wire screening of 1/4 by 1/4 inch openings. Two layers of cellophane provided the top covering. Measurements of dosage were made over the screening to allow the back-scatter to be included in the dose rate. No more than 16 to 18 mice were irradiated at any one time in this frame.

The radiation factors were: 98 pKV, 2 ma., with no filtration except that inherent in the glass wall of the tube. The tube was an air-cooled Coolidge-type tube with a tungsten target. The distance from the target to the mouse was 36.5 centimeters. Dose-rate of the machine was 22.5 roentgens per 30 seconds. The exposure times for the various doses were; 20r: 27 seonds; 200r: 4 minutes, 27 seconds; 400r: 8 minutes, 54 seconds; 800r: 17 minutes, 48 seconds.

Statistical

A balanced experimental design has been utilized in order to best estimate the effectiveness of the several variables that are involved. The 600 mice in this experiment are equally distributed among the six strains, five radiation levels, and the two sexes. Each strain has 20 mice at each dosage level, these 20 animals being sampled from ten different litters. Two mice were taken from a litter, one male and one female. The litter-mates were irradiated at the same time and at the same dosage level. Care was taken to avoid irradiating more than one litter-pair of any one strain and dosage at the same time. In this way, the variation between litters, within a strain and dosage level, can be considered as random environmental variation.

The experimental design is essentially a factorial type. With six strains and five dosage or treatment levels, there are 30 strain by treatment cells which are the crux of the experiment. It is the variation among these that is due to differences in radiation response of the several strains. The general breakdown for the analysis is given in Table 1.

Included are the expectations of the estimated mean squares or the linear components of variation. These are composed of the different components of the total variation and are used as algebraic equivalents of the respective mean squares. The methods are described by Snedecor (1946).

Table 1. Breakdown for the Statistical Analysis

Source of variation	df	Components of variation
Between strains	5	E + 2L + 10FST + 20ST + 50FS + 100S
Between treatments	4	E + 2L + 10FST + 20ST + 60FT + 120T
Strain x treatment	20	E + 2L + 10FST + 20ST
Between litters, within strain and treatment	270	E + 2L
Between sexes	1	E + 10FST + 50FS + 60FT + 300F
Sex x strain	5	E + 10FST + 50FS
Sex x treatment	4	E + 10FST + 60FT
Sex x strain x treatment	20	E + 10FST
Sex x litter, within strain and treatment	270	E
	599	

The components can be interpreted as follows: S is the variation due to strain differences, T is due to the differences between the effects of the radiation levels, and F is the basic variation between sexes. The interaction terms are interpreted as arising from differential responses of either the strains or sexes from one dosage level to the next.

The component L, due to variation between litters, and the component E, due to a sex by litter interaction, are both considered attributable to uncontrollable environmental variation. The latter term, E, has its biological basis in the random variation of individual sex differences that exist between the litter-mates which have been treated alike. Butler (1952) has shown that such within-litter sex differences, in body weight, are positively correlated with the body weight of the male. That is, as the body weight increases, the sex difference will increase. The same effect is seen in these data. However, it if is assumed that the body weights are randomly distributed, then the individual within-litter sex differences are very likely randomly distributed as well.

The component, L, is due to various factors of the biological environment, such as litter size, lactation number, and age of dam. It also includes variation attributable to fluctuation in x-ray machine output, although this is probably not a major effect. Fluctuations in the physical environment, such as temperature, are also included.

All of these components can be expressed in terms of a percentage of total variation, such that, with a fixed scale, a measure of the relative importance of the different effects and interactions can be observed. The general mathematical model, upon which this component analysis is based, is as follows:

$$x_{ijkl} = u + s_i + t_j + (st)_{ij} + l_{ijk} + f_l + (fs)_{il} + (ft)_{jl} + (fst)_{ijl} + e_{ijkl},$$

where u = the overall mean,

i = 1,2,...6 - the strains,

j = 1,2,...5 - the treatments, or dosage levels,

k = 1,2,...10 - the litters per strain and dosage,

l = 1,2 - the sexes.

In all of the analyses, the method of covariance is used. For the body weights, the initial or 40-day weight is held as the independent variable. The 60-day body weight is the independent variate for analyzing the organ weights. Since all of the mean squares are adjusted to the estimated regressions involved, two terms are added to the above mathematical model:

$$y_{ijkl} = u + s_i + t_j + (st)_{ij} + \beta_1(x_{ijk}) + l_{ijk} + f_l + (fs)_{il} + (ft)_{jl} + (fst)_{ijl} + \beta_2(x_{ijkl}) + e_{ijkl}.$$

The β_1 is the regression derived from the between-litter source, while β_2 is from the sex by litter interaction. The mean squares for strain, treatment, and strain by treatment have been adjusted to the average between-litter regression, in order to eliminate variation due to the independent variable. The mean squares for the sex effect and all the interactions with sex have been adjusted to the average regression from the sex by litter term. The adjusted mean squares are used for estimating the components. The method of adjustment is given by Snedecor (1946).

Two major sets of correlations have been derived from these data in an effort to determine the effects of irradiation upon the integrating forces of the animal body. One set of correlations is obtained from the between-litter source and is an environmentally produced correlation. The other set is the between-strain or phenotypic correlation which measures the degree of co-existence of two characteristics as seen from one strain to the next. As only six strains are involved, the phenotypic correlations are very susceptible to sampling variation. The trends or shifts of such correlation from one dosage level to the next can be of value, however. Genetic correlations, obtained from the estimated strain components of variance and covariance, can also be determined, but they paralleled the phenotypic correlations so completely that it is felt that the method is basically inadequate. Phenotypic correlations can be expected to shift under the effects of irradiation, but similar shifts in the genetic correlations are not always logical.

Between-strain and between-litter inter-organ correlations are also presented. These are given as first-order partial correlations, wherein the variation in body weight has been removed. All partial correlations have been derived through use of Pearson's formula:

$$r_{12.3} = \frac{r_{12}-r_{13}r_{23}}{\sqrt{(1-r_{13}^2)(1-r_{23}^2)}}.$$

Standard errors for the means have been derived from the between-litter mean squares. For the standard errors of the sex means, the between-litter mean squares have been determined on a within-sex basis. Tests of significance are largely limited to "t" tests of the differences between control and treatment means. The method used is described by Wishart (1950).

As the data taken in this investigation involve growth in body weight, it has been found that a transformation of the observed values to their common logarithmic equivalents is justified. This tends to eliminate the metrical bias that exists where the mean and the variance are positively correlated. Invariably, the heavy strains will show greater variation among their individual observations. This feature implies that the weight differences are multiplicative and basically due to differences in rate of growth. The logarithmic transformation is consistent with this assumption and acts to create a more uniform range of variation.

The organ weight data has been similarly transformed, as in a previous study on these mice (Grahn, 1950). It was pointed out, then, that this permits the organ weight analysis to be considered as a study in relative growth, as outlined by Huxley (1932).

Additional features of the analysis will be brought up with the presentation of results, wherein specific details can be more clearly explained.

RESULTS OF INVESTIGATION

Body Weight

Before pointing out the major findings of interest, the statistical approach should be described. The results of an analysis of variance of the observed body weights indicated that very little of the variation in body weight could be attributed to the effects of the irradiation. Simple observation of the data does not bear this out. The crux of this problem lies in the small amount of sampling variation that exists among the five dosage means at 40 days of age. The mean initial weight for the 800r sample is 16.8 grams, while that for the control group is 16.0 grams. One day after exposure, the 800r mice have lost about 0.6 grams, while the controls have gained about 0.3 grams, yielding weights of 16.2 and 16.3 grams for the 800r and 0r groups, respectively. Obviously, the statistical result would indicate a greater effect of irradiation before the mice were even irradiated.

The above situation, however, points out that it is the amount of weight gain or loss that is the sensitive criterion of radiation effects. Two approaches can be made, each providing supplementary information to the other. In both analyses, the initial weight is held as the independent variable. If the dependent variable is the post-irradiation weight, then, with two exceptions, the results are identical to those attained by using the weight change from initial weight as the dependent variable.

The exceptions to this similarity are in the regressions and correlations derived from the analyses. The regressions and correlations of weight on weight are always positive, are initially high, and progressively decline toward zero with increasing age. The regressions and correlations of weight change on weight are negative, initially low, and progressively rise toward minus one with increasing age. The adjustment of the body weight to a constant initial weight can be determined directly from the regression of weight on weight. If the weight change is adjusted, then added to the constant initial weight, the results are the same as for the direct adjustment of the body weight.

At most age levels, the regressions within each dosage level are significantly different. As a result, the individual regressions for each dose and age level are used for adjustment of the body weight means, a procedure that succeeds in removing the sampling variation in the initial weights.

<u>Over-all radiation response</u>

Examination of the data in Table 2 and Figure 1 shows

Table 2. Over-all Body Weight Means; Adjusted to the 40-day Weight

Dose	Age days	Mean log	S.E.	Mean[1] grams	Weight change[2] grams	per cent
IW*	40	1.210	±.003	16.22		
0r	41	1.217	±.001	16.48	+0.26	+1.6
	42	1.223	±.002	16.71	+0.49	+3.0
	45	1.246	±.002	17.62	+1.40	+8.6
	50	1.276	±.002	18.88	+2.66	+16.4
	55	1.298	±.002	19.86	+3.64	+22.4
	60	1.302	±.002	20.04	+3.82	+23.6
20r	41	1.210	±.001	16.22	0.00	0.0
	42	1.217	±.002	16.48	+0.26	+ 1.6
	45	1.242	±.002	17.46	+1.24	+ 7.6
	50	1.274	±.002	18.79	+2.57	+15.8
	55	1.299	±.003	19.91	+3.69	+22.7
	60	1.302	±.003	20.04	+3.82	+23.6
200r	41	1.202	±.001	15.92	-0.30	- 1.8
	42	1.207	±.002	16.11	-0.11	- 0.7
	45	1.233	±.002	17.10	+0.88	+ 5.4
	50	1.263	±.003	18.32	+2.10	+12.9
	55	1.289	±.004	19.45	+3.23	+19.9
	60	1.293	±.004	19.63	+3.41	+21.0
400r	41	1.197	±.001	15.74	-0.48	- 3.0
	42	1.195	±.002	15.67	-0.55	- 3.4
	45	1.214	±.002	16.37	+0.15	+ 0.9
	50	1.253	±.002	17.91	+1.69	+10.4
	55	1.282	±.003	19.14	+2.92	+18.0
	60	1.289	±.003	19.45	+3.23	+19.9
800r	41	1.195	±.001	15.67	-0.55	- 3.4
	42	1.184	±.002	15.28	-0.94	- 5.8
	45	1.185	±.003	15.31	-0.91	- 5.6
	50	1.203	±.003	15.96	-0.26	- 1.6
	55	1.224	±.004	16.75	+0.53	+ 3.3
	60	1.242	±.004	17.46	+1.24	+ 7.6

[1]Antilog of mean logarithm in column 3.

[2]Measured from the 40-day weight, column 5.

*IW = pre-irradiation mean initial weight for all mice.

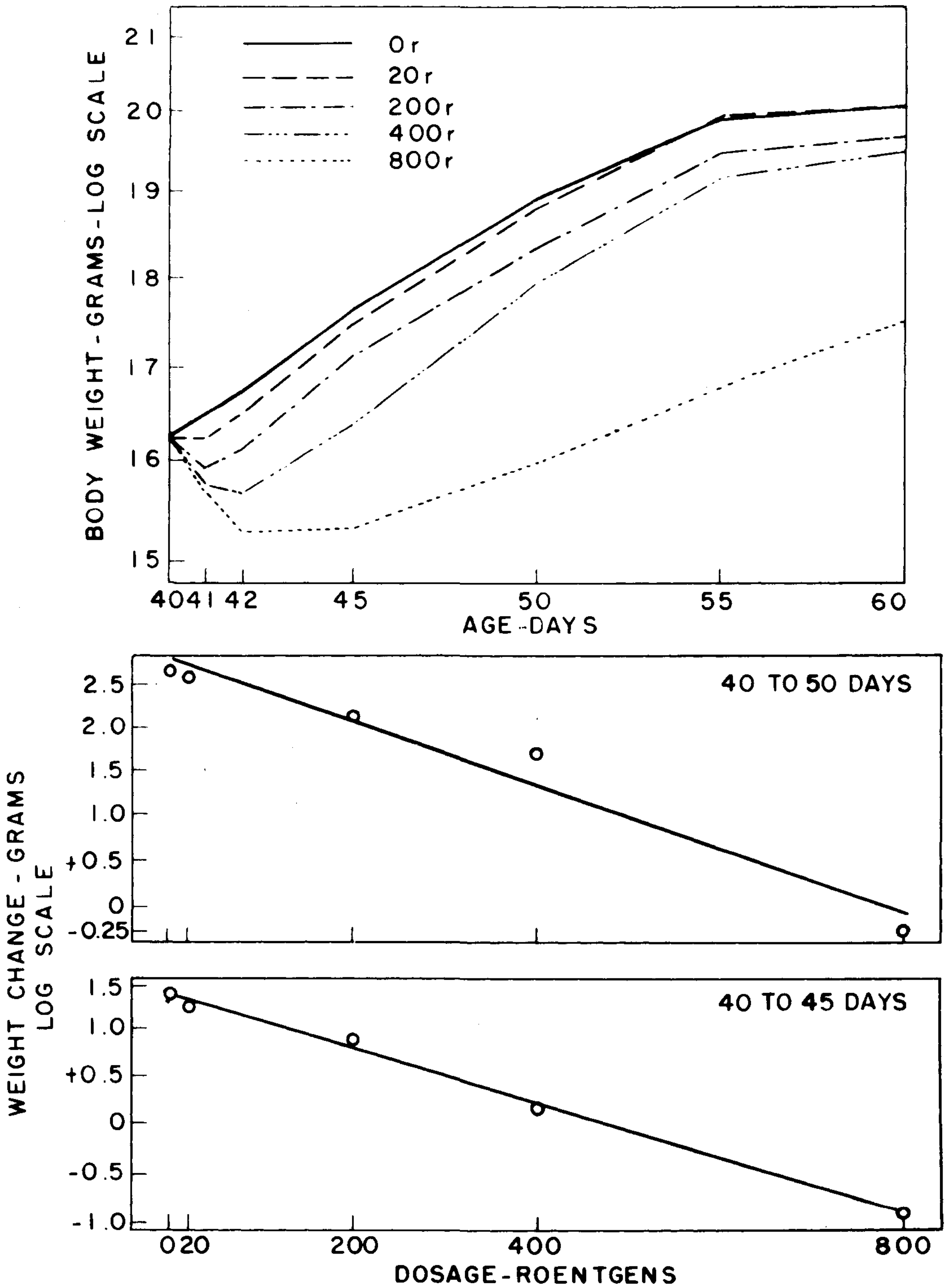

Figure 1. Over-all body weight means (upper); regression of weight change on dose (lower). All values adjusted to a constant 40-day weight.

that a definite body weight response exists, even at the lowest exposure level of 20r. A series of significance tests on the differences between the control and 20r means and the control and 200r means, at each of the age levels, are given in Table 3.

Table 3. Significance of the Differences Between Adjusted Body Weight Means; 0-20r, 0-200r.

Age days	Mean difference (log)	$S.E._{diff.}$	t	P level*
0-20r				
41	.0077	±.0018	4.18	<.0001
42	.0067	±.0025	2.64	.008
45	.0039	±.0028	1.36	.17
50	.0026	±.0037	0.72	.47
55	.0004	±.0043	0.10	.92
60	.0007	±.0045	0.15	.88
0-200r				
41	.0154	±.0018	8.36	<.0001
42	.0166	±.0025	6.52	<.0001
45	.0136	±.0028	4.79	<.0001
50	.0128	±.0037	3.47	.0006
55	.0096	±.0043	2.23	.026
60	.0090	±.0045	1.99	.047

*238 degrees of freedom.

For the first 48 hours after exposure, a dose of 20r can be expected to create a significant weight response in 40-day-old mice. Beyond that point, the differences are well within the limits of random deviation. The differences between the

Or and 200 r means are always significant.

The correlation between the adjusted means and the dosage of radiation is always high. The greatest degree of linearity of this relationship is seen at 45 and 50 days of age. When adjusted means are used, the correlations and regressions that are derived are the same for either body weight or weight change. The presentation is in terms of weight change, as this is a more sensitive measure without prior statistical adjustments. The use of unadjusted mean weight changes gives correlations that are not significantly different from those derived from adjusted values. The use of unadjusted body weights, however, because of sampling variation, may even yield positive correlations with dosage, when in actuality, the response is negatively correlated with dose to a nearly perfect degree.

Table 4. Regressions and Correlations of Weight Change with Dosage. Over-all Means.

Weight change interval days	Regression per roentgen	Correlation	P level*
40-41	-.0000246/mouse	-.870	.10-.05
40-42	-.0000463/mouse	-.969	.01-.001
40-45	-.0000764/mouse	-.998	<.001
40-50	-.0000886/mouse	-.982	.01-.001
40-55	-.0000905/mouse	-.961	.01-.001
40-60	-.0000718/mouse	-.956	.02-.01

*3 degrees of freedom.

The regressions of weight change on dosage and their accompanying correlations are presented in Table 4. These data will be discussed in more detail in a later section, since they will be used in an empirical procedure designed to determine the relative resistance levels of the six strains used in this study.

Radiation response by sex

A small difference in weight response of the two sexes exists. If the data for the males (Table 5 and Figure 2) is compared with that for the females (Table 6 and Figure 3), the females show a more complete recovery from weight loss. By the 15th day after exposure, there is little or no difference between the female body weights at the control, 20r, and 200r levels, while in the males, only the control and 20r mice have converged by the 15th day. Initially, the effect in the two sexes is nearly the same, but this similarity is gone by the fifth post-irradiation day.

If one looks at the actual weight changes given in Tables 5 and 6, the females consistently present a greater loss than the males in both absolute and relative terms. However, this apparent paradox is resolved by the fact that the females have a strikingly lower total gain at 60 days, 20 per cent of the initial weight as compared to 28 per cent in the males. This fact completely counterbalances the slightly greater

Table 5. Males - Body Weight Means; Adjusted to the 40-day Weight.

Dose	Age days	Mean log	S.E.	Mean[1] grams	Weight change[2] grams	per cent
IW*	40	1.234	±.004	17.14		
0r	41	1.242	±.002	17.46	+0.32	+ 1.9
	42	1.251	±.002	17.82	+0.68	+ 4.0
	45	1.278	±.002	18.97	+1.83	+10.7
	50	1.310	±.003	20.42	+3.28	+19.1
	55	1.334	±.003	21.58	+4.44	+25.9
	60	1.340	±.002	21.88	+4.74	+27.7
20r	41	1.236	±.002	17.22	+0.08	+ 0.5
	42	1.243	±.002	17.50	+0.36	+ 2.1
	45	1.272	±.002	18.71	+1.57	+ 9.2
	50	1.306	±.003	20.23	+3.09	+18.0
	55	1.334	±.004	21.58	+4.44	+25.9
	60	1.338	±.004	21.78	+4.64	+27.1
200r	41	1.228	±.002	16.90	-0.24	- 1.4
	42	1.232	±.002	17.06	-0.08	- 0.5
	45	1.260	±.002	18.20	+1.06	+ 6.2
	50	1.290	±.005	19.50	+2.36	+13.8
	55	1.317	±.006	20.75	+3.61	+21.1
	60	1.321	±.006	20.94	+3.80	+22.2
400r	41	1.222	±.002	16.67	-0.47	- 2.7
	42	1.222	±.002	16.67	-0.47	- 2.7
	45	1.243	±.003	17.50	+0.36	+ 2.1
	50	1.284	±.003	19.23	+2.09	+12.2
	55	1.314	±.003	20.61	+3.47	+20.2
	60	1.322	±.003	20.99	+3.85	+22.5
800r	41	1.221	±.002	16.63	-0.51	- 3.0
	42	1.210	±.002	16.22	-0.92	- 5.4
	45	1.211	±.003	16.26	-0.88	- 5.1
	50	1.231	±.004	17.02	-0.12	- 0.7
	55	1.251	±.004	17.82	+0.68	+ 4.0
	60	1.268	±.005	18.54	+1.40	+ 8.2

[1]Antilog of mean logarith - column 3.

[2]Measured from the 40-day weight - column 5.

*IW = pre-irradiation mean initial weight for all males.

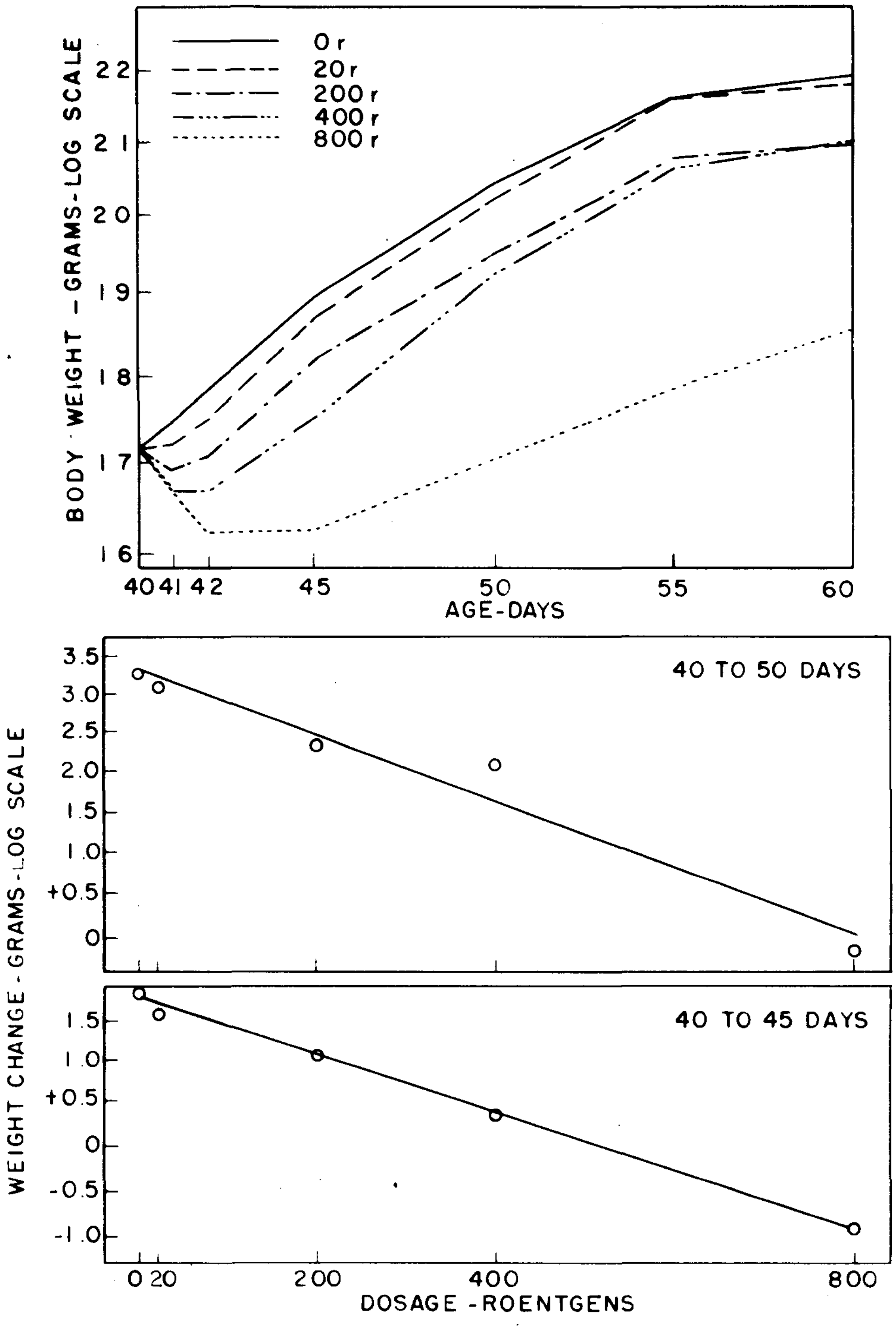

Figure 2. Male body weight means (upper); regression of weight change on dose (lower). All values adjusted to a constant 40-day weight.

Table 6. Females - Body Weight Means; Adjusted to the 40-day Weight.

Dose	Age days	Mean log	S.E.	Mean[1] grams	Weight change[2] grams	per cent
IW*	40	1.186	±.004	15.35		
0r	41	1.193	±.001	15.60	+0.25	+ 1.6
	42	1.196	±.002	15.70	+0.35	+ 2.3
	45	1.214	±.002	16.37	+1.02	+ 6.6
	50	1.242	±.003	17.46	+2.11	+13.7
	55	1.264	±.003	18.37	+3.02	+19.7
	60	1.265	±.003	18.41	+3.06	+19.9
20r	41	1.183	±.002	15.24	-0.11	- 0.7
	42	1.190	±.003	15.49	+0.14	+ 0.9
	45	1.212	±.002	16.29	+0.94	+ 6.1
	50	1.241	±.003	17.42	+2.07	+13.5
	55	1.264	±.003	18.37	+3.02	+19.7
	60	1.265	±.003	18.41	+3.06	+19.9
200r	41	1.176	±.002	15.00	-0.35	- 2.3
	42	1.182	±.002	15.21	-0.14	- 0.9
	45	1.206	±.003	16.07	+0.72	+ 4.7
	50	1.238	±.003	17.30	+1.95	+12.7
	55	1.263	±.003	18.32	+2.97	+19.3
	60	1.267	±.003	18.49	+3.14	+20.5
400r	41	1.172	±.001	14.86	-0.49	- 3.2
	42	1.168	±.002	14.72	-0.63	- 4.1
	45	1.186	±.002	15.35	0.00	0.0
	50	1.221	±.003	16.63	+1.28	+ 8.3
	55	1.249	±.003	17.74	+2.39	+15.6
	60	1.257	±.003	18.07	+2.72	+17.7
800r	41	1.169	±.002	14.76	-0.59	- 3.8
	42	1.159	±.002	14.42	-0.93	- 6.1
	45	1.159	±.003	14.42	-0.93	- 6.1
	50	1.177	±.004	15.03	-0.32	- 2.1
	55	1.197	±.005	15.74	+0.39	+ 2.5
	60	1.217	±.005	16.48	+1.13	+ 7.4

[1]Antilog of mean logarithm - column 3.

[2]Measured from the 40-day weight - column 5.

*IW = Pre-irradiation mean initial weight for all females.

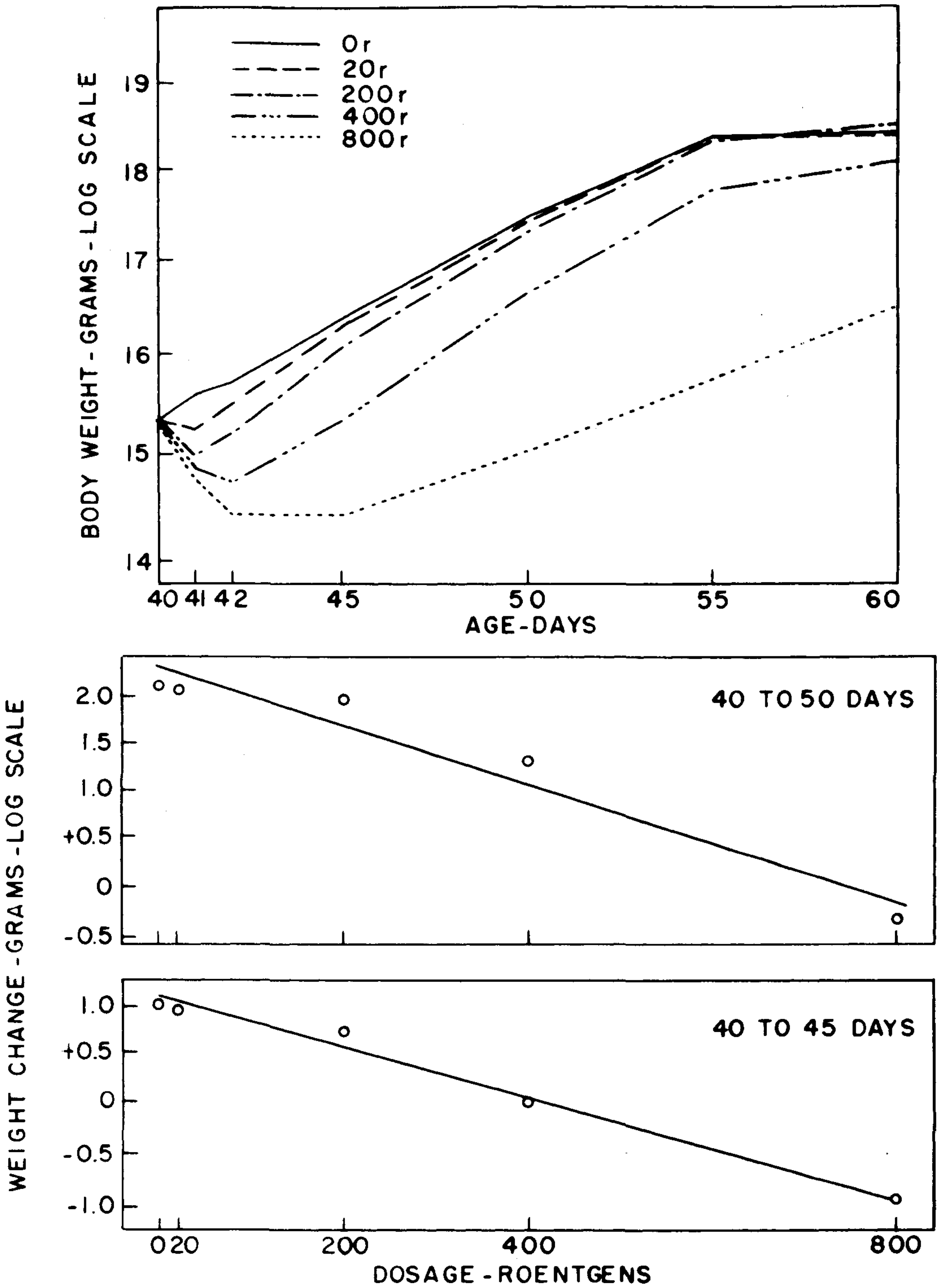

Figure 3. Female body weight means (upper); regression of weight change on dose (lower). All values adjusted to a constant 40-day weight.

losses sustained by the females, since these losses are less severe with respect to their normal weight. For example, ten days after exposure to 800r, the males are 3.40 grams below their controls, but the females are only 2.43 grams below their controls. In addition, by twenty days after exposure, the females are 1.13 grams over their starting weight as compared to 1.40 grams for the males; however, the latter are still 3.34 grams, or 70 per cent, below the normal gain, while the females are only 1.93 grams, or 63 per cent, below their normal gain.

Table 7. Regressions of Weight Change on Dosage by Sex

Weight change interval days	Regressions per r per mouse	
	Male	Female
40-41	-.0000242	-.0000246
40-42	-.0000478	-.0000444
40-45	-.0000819	-.0000701
40-50	-.0000948	-.0000815
40-55	-.0000992	-.0000820
40-60	-.0000852	-.0000593

The female regressions of weight change on dosage are, with one exception, lower than those of the males. A comparison of these regressions is given in Table 7.

Only at the first post-irradiation interval does the male show a lower regression than the female. The differences between the two regressions are never statistically significant, but the consistency of the difference would bolster the assumption that the female is slightly more resistant to weight change, at least, on a roentgen by roentgen basis. The importance of the expected normal gain in weight is demonstrated in this comparison, as it constitutes one of the points on the regression. Ignorance of the control gain could lead to the assumption that the male can more effectively resist the irradiation.

Radiation response by strain

Strain RI. This strain is characterized by its rather high resistance to weight change. As seen in Table 8 and Figure 4, only the 800r mice continue to show a depression below the normal at 60-days of age. In addition, a very definite and rapid recovery sets in at all doses by the second post-irradiation day at the latest.

Strain Z. The data in Table 9 and Figure 5 relate a comparatively more extended response, particularly at 800r. However, this strain also shows a rapid recovery, but in a different manner than strain RI. The latter strain has a consistent, progressive recovery at 800r, while the Z mice show a very sudden regain of weight loss between the tenth and fifteenth post-irradiation days.

Strain S. The S mice are another relatively resistant group of animals. This strain is more uniform in its response

Table 8. Strain RI - Body Weight Means; Adjusted to the 40-day Weight.

Dose	Age days	Mean log	S.E.	Mean[1] grams	Weight change[2] grams	per cent
IW*	40	1.299	±.010	19.91		
0r	41	1.307	±.002	20.28	+0.37	+ 1.9
	42	1.316	±.003	20.70	+0.79	+ 4.0
	45	1.336	±.005	21.68	+1.77	+ 8.9
	50	1.368	±.005	23.33	+3.42	+17.2
	55	1.385	±.005	24.27	+4.36	+21.9
	60	1.390	±.003	24.55	+4.64	+23.3
20r	41	1.298	±.003	19.86	-0.05	- 0.3
	42	1.304	±.003	20.14	+0.23	+ 1.2
	45	1.333	±.003	21.53	+1.62	+ 8.1
	50	1.365	±.004	23.17	+3.26	+16.4
	55	1.386	±.003	24.32	+4.41	+22.1
	60	1.397	±.004	24.95	+5.04	+25.3
200r	41	1.294	±.004	19.68	-0.23	- 1.2
	42	1.296	±.006	19.77	-0.14	- 0.7
	45	1.336	±.003	21.68	+1.77	+ 8.9
	50	1.358	±.004	22.80	+2.89	+14.5
	55	1.384	±.003	24.21	+4.30	+21.6
	60	1.396	±.005	24.89	+4.98	+25.0
400r	41	1.291	±.002	19.54	-0.37	- 1.9
	42	1.287	±.002	19.36	-0.55	- 2.8
	45	1.310	±.004	20.42	+0.51	+ 2.6
	50	1.351	±.004	22.44	+2.53	+12.7
	55	1.378	±.004	23.88	+3.97	+19.9
	60	1.383	±.004	24.15	+4.24	+21.3
800r	41	1.292	±.003	19.59	-0.32	- 1.6
	42	1.274	±.005	18.74	-1.17	- 5.9
	45	1.289	±.005	19.45	-0.46	- 2.3
	50	1.319	±.005	20.84	+0.93	+ 4.7
	55	1.346	±.007	22.18	+2.27	+11.4
	60	1.367	±.007	23.28	+3.37	+16.9

[1]Antilog of mean logarithm in column 3.

[2]Measured from the 40-day weight - column 5.

*IW = Pre-irradiation mean initial weight for all RI mice.

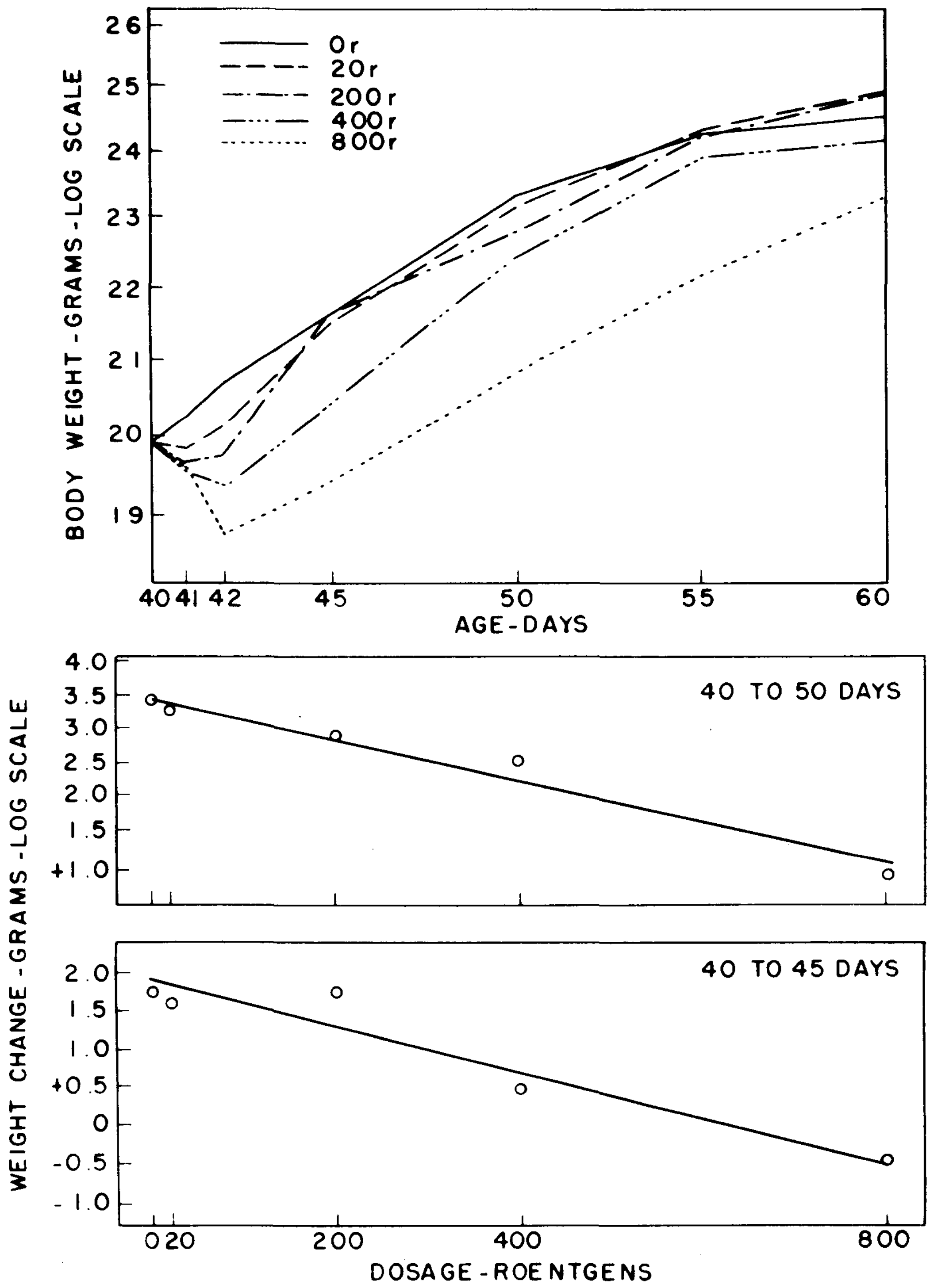

Figure 4. Strain RI body weight means (upper); regression of weight change on dose (lower). All values adjusted to a constant 40-day weight.

Table 9. Strain Z - Body Weight Means; Adjusted to the 40-day Weight.

Dose	Age days	Mean log	S.E.	Mean[1] grams	Weight grams	change[2] per cent
IW*	40	1.236	±.008	17.22		
0r	41	1.251	±.005	17.82	+0.60	+ 3.5
	42	1.254	±.005	17.95	+0.73	+ 4.2
	45	1.269	±.004	18.58	+1.36	+ 7.9
	50	1.296	±.006	19.77	+2.55	+14.8
	55	1.304	±.003	20.14	+2.92	+17.0
	60	1.308	±.005	20.32	+3.10	+18.0
20r	41	1.237	±.004	17.26	+0.04	+ 0.2
	42	1.242	±.005	17.46	+0.24	+ 1.4
	45	1.261	±.005	18.24	+1.02	+ 5.9
	50	1.294	±.005	19.68	+2.46	+14.3
	55	1.320	±.005	20.89	+3.67	+21.3
	60	1.320	±.005	20.89	+3.67	+21.3
200r	41	1.223	±.005	16.71	-0.51	- 3.0
	42	1.226	±.006	16.83	-0.39	- 2.3
	45	1.248	±.006	17.70	+0.48	+ 2.8
	50	1.285	±.009	19.28	+2.06	+12.0
	55	1.315	±.013	20.65	+3.43	+19.9
	60	1.308	±.013	20.32	+3.10	+18.0
400r	41	1.221	±.003	16.63	-0.59	- 3.4
	42	1.224	±.003	16.75	-0.47	- 2.7
	45	1.243	±.004	17.50	+0.28	+ 1.6
	50	1.273	±.003	18.75	+1.53	+ 8.9
	55	1.304	±.004	20.14	+2.92	+17.0
	60	1.310	±.004	20.42	+3.20	+18.6
800r	41	1.219	±.004	16.56	-0.66	- 3.8
	42	1.214	±.004	16.37	-0.85	- 4.9
	45	1.219	±.008	16.56	-0.66	- 3.8
	50	1.227	±.006	16.87	-0.35	- 2.0
	55	1.274	±.006	18.79	+1.57	+ 9.1
	60	1.292	±.005	19.59	+2.37	+13.8

[1]Antilog of mean logarithm in column 3.

[2]Measured from the 40-day weight - column 5.

*IW = Pre-irradiation mean initial weight for all Z mice.

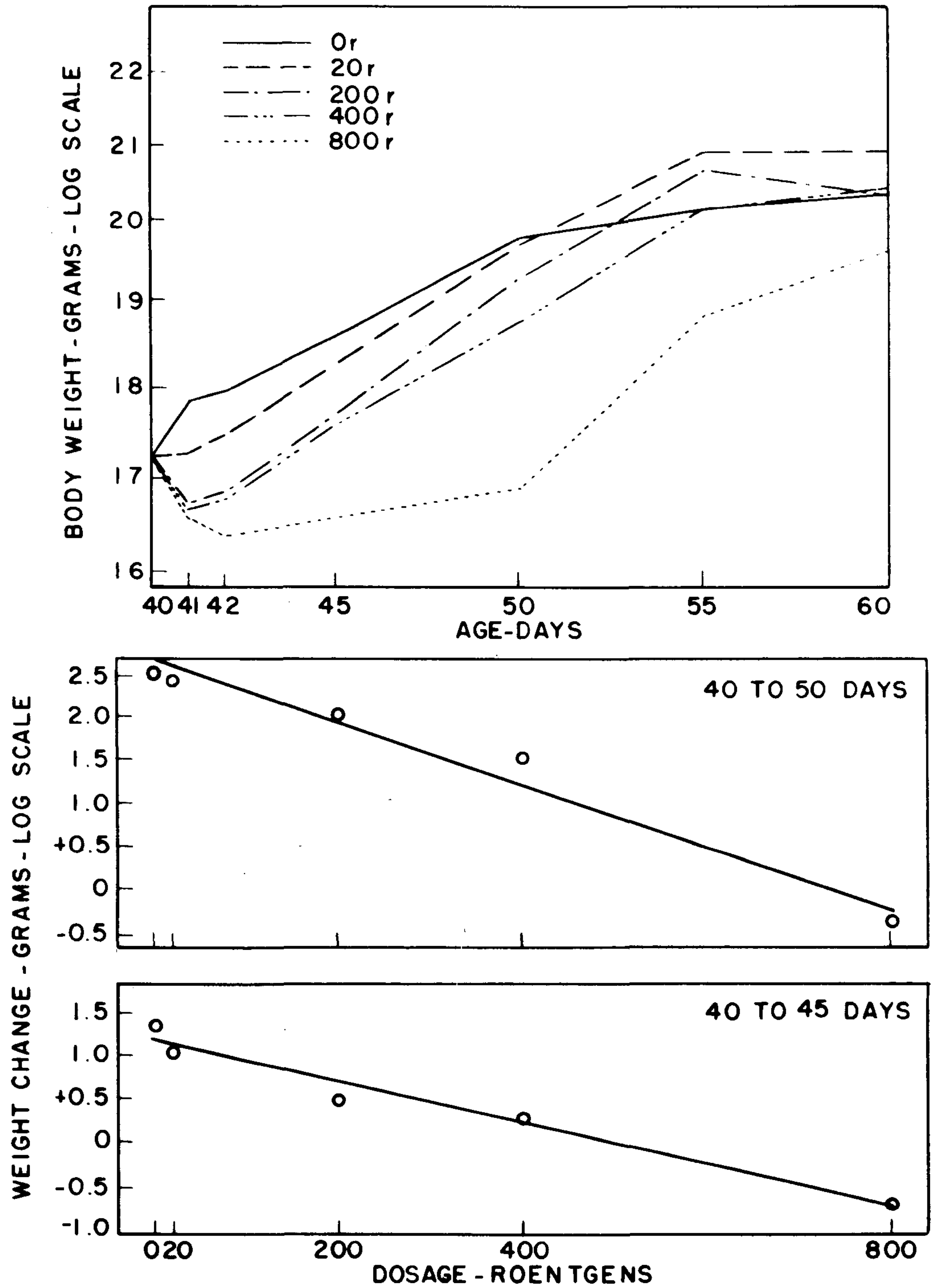

Figure 5. Strain Z body weight means (upper); regression of weight change on dose (lower). All values adjusted to a constant 40-day weight.

(Table 10 and Figure 6). However, by the tenth day after exposure, the only mice showing a continued reaction are those at 800r. Here, as in strain RI, the recovery is progressive and steady. In all three of these strains (RI, Z, and S), body weight recovery has set in by the second day after exposure, at the latest. By 60 days of age, at 800r, the Z mice are only 24 per cent below the control gain, the RI mice are 27 per cent below, and the S mice 36 per cent below the control. An equivalence of gain at 800r in the S and Z mice, 2.4 grams, is a more favorable quantity in strain Z which has the smaller normal rate of gain.

Strain E. Table 11 and Figure 7 present the data on strain E. A somewhat more severe response is indicated. At all exposure levels, the mice remain depressed below the normal. Recovery in the 800r mice is delayed until the 45th day of age. These mice show a maximum loss at 800r that is similar to strain S; however, a difference in the rate of loss exists. The S mice lose 0.67 grams in two days, while the E mice lose 0.72 grams over the first five days.

Strain E, in addition, shows the greatest proportionate normal weight gain, 31 per cent of the initial weight by 60 days of age. Even though the RI mice have a higher absolute gain, 4.64 grams to the 4.16 grams in the E mice, it only constitutes a gain of 23 per cent of their initial weight.

Strain L. This strain is decidedly more susceptible to a weight loss following x-irradiation. Table 12 and Figure 8

Table 10. Strain S - Body Weight Means; Adjusted to the 40-day Weight.

Dose	Age days	Mean log	S.E.	Mean[1] grams	Weight change[2] grams	per cent
IW*	40	1.194	±.009	15.63		
0r	41	1.196	±.005	15.70	+0.07	+ 0.4
	42	1.207	±.010	16.11	+0.48	+ 3.1
	45	1.235	±.007	17.18	+1.55	+ 9.9
	50	1.262	±.007	18.28	+2.65	+17.0
	55	1.286	±.007	19.32	+3.69	+23.6
	60	1.287	±.009	19.36	+3.73	+23.9
20r	41	1.195	±.002	15.67	+0.04	+ 0.3
	42	1.202	±.006	15.92	+0.29	+ 1.9
	45	1.232	±.003	17.06	+1.43	+ 9.1
	50	1.262	±.003	18.28	+2.65	+17.0
	55	1.292	±.003	19.59	+3.96	+25.3
	60	1.290	±.007	19.50	+3.87	+24.8
200r	41	1.189	±.004	15.45	-0.18	- 1.2
	42	1.192	±.005	15.56	-0.07	- 0.4
	45	1.222	±.007	16.67	+1.04	+ 6.7
	50	1.264	±.006	18.37	+2.74	+17.5
	55	1.289	±.006	19.45	+3.82	+24.4
	60	1.290	±.006	19.50	+3.87	+24.8
400r	41	1.187	±.004	15.38	-0.25	- 1.6
	42	1.188	±.005	15.42	-0.21	- 1.3
	45	1.209	±.006	16.18	+0.55	+ 3.5
	50	1.255	±.003	17.99	+2.36	+15.1
	55	1.286	±.003	19.32	+3.69	+23.6
	60	1.291	±.003	19.54	+3.91	+25.0
800r	41	1.181	±.004	15.17	-0.46	- 2.9
	42	1.175	±.005	14.96	-0.67	- 4.3
	45	1.183	±.004	15.24	-0.39	- 2.5
	50	1.209	±.004	16.18	+0.55	+ 3.5
	55	1.236	±.004	17.22	+1.59	+10.2
	60	1.256	±.004	18.03	+2.40	+15.4

[1]Antilog of mean logarithm in column 3.

[2]Measured from 40-day weight - column 5.

*IW = Pre-irradiation mean initial weight for all S mice.

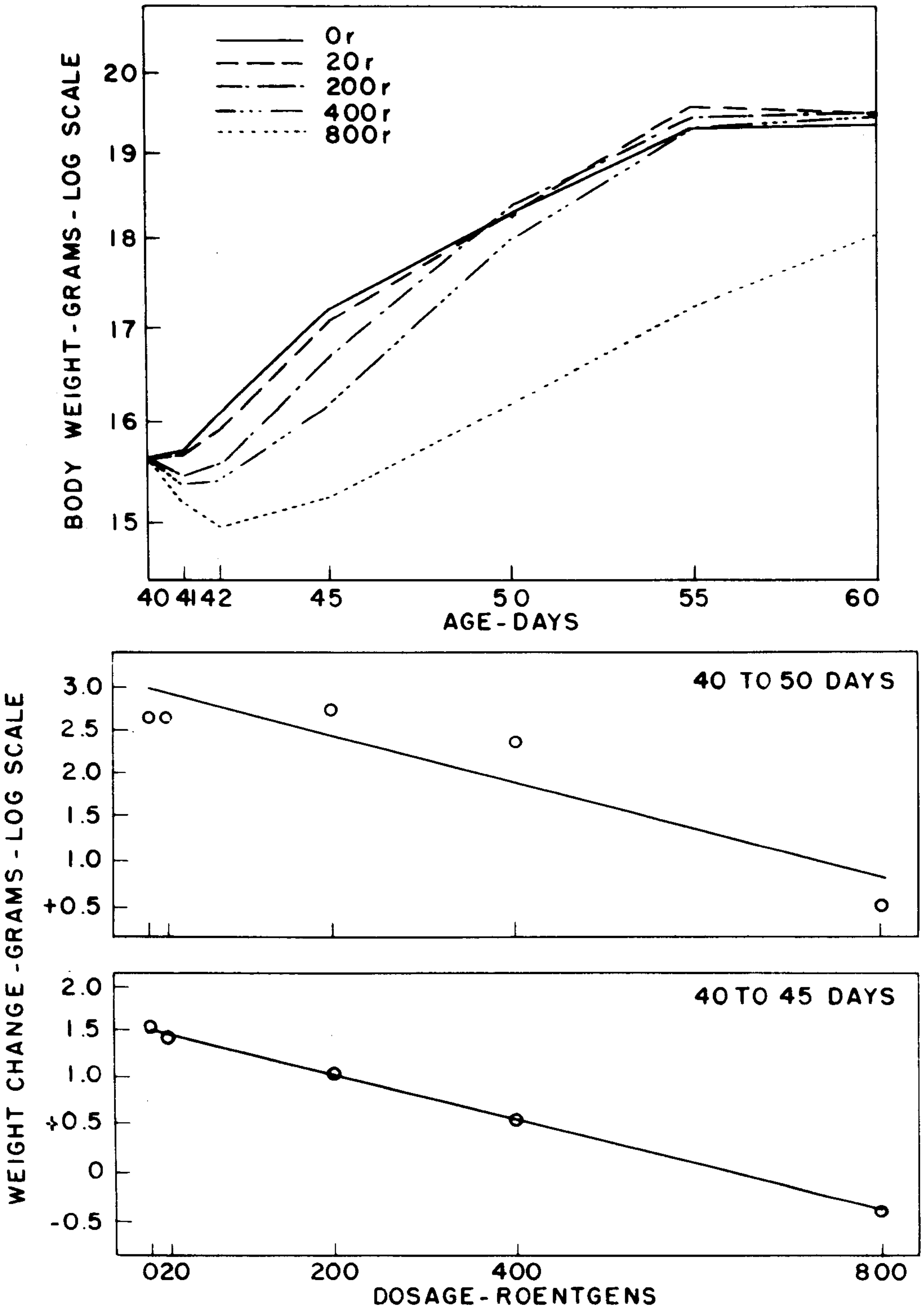

Figure 6. Strain S body weight means (upper); regression of weight change on dose (lower). All values adjusted to a constant 40-day weight.

Table 11. Strain E - Body Weight Means; Adjusted to the 40-day Weight.

Dose	Age days	Mean log	S.E.	Mean[1] grams	Weight change[2] grams	per cent
IW*	40	1.125	±.009	13.34		
0r	41	1.131	±.004	13.52	+0.18	+ 1.3
	42	1.137	±.005	13.71	+0.37	+ 2.8
	45	1.168	±.006	14.72	+1.38	+10.3
	50	1.197	±.006	15.74	+2.40	+18.0
	55	1.228	±.007	16.90	+3.56	+26.7
	60	1.243	±.006	17.50	+4.16	+31.2
20r	41	1.124	±.004	13.30	-0.04	- 0.3
	42	1.133	±.005	13.58	+0.24	+ 1.8
	45	1.163	±.006	14.55	+1.21	+ 9.1
	50	1.199	±.008	15.81	+2.47	+18.5
	55	1.225	±.010	16.79	+3.45	+25.9
	60	1.230	±.009	16.98	+3.64	+27.3
200r	41	1.123	±.003	13.27	-0.07	- 0.5
	42	1.130	±.002	13.49	+0.15	+ 1.1
	45	1.158	±.006	14.39	+1.05	+ 7.9
	50	1.191	±.007	15.52	+2.18	+16.3
	55	1.223	±.007	16.71	+3.37	+25.3
	60	1.232	±.007	17.06	+3.72	+27.9
400r	41	1.113	±.004	12.97	-0.37	- 2.8
	42	1.110	±.004	12.88	-0.46	- 3.4
	45	1.129	±.007	13.46	+0.12	+ 0.9
	50	1.172	±.008	14.86	+1.52	+11.4
	55	1.209	±.009	16.18	+2.84	+21.3
	60	1.219	±.009	16.56	+3.22	+24.1
800r	41	1.109	±.003	12.85	-0.49	- 3.7
	42	1.104	±.005	12.71	-0.63	- 4.7
	45	1.101	±.007	12.62	-0.72	- 5.4
	50	1.134	±.008	13.61	+0.27	+ 2.0
	55	1.167	±.011	14.69	+1.35	+10.1
	60	1.177	±.012	15.03	+1.69	+12.7

[1]Antilog of mean logarithm in column 3.

[2]Measured from the 40-day weight - column 5.

*IW = Pre-irradiation mean initial weight for all E mice.

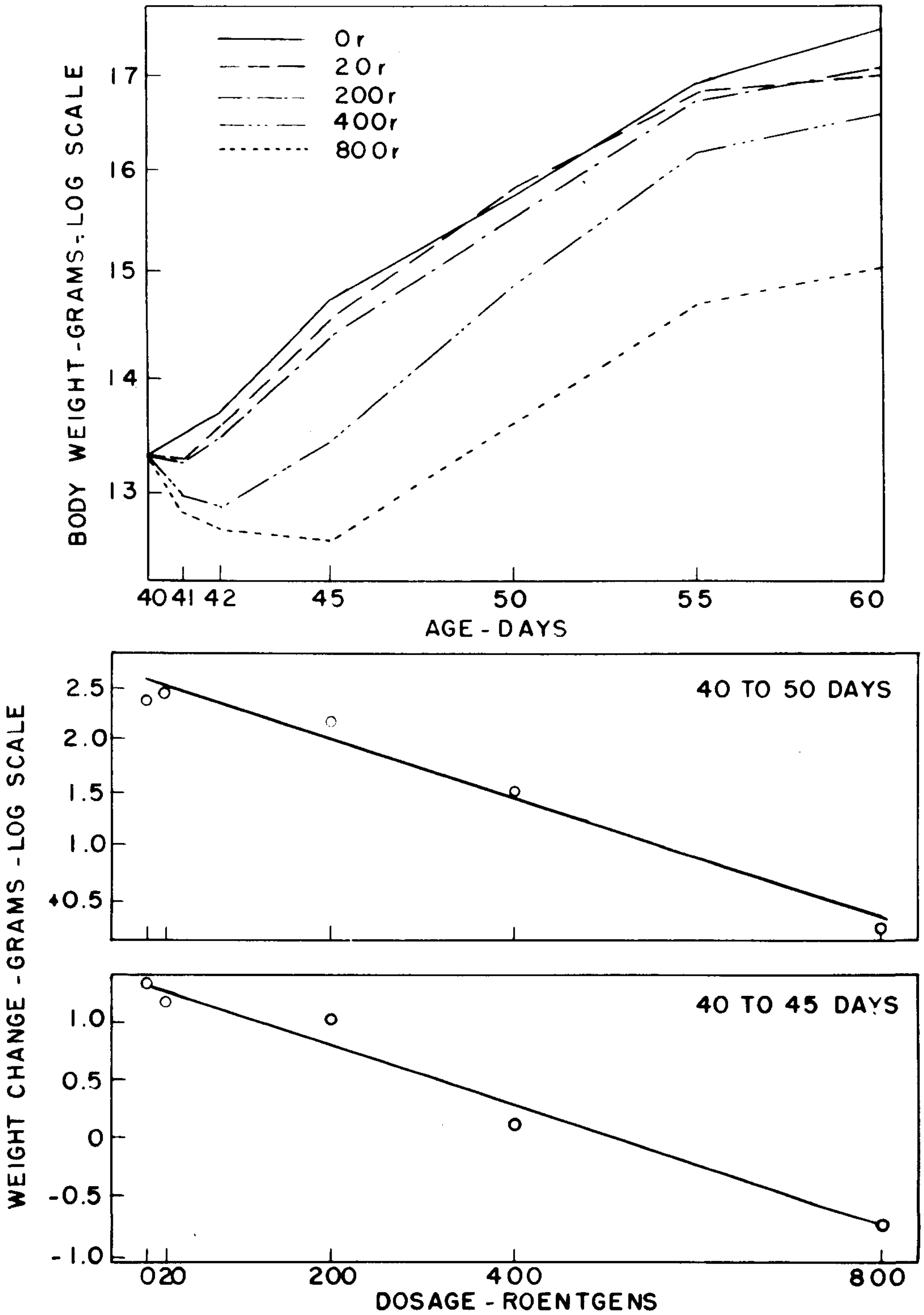

Figure 7. Strain E body weight means (upper); regression of weight change on dose (lower). All values adjusted to a constant 40-day weight.

Table 12. Strain L - Body Weight Means; Adjusted to the 40-day Weight.

Dose	Age days	Mean log	S.E.	Mean[1] grams	Weight change[2] grams	per cent
IW*	40	1.191	±.007	15.52		
0r	41	1.195	±.002	15.67	+0.15	+ 1.0
	42	1.196	±.002	15.70	+0.18	+ 1.2
	45	1.220	±.002	16.60	+1.08	+ 7.0
	50	1.255	±.004	17.99	+2.47	+15.9
	55	1.277	±.004	18.92	+3.40	+21.9
	60	1.279	±.006	19.01	+3.49	+22.5
20r	41	1.192	±.004	15.56	+0.04	+ 0.3
	42	1.204	±.004	16.00	+0.48	+ 3.1
	45	1.225	±.005	16.79	+1.27	+ 8.2
	50	1.256	±.004	18.03	+2.51	+16.2
	55	1.283	±.005	19.19	+3.67	+23.6
	60	1.283	±.004	19.19	+3.67	+23.6
200r	41	1.181	±.004	15.17	-0.35	- 2.3
	42	1.187	±.005	15.38	-0.14	- 0.9
	45	1.208	±.007	16.14	+0.62	+ 4.0
	50	1.235	±.013	17.18	+1.66	+10.7
	55	1.258	±.012	18.11	+2.59	+16.7
	60	1.263	±.013	18.32	+2.80	+18.0
400r	41	1.175	±.004	14.96	-0.56	- 3.6
	42	1.172	±.002	14.86	-0.66	- 4.3
	45	1.191	±.004	15.52	0.00	0.0
	50	1.230	±.007	16.98	+1.46	+ 9.4
	55	1.254	±.009	17.95	+2.43	+15.7
	60	1.271	±.010	18.66	+3.14	+20.2
800r	41	1.169	±.004	14.76	-0.76	- 4.9
	42	1.158	±.004	14.39	-1.13	- 7.3
	45	1.160	±.007	14.45	-1.07	- 6.9
	50	1.177	±.003	15.03	-0.49	- 3.2
	55	1.187	±.015	15.38	-0.14	- 0.9
	60	1.205	±.012	16.03	+0.51	+ 3.3

[1]Antilog of mean logarithm in column 3.

[2]Measured from the 40-day weight - column 5.

*IW = Pre-irradiation mean initial weight for all L mice.

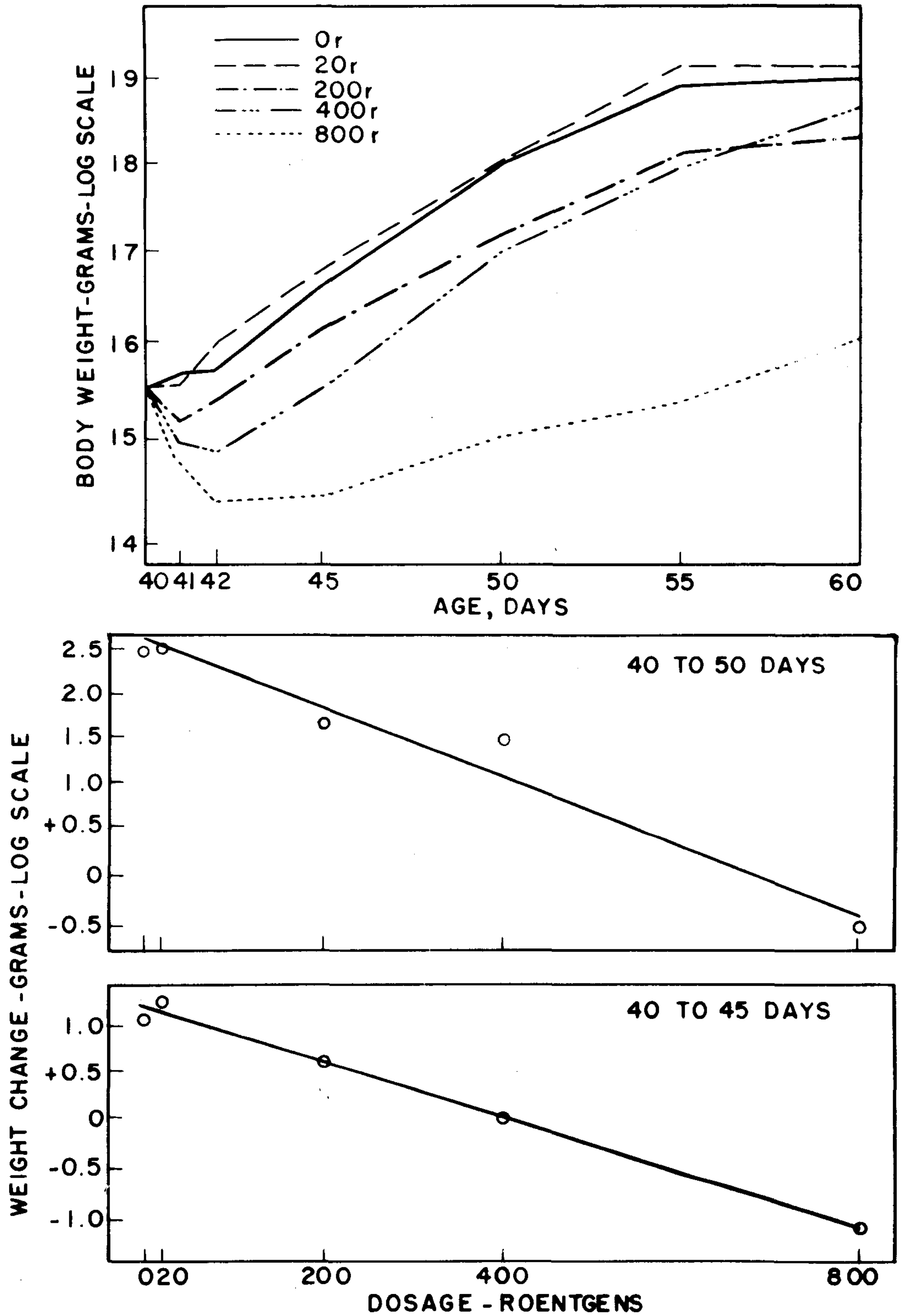

Figure 3. Strain L body weight means (upper); regression of weight change on dose (lower). All values adjusted to a constant 40-day weight.

indicate that, excepting the 20r group, the 200r, 400r and 800r mice are considerably depressed in their growth. Recovery sets in, even at 800r, as early as 42 days of age, but the rate of regain is very slow. Thus, by 60 days of age, the 800r mice are only 0.51 grams above the initial weight. This constitutes an 85 per cent depression from the normal gain of the controls. Comparatively, the E strain, at 800r, is 59 per cent below the expected normal gain.

Since the L mice have a considerably lower control rate of gain, they are not as severely affected as are the E mice at the lower doses. At 400r, 60 days of age, this is clearly brought out. The L mice have attained 90 per cent of their expected normal gain, while the E mice have only gained 77 per cent of their normal. Both strains have an absolute gain of about 3.2 grams at this dose and age level. The greater susceptibility of the L strain lies in the 800r response, not only through greater absolute and relative losses, but also because of a slower rate of recovery.

Strain Ba. These mice are unquestionably the most susceptible to weight loss. At all exposure levels, they are consistently retarded in their growth (Table 13 and Figure 9). The most striking difference from the other strains lies in the 800r level. The Ba mice continue to lose weight through the first 15 days after exposure, as compared to the usual two days in the other strains. Even though recovery sets in between the 55th and 60th days of age, they still

Table 13. Strain Ba - Body Weight Means; Adjusted to the 40-day Weight.

Dose	Age days	Mean log	S.E.	Mean[1] grams	Weight change[2] grams	per cent
IW*	40	1.214	±.007	16.37		
0r	41	1.221	±.002	16.63	+0.26	+ 1.6
	42	1.231	±.003	17.02	+0.65	+ 4.0
	45	1.251	±.003	17.82	+1.45	+ 8.9
	50	1.280	±.005	19.05	+2.68	+16.4
	55	1.303	±.005	20.09	+3.72	+22.7
	60	1.300	±.005	19.95	+3.58	+21.9
20r	41	1.212	±.002	16.29	-0.08	- 0.5
	42	1.214	±.006	16.37	0.00	0.0
	45	1.238	±.007	17.30	+0.93	+ 5.7
	50	1.265	±.008	18.41	+2.04	+12.5
	55	1.286	±.010	19.32	+2.95	+18.0
	60	1.289	±.011	19.45	+3.08	+18.8
200r	41	1.200	±.002	15.85	-0.52	- 3.2
	42	1.203	±.003	15.96	-0.41	- 2.5
	45	1.226	±.004	16.83	+0.46	+ 2.8
	50	1.258	±.005	18.11	+1.74	+10.6
	55	1.283	±.008	19.19	+2.82	+17.2
	60	1.291	±.008	19.54	+3.17	+19.4
400r	41	1.199	±.003	15.81	-0.56	- 3.4
	42	1.198	±.005	15.78	-0.59	- 3.6
	45	1.206	±.008	16.07	-0.30	- 1.8
	50	1.243	±.005	17.50	+1.13	+ 6.9
	55	1.266	±.006	18.45	+2.08	+12.7
	60	1.272	±.007	18.71	+2.34	+14.3
800r	41	1.190	±.002	15.49	-0.88	- 5.4
	42	1.174	±.003	14.93	-1.44	- 8.8
	45	1.148	±.008	14.06	-2.31	-14.1
	50	1.138	±.010	13.74	-2.63	-16.1
	55	1.119	±.012	13.15	-3.22	-19.7
	60	1.152	±.015	14.19	-2.18	-13.3

[1]Antilog of mean logarithm in column 3.

[2]Measured from the 40-day weight - column 5.

*IW = Pre-irradiation mean initial weight for all Ba mice.

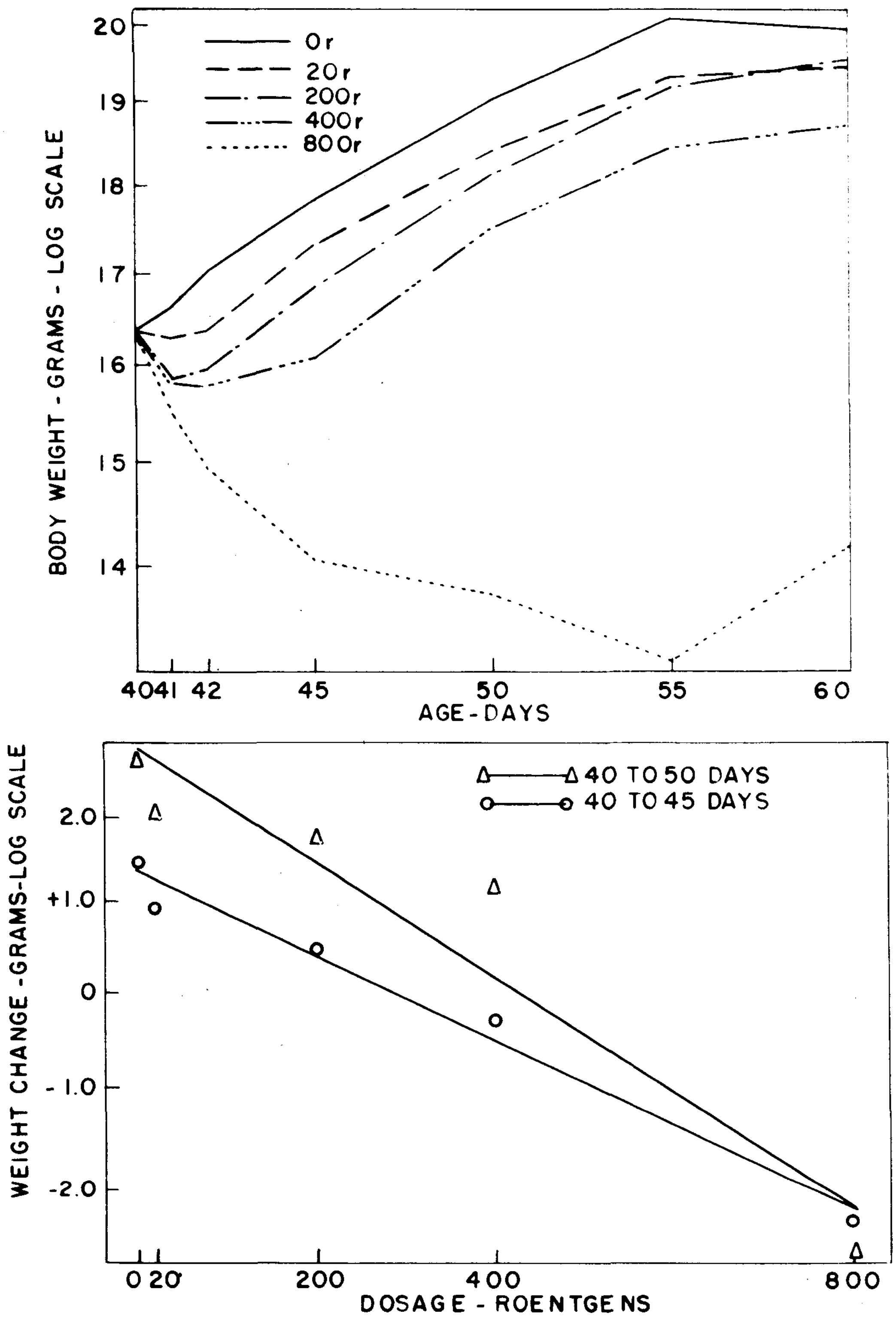

Figure 9. Strain Ba body weight means (upper); regression of weight change on dose (lower). All values adjusted to a constant 40-day weight.

show a weight loss of over two grams, or 13.3 per cent of the initial weight. At the maximum loss, nearly a 20 per cent reduction in the starting weight occurs. With respect to their control gain at 60-days, the 800r mice are 161 per cent below their expected weight gain. Comparatively, the different strains at 800r and 60 days of age show the following depressions below their expected gains; Z: 24 per cent; RI: 27 per cent; S: 36 per cent; E: 59 per cent; L: 85 per cent; Ba: 161 per cent.

Although strain differences in response appear to be most expressive at the 800r dosage level, direct comparison of a susceptible and a resistant strain points out that a genetic difference in raio-sensitivity can even exist at 20r.

Figure 10 graphically emphasizes the importance of the individual's genotype in investigating radiation response, at least with respect to body weight. The two strains compared, Ba and S, show many outward similarities. At 40 days of age, they differ by only about 0.8 grams of body weight, strain Ba being the heavier. The Ba mice gain 3.58 grams over the 20-day period, or 21.9 per cent of their initial weight. Strain S gains 3.73 grams, or 23.9 per cent of the initial weight. Consequently, the control growth curves are nearly parallel, with the Ba mice maintaining their weight superiority. The curves only include data up to the 55th day of age, as this range covers all the estimates of live weights.

At 20r, the more susceptible Ba mice are depressed in

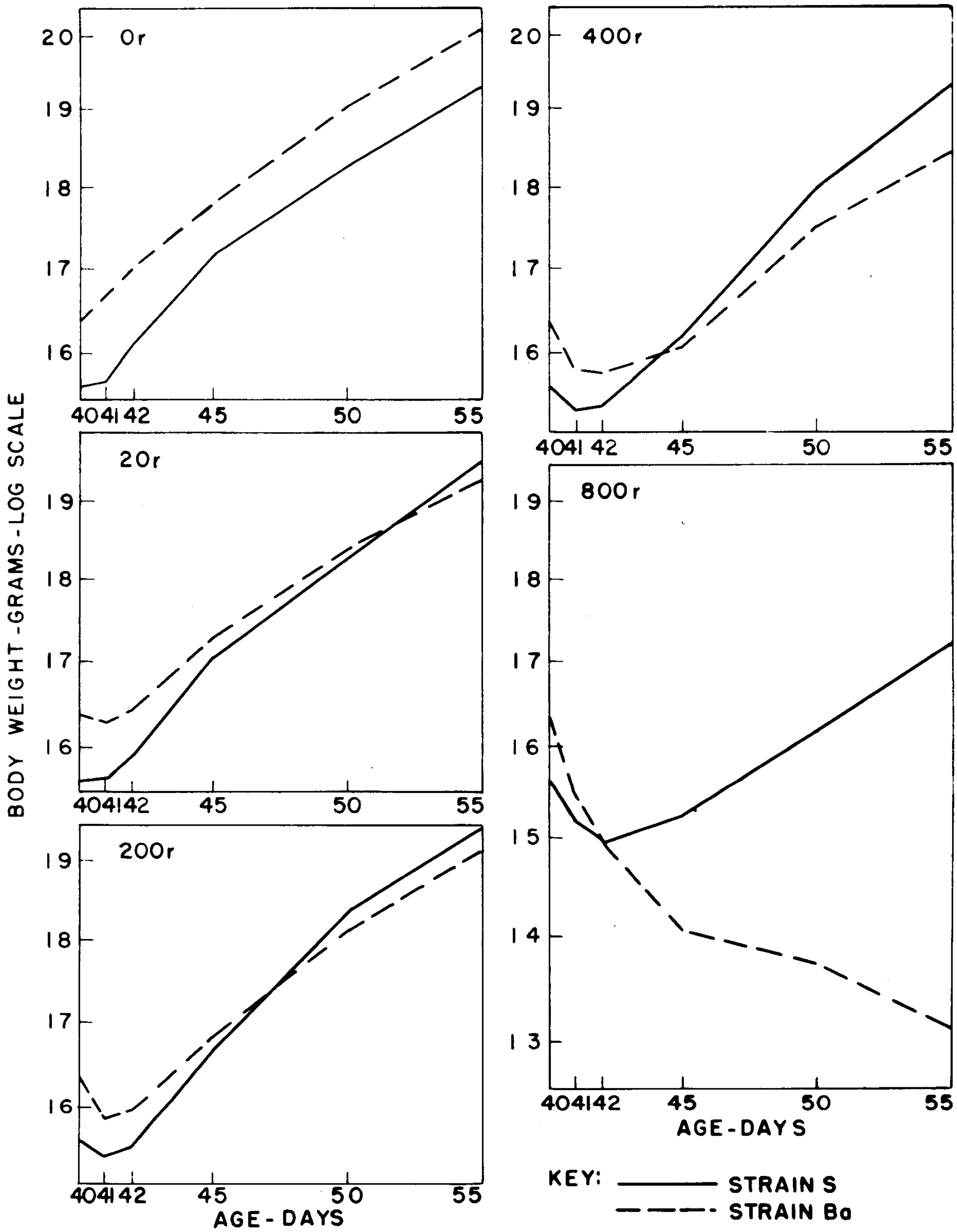

Figure 10. Growth in body weight of resistant (S) and susceptible (Ba) strains of mice.

their growth so that by 55 days of age they have become lighter than the S mice. This differential growth inhibition becomes more completely expressed at 200r and 400r. At 800r, the difference is extreme. The point where the Ba curve drops below the S curve appears progressively sooner after exposure with increasing dosage. As these data indicate, body weight and normal weight gain, alone, could be disastrous criteria for assuming any extensive amount of genetic similarity.

Table 14. Significance of the 0-20r Body Weight Differences in Strains Ba and S.

Age days	Strain	Mean weight difference log	$S.E._{diff.}$	t	P level*
41	S	.0022	±.0046	0.48	.70-.60
	Ba	.0094	±.0031	3.07	.01-.001
42	S	.0016	±.0091	0.17	.90-.80
	Ba	.0178	±.0067	2.64	.02-.01

*38 degrees of freedom.

The genetic dissimilarity of these two strains can be further substantiated by the significance of the weight response at 20r when compared to the controls. This is summarized in Table 14. The data clearly indicate that the mean weight differences are highly significant in the case of the susceptible Ba strain, but that the 20r response is within the limits of sampling variation in the resistant S mice.

On this basis, the minimum level at which radiation effects may be observed will depend upon the genetic constitution of the materials studied.

Quantitation of body weight response to irradiation

The amount of variation in weight change that is due to these genetic differences can be given a quantitative expression. As previously described, the estimated components of variance can be utilized to express the amount of variation in weight response attributable to the various effects and interactions. The derived values for the components must be considered as somewhat tentative due to the known heterogeneity of the within-dosage regressions that enter into the estimates. Similarly, a heterogeneity of variance between the dosage levels and between the strains is recognized but put aside in an effort to provide the best available estimates of the different components.

The results of the component analysis are presented in Table 15 and Figure 11. These data substantiate the indicated strain differences in radiation response, as depicted by the strain by treatment (ST) component. A maximum occurs 15 days after exposure, when 17 per cent of the total variation is attributable to these genetic differences in response.

The over-all weight response to the radiation is maximum five days after exposure, rising rapidly to a peak of 43 per cent. A progressive decline then is established. Strain

Table 15. Breakdown of Variation in Weight Change into the Components; Absolute Variance and Percentage of Total Variation

Component of variation		Weight change interval - days					
		40-41	40-42	40-45	40-50	40-55	40-60
Strain effect	S	.0000184	.0000159	.0001078	.0002411	.0003738	.0005306
	%	6.2	2.8	8.2	11.5	12.8	19.3
Treatment effect	T	.0000827	.0002358	.0005641	.0007638	.0008074	.0004773
	%	27.7	42.1	43.0	36.4	27.7	17.4
Strain x treatment effect	ST	.0000048	.0000117	.0000790	.0001933	.0004978	.0003745
	%	1.6	2.1	6.0	9.2	17.0	13.6
Between litter effect	L	.0000440	.0000880	.0001745	.0001765	.0002055	.0002890
	%	14.7	15.7	13.3	8.4	7.0	10.5
Sex effect	F	.0000240	.0000361	.0001101	.0002060	.0002875	.0003330
	%	8.0	6.5	8.4	9.8	9.8	12.1
Sex x strain effect	FS	.0	.0	.0000083	.0000071	.0000020	.0000183
	%	0	0	0.6	0.3	0.1	0.7
Sex x treatment effect	FT	.0	.0	.0000079	.0000206	.0000220	.0000404
	%	0	0	0.6	1.0	0.8	1.5
Sex x strain x treatment	FST	.0	.0000004	.0	.0	.0	.0
	%	0	0.1	0	0	0	0
Sex x litter effect	E	.0001250	.0001720	.0002610	.0004900	.0007240	.0006830
	%	41.8	30.7	19.9	23.4	24.8	24.9
Total variation		.0002989	.0005599	.0013127	.0020984	.0029200	.0027461

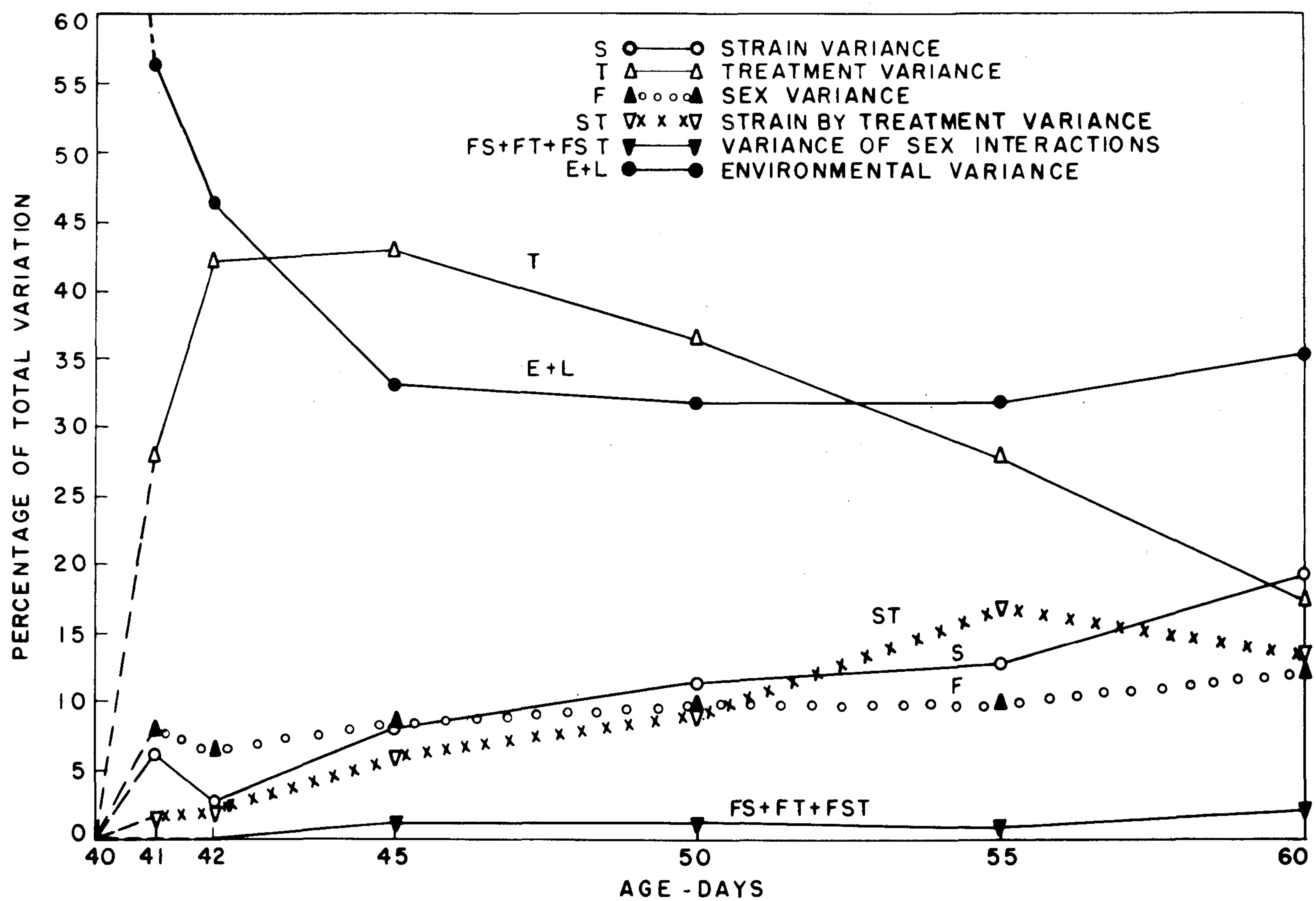

Figure 11. Breakdown of variation in weight change from the 40-day weight to each subsequent age level. Components expressed as a percentage of total variation.

differences in weight change progressively increase throughout the 20-day period. The sex difference in gain is also progressively increasing to its final value of 12 per cent as compared to 19 per cent between strains. The interactions of sex with strains and with treatments are negligible.

Uncontrollable variation drops sharply to a minimum between the 50th and 55th days of age. From Table 15, it is apparent that the variation between litters is not a serious source of variation in these data, indicating a high degree of within-strain uniformity in response. This is very different from a recent dosage-mortality study on an inbred strain of mice (Kaplan and Brown, 1952), wherein a significant amount of heterogeneous response was encountered on a between-litter basis. However, an all-or-none type of response, such as lethality, intrinsically carries the threat of greater variation between litters, particularly in the mid-lethal range. A body weight or weight change response, on the other hand, entailing only living animals, can reasonably be expected to show more uniformity.

The sex by litter interaction, essentially a within-litter source of variation, contributes from one-fifth to two-fifths of the total variation, as seen in Table 15. Since this is due to the variation around the mean within-litter sex difference in body weight or weight change, it then seems plausible that sex differences in radiation response have been erratic and difficult to isolate. When they do exist, the female has generally been favored as the more resistant sex (Cronkite and Chapman, 1949).

In summary, the following variables appear to enter into the body weight response to x-irradiation: basic genetic differences in initial body weight, genetic differences in the normal gain, and genetic differences in the actual weight response to x-ray. The latter factor can be broken down into additional variables. At any given dose, these are: differences in maximum loss, rate of loss, time of inception of recovery, and the rate of recovery. The similarity of the type of response shown by these strains would not permit the assumption that the genotype is capable of causing qualitatively different responses. However, genetic factors appear capable of exerting some control over the degree or quantity of expression of these response characteristics.

The observation of genetic differences in radiation response leads to the problem of deriving the relative resistance of these strains to each other. Any method of scaling must reasonably integrate all of the different aspects of the weight response. The best prodedure involves the regressions of weight change on dosage. These regressions do integrate and reflect the rate of gain, rate and maximum amount of loss, and the rate and time of recovery. They do not reflect the initial weight as a single factor but will contain any influence it has upon the other response factors. The regressions and their respective correlations, are given in Table 16.

The differences between the strain regressions at the first two age intervals are not statistically significant, but the differences are highly significant ($P < .001$) at all other ages. At any age level, these regressions indicate the strain differences in the amount of loss per unit of dosage as it is inter-related with normal gain. Within a strain, the comparison across the age levels reflects the rate and time of loss and recovery. Thus, a strain comparison across the age levels should bring in all the response factors.

The weakness of this procedure lies in the non-linearity of the response with dosage at several of the age levels. The derivation of the regressions is based on the assumption of an existing linear function. However, there is apparently no legitimate scale that renders the data completely linear throughout. Figure 12 plots the over-all mean weight changes with dosage. It can be seen that the weight change over the first day is decidedly curvilinear and that the radiation effect becomes proportionately less with increasing dose. At the 42nd and 45th days of age, the response is quite linear, while at the last three age levels it becomes curvilinear again. The latter situation is due to the lag in gain of the 800r mice.

The correlations of weight change and dose have been determined when using three different scales for dosage. These scales are the logarithm of the dose, the arithmetic value of

Table 16. Regressions and Correlations of Weight Change on Dosage by Strain and Age Interval

Strain		Weight change interval - days					
		40-41	40-42	40-45	40-50	40-55	40-60
RI	b x 10^6	-13.6	-45.7	-60.8	-58.1	-49.1	-34.4
	r	- .706	- .951	- .963	- .985	- .950	- .923
Z	b x 10^6	-32.6	-43.0	-57.6	-84.3	-46.7	-25.1
	r	- .779	- .887	- .984	- .983	- .873	- .835
S	b x 10^6	-18.8	-37.5	-63.3	-64.7	-62.6	-38.3
	r	- .970	- .977	- .999	- .918	- .888	- .837
E	b x 10^6	-25.4	-42.9	-84.0	-81.6	-74.3	-73.9
	r	- .925	- .944	- .986	- .988	- .968	- .960
L	b x 10^6	-31.2	-54.0	-79.2	-95.2	-112.0	-89.1
	r	- .938	- .967	- .995	- .982	- .972	- .924
Ba	b x 10^6	-32.3	-60.3	-121.1	-163.6	-213.1	-173.9
	r	- .902	- .952	- .989	- .955	- .937	- .931

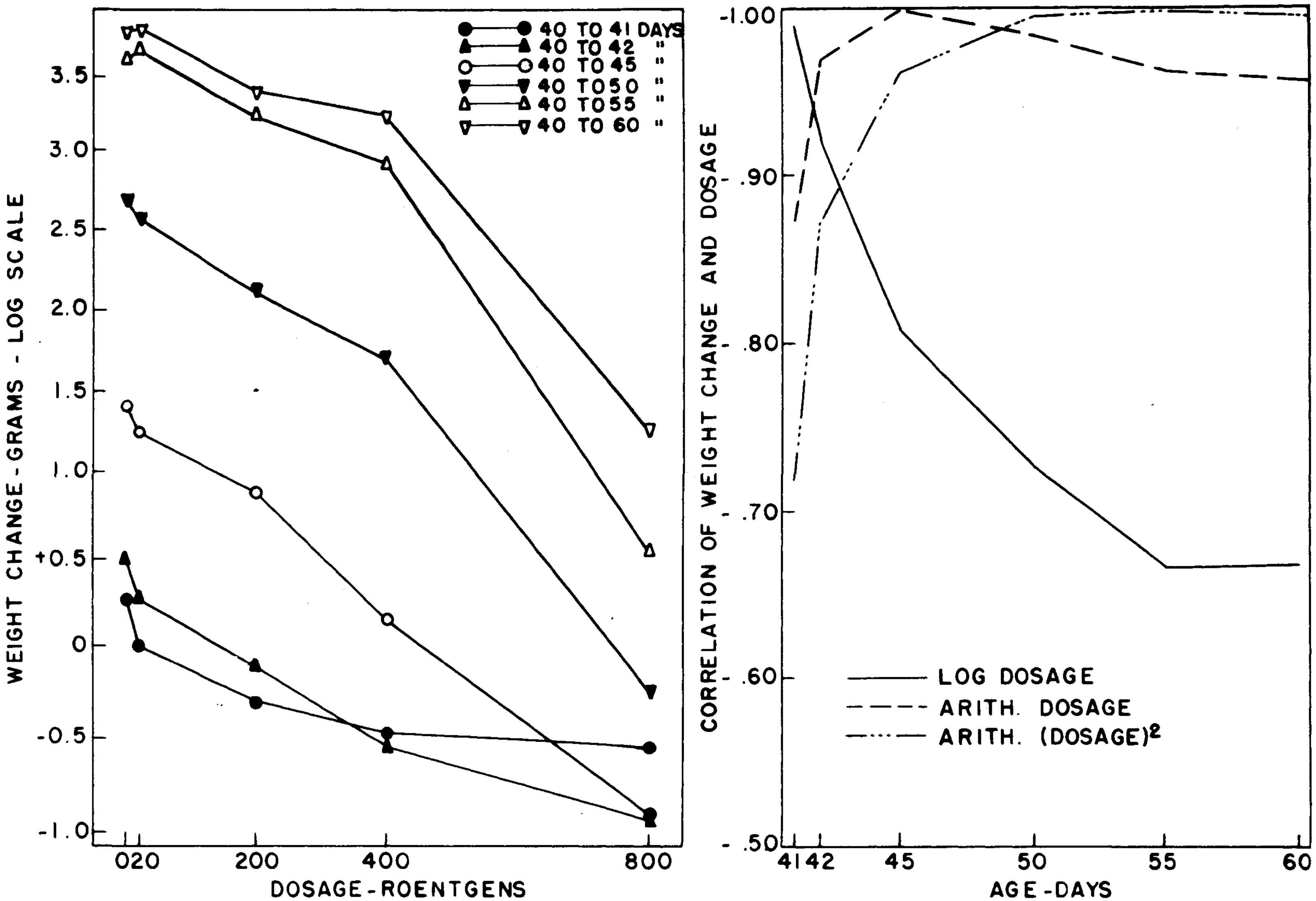

Figure 12. Relation of weight change and dosage (left); correlation of weight change with dosage on several scales (right).

the dose, and the square of the arithmetic value. The three sets of correlations are plotted in Figure 12.

If the highest correlations indicate the most linear relationship, then the straight arithmetic scale yields the best results. It is of interest to note, however, that the logarithm of the dose initially fits a linear function, while a square of the dose is most linear terminally. The results indicate that there is a triphastic response with time, while the break in response at 400r relates a biphasic response with dosage.

The strain regressions have been plotted at each age and the areas under the resulting curves graphically estimated. Figure 13 gives the curves and emphasizes the genetic disparity that exists.

The area under the curve derived from the regressions in the over-all mean data (Table 4) was arbitrarily given a value of 1.0. The areas determined for each of the strains and for the sexes were then expressed as a proportion of this average area. In order to re-express these relative areas on a scale running from 0 to 100, the values were plotted as in Figure 14. The slope used to determine the vertices of the 90 degree angles had to be arbitrarily fixed by two points. The average area is considered as the 50 per cent point, and the most susceptible strain (Ba) is fixed at 0 per cent. The remaining strains and the sexes are plotted on the ordinate and a

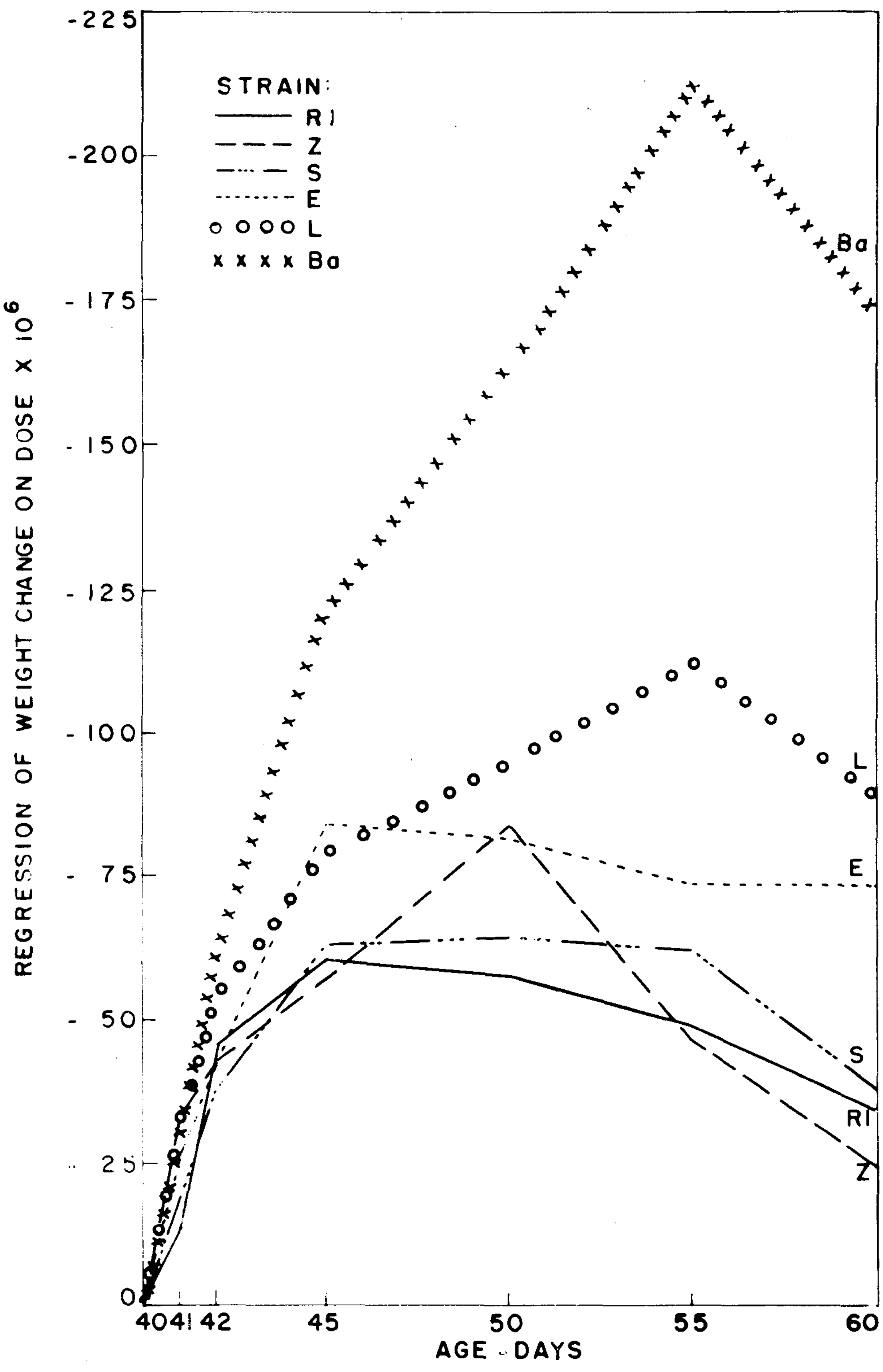

Figure 13. Strain regressions of weight change on dose for each age level. Areas under curves used to determine relative resistance levels.

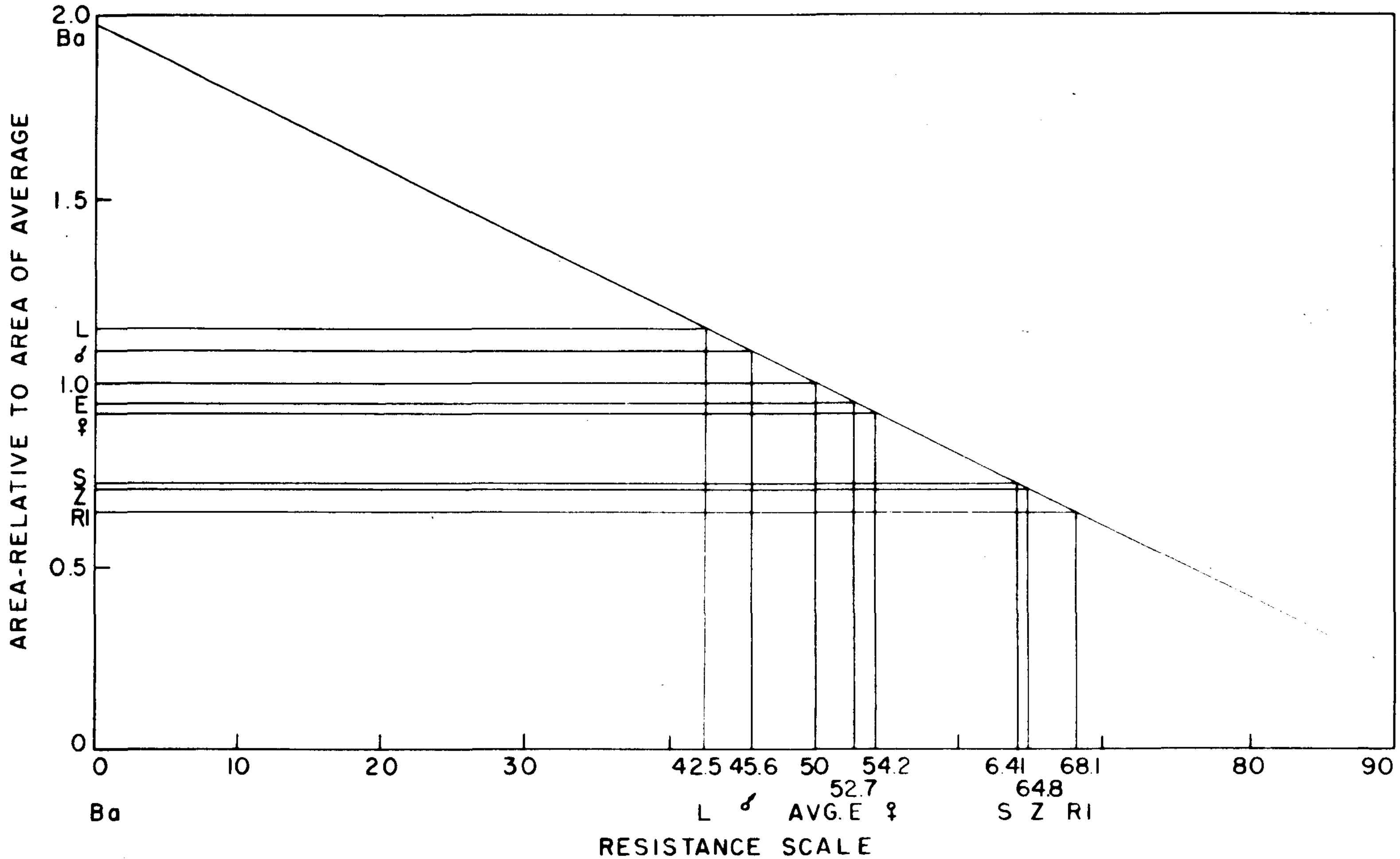

Figure 14. Determination of relative resistance of mouse strains to alteration of the normal gain in body weight after exposure to x-ray.

line parallel to the abscissa is run to the slope for each value. A perpendicular is then dropped to the abscissa and the percentage resistance is determined. The final resistance levels and the relative areas are given in Table 17.

Table 17. Relative Areas and Final Resistance Levels of the Strains and Sexes

Sex or strain	Relative area	Resistance level
		%
Average	1.000	50.0
Males	1.085	45.6
Females	0.916	54.2
RI	0.647	68.1
Z	0.714	64.8
S	0.723	64.1
E	0.942	52.7
L	1.145	42.5
Ba	1.974	0.0

Of particular interest are the final estimates for strains Z and S. Though nearly identical in their final resistance, their individual patterns of response show specific differences. As seen from Table 16, for the first ten days after exposure the Z mice have a proportionately greater loss in weight than the S mice, and consequently, much steeper regressions of weight change on dose. The rapid recovery phase that the Z mice enter between 50 and 55 days of age completely counterbalances their more severe early losses. Their regressions, at the last two age levels, are lower than all other strains. This feature emphasizes the importance of the time and rate of recovery as a genetic differential.

The final resistance levels cannot be considered as definitive, since one strain is fixed at 0 per cent. The use of strains with lesser or greater resistances would shift all of the estimates. As well, estimates from a different set of dosage levels would cause some changes. Nevertheless, for a given set of data, it permits a working scale for comparative study and interpretation.

A method like this does not need to be limited to radiation studies alone. Any investigation that involves a range of dosage levels of some agent--chemical, physical, or biological--that is capable of producing a set of correlated and measurable responses can utilize a procedure similar to this one. Its particular value lies in the use of living animals, which avoids losing experimental material as in mortality studies. Obviously, a living scale is of greater practical and theoretical value for integrated and quantitative biological investigation.

Organ Weight

An analysis of covariance, eliminating the variation in body weight, has been used to analyze the organ weights. In presenting and interpreting the results, the mean organ weights at each dosage level have been adjusted to a constant 60-day body weight. The appropriate organ:body weight regressions have been used to adjust the over-all, sex, and strain means. Standard errors are attached to these adjusted means.

For the most part, the inter-dosage variation in the 60-day body weights is not great, so that the extent of the adjustment is not serious. The 60-day body weights are not adjusted weights themselves and still express the initial sampling variation that was referred to earlier, upon which has been super-imposed the effects of the radiation. As a result of sampling, in one strain, Z, the observed 800r mean 60-day body weight is slightly heavier than that of the controls. Most strains, however, express the 800r growth suppression at 60 days, particularly strain Ba. In the latter strain, the organ weight adjustment requires an estimation across a four-gram body weight shift. The standard errors of such estimates are noticeably larger, however.

As Walter and Addis (1939) effectively pointed out, the comparison of organ weights, between any treated and untreated animals, must be done with care when the organs are expressed as a function of the body weight. Unequivalent losses in fat and body water in the treated and untreated body weights can create the estimation of aberrant organ weights by over-correction. In this respect, adjusted organ weights of the Ba mice at 800r may well be unreliable estimates, since these mice were characterized by an emaciated appearance. However, this should not detract from the large majority of the other estimates.

Heart weight - over-all radiation response

The over-all mean radiation effects on heart weight are presented in Table 18 and Figure 15. The effect of the adjustment of the organ weights is clearly depicted. In column 3, the observed mean heart weights show a progressive decline with increasing dose. Similarly, the body weights (column 2) show this decline. Adjustment to the over-all mean body weight (19.34 grams, column 2) completely eliminates the weight differences in the hearts. The adjusted means vary by only 0.5 milligrams at the most. The weights from the irradiated mice are consistently lower than the control weight, but these changes are not significant. The average effect upon the unadjusted heart weight is probably entirely due to inanition.

Radiation response by sex

The data of Table 18 and Figure 15 indicate that the two sexes respond in an essentially parallel manner, with no significant effects arising.

Radiation response by strain

Several minor changes in heart weight occur after

Table 18. Heart Weight and 60-day Body Weight Means; by Dosage and by Sex and Dosage

Dose r	Sex	Observed means[1] Body wt. grams	Observed means[1] H. wt. mgs.	Adj. means[2] Heart wt. log	S.E.	Adj. means[1] Heart wt. mgs.	Change from 0r mgs.	Change from 0r %	P[3] level
0		19.92	114.0	2.047	±.003	111.4			at 238 df
20		19.90	113.4	2.046	±.003	111.2	-0.2	-0.2	*
200		19.74	112.8	2.046	±.003	111.2	-0.2	-0.2	
400		19.33	110.8	2.045	±.003	110.9	-0.5	-0.4	
800		17.87	105.0	2.046	±.003	111.2	-0.2	-0.2	
Over-all means[1]		19.34	111.2						
0	♂	21.84	123.5	2.076	±.004	119.1			at 118 df
20		21.73	122.8	2.075	±.004	118.9	-0.2	-0.2	
200		20.86	118.3	2.072	±.003	118.0	-1.1	-0.9	
400		20.77	118.1	2.073	±.003	118.3	-0.8	-0.7	
800		18.99	110.4	2.073	±.004	118.3	-0.8	-0.7	
Male means[1]		20.81	118.5						
0	♀	18.18	105.2	2.019	±.004	104.5			at 118 df
20		18.22	104.7	2.016	±.004	103.8	-0.7	-0.7	
200		18.69	107.5	2.019	±.004	104.5	0.0	0.0	
400		17.99	104.0	2.016	±.004	103.8	-0.7	-0.7	
800		16.81	99.9	2.020	±.004	104.7	+0.2	+0.2	
Female means[1]		17.97	104.2						

[1]Geometric means

[2]Adjusted to the mean 60-day body weight

[3]Significance of the difference between adjusted means; 0-20r, 0-200r, etc.
*Absence of entry here and in subsequent tables indicates insignificant change.

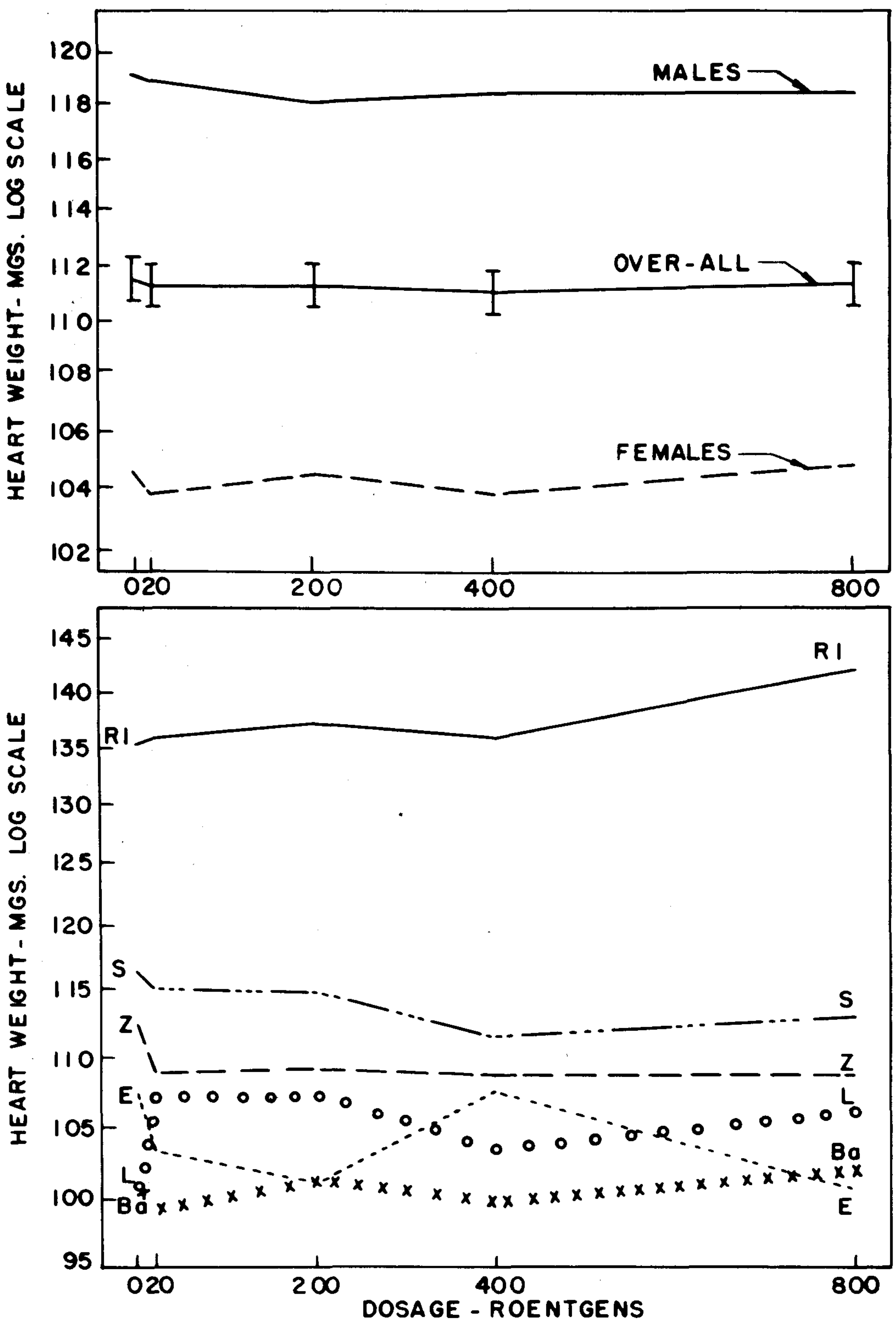

Figure 15. Heart weight. Sex and strain means by dosage. Over-all means shown with ± one standard error. Each set of values adjusted to its respective constant 60-day body weight.

Table 19. Heart Weight and 60-day Body Weight Means; by Strain and Dosage

Dose r	Strain	Observed means[1] Body wt. grams	Observed means[1] H. wt. mgs.	Adj. means[2] Heart wt. log	S.E.	Adj. means[1] Heart wt. mgs.	Change from Or mgs.	Change from Or %	P[3] level
0	RI	24.35	134.9	2.131	±.006	135.2			at 38 df
20		24.74	137.2	2.133	±.006	135.8	+ 0.6	+ 0.4	
200		26.37	144.2	2.137	±.006	137.1	+ 1.9	+ 1.4	
400		23.47	132.4	2.133	±.006	135.8	+ 0.6	+ 0.4	
800		23.26	137.4	2.152	±.006	141.9	+ 6.7	+ 5.0	.02-.01
Strain means[1]		24.41	137.2						
0	Z	20.10	112.0	2.051	±.006	112.5			at 38 df
20		21.11	113.0	2.037	±.006	108.9	- 3.6	- 3.2	
200		19.25	104.5	2.038	±.006	109.1	- 3.4	- 3.0	
400		20.42	109.5	2.036	±.006	108.6	- 3.9	- 3.5	.10-.05
800		20.26	108.9	2.036	±.006	108.6	- 3.9	- 3.5	.20-.10
Strain means[1]		20.22	109.5						
0	S	19.81	119.5	2.066	±.007	116.4			at 38 df
20		19.12	114.9	2.061	±.007	115.1	- 1.3	- 1.1	
200		18.85	113.2	2.060	±.007	114.8	- 1.6	- 1.4	
400		19.81	114.5	2.047	±.007	111.4	- 5.0	- 4.3	.10-.05
800		18.37	109.0	2.053	±.007	113.0	- 3.4	- 2.9	
Strain means[1]		19.18	114.2						

[1]Geometric means

[2]Adjusted to the mean 60-day body weight

[3]Significance of the difference between adjusted means; 0-20r, 0-200r, etc.

Table 20. Heart Weight and 60-day Body Weight Means; by Strain and Dosage

Dose r	Strain	Observed means[1] Body wt. grams	H. wt. mgs.	Adj. means[2] Heart wt. log	S.E.	Adj. means[1] Heart wt. mgs.	Change from Or mgs.	%	P[3] level
0	E	17.08	109.1	2.031	±.008	107.4			at 38 df
20		17.19	105.4	2.014	±.008	103.3	- 4.1	- 3.8	.20-.10
200		17.31	103.8	2.005	±.008	101.2	- 6.2	- 5.8	.05-.02
400		16.21	105.9	2.031	±.008	107.4	0.0	0.0	
800		15.42	96.3	2.003	±.008	100.7	- 6.7	- 6.2	.05-.02
Strain means[1]		16.63	104.0						
0	L	19.30	104.2	2.004	±.008	100.9			at 38 df
20		19.05	109.9	2.030	±.007	107.2	+ 6.3	+ 6.2	.02-.01
200		17.84	105.9	2.031	±.007	107.4	+ 6.5	+ 6.4	.02-.01
400		17.93	102.3	2.015	±.007	103.5	+ 2.6	+ 2.6	.40-.30
800		17.30	102.7	2.026	±.008	106.2	+ 5.3	+ 5.3	.10-.05
Strain means[1]		18.27	105.0						
0	Ba	19.57	107.0	2.004	±.008	100.9			at 38 df
20		18.98	103.1	1.998	±.007	99.5	- 1.4	- 1.4	
200		20.05	109.7	2.006	±.008	101.4	+ 0.5	+ 0.5	
400		18.91	103.2	2.000	±.007	100.0	- 0.9	- 0.9	
800		14.11	83.2	2.009	±.011	102.1	+ 1.2	+ 1.2	
Strain means[1]		18.18	100.8						

[1]Geometric means

[2]Adjusted to the mean 60-day body weight

[3]Significance of the difference between adjusted means; 0-20r, 0-200r, etc.

x-irradiation in some of the strains (Tables 19 and 20). Strains RI and L show an increase in weight at all irradiation levels. This is a significant increase at 800r in the RI mice, and at 20r and 200r in the L mice.

Strains Z, S, and E have lower mean weights after irradiation, but only those of the E mice are significant. The Ba strain shows no change in adjusted heart weight, in spite of their gross body weight response to the x-ray.

Table 21. Heart Weight - Component Analysis

Component of variation	Percentage of total variation	Absolute variance
S - Strain effect	28.3	.0003281
T - Treatment effect	0.0	.0
ST - Strain x treatment effect	5.7	.0000660
L - Between litter effect	21.1	.0002445
F - Sex effect	0.0	.0
FS - Sex x strain effect	2.8	.0000327
FT - Sex x treatment effect	0.0	.0
FST- Sex x strain x treatment	0.0	.0
E - Sex x litter effect	42.1	.0004880
		.0011593

The increases in heart weight may be an indirect reflection of a radiation induced anemia. Grossly, some of the hearts of the RI mice were flabby and obviously larger than normal. Cardiac dilatation and hypertrophy are sometimes seen in anemic states (Hull, 1950).

The depressions in organ weight may reflect the general growth retardation induced by the x-ray. In strains exhibiting this, it may prove to be a greater physiologic antagonist than any anemic condition that may exist.

The component analysis of the heart weights is given in Table 21. The uncontrollable variation takes out 63 per cent of the total, one-third of this lying between the litters. Basic strain differences in heart weight contribute 28 per cent to the total variation, while the average radiation effects are zero. However, as has been demonstrated, some strain differentials in response do exist which amount to nearly 6 per cent of the total variation.

Kidney weight - over-all radiation response

The kidneys, like the heart, are relatively resistant organs. Table 22 and Figure 16 show that after body weight variation is eliminated, little or no response occurs in kidney weight. Again, there is a tendency for a weight depression to exist after exposure, with the exception of the mice at 800r.

Radiation response by sex

The two sexes respond in a nearly parallel manner, with neither showing a significant change from the control weight. The basic difference in body weight conceals the existence of a very significant sex difference in kidney weight. The female has a strikingly lighter mean kidney weight, which has

Table 22. Kidney Weight and 60-day Body Weight Means; by Dosage and by Sex and Dosage

Dose r	Sex	Observed means[1] Body wt. grams	Observed means[1] K. wt. mgs.	Adj. means[2] Kidney wt. log	S.E.	Adj. means[1] Kidney wt. mgs.	Change from Or mgs.	Change from Or %	P[3] level
0		19.92	334.6	2.510	±.003	323.6			at 238 df
20		19.90	331.9	2.507	±.003	321.4	- 2.2	- 0.7	
200		19.74	327.8	2.505	±.003	319.9	- 3.7	- 1.1	
400		19.33	319.1	2.504	±.003	319.2	- 4.4	- 1.4	
800		17.87	299.2	2.514	±.004	326.6	+ 3.0	+ 0.9	
Over-all means[1]		19.34	322.3						
0	♂	21.84	390.6	2.567	±.005	369.0			at 118 df
20		21.73	387.9	2.566	±.005	368.1	- 0.9	- 0.2	
200		20.86	364.6	2.561	±.005	363.9	- 5.1	- 1.4	
400		20.77	362.5	2.560	±.005	363.1	- 5.9	- 1.6	
800		18.99	334.6	2.572	±.005	373.3	+ 4.3	+ 1.2	
Male means[1]		20.81	367.5						
0	♀	18.18	286.6	2.452	±.004	283.1			at 118 df
20		18.22	284.0	2.448	±.004	280.5	- 2.6	- 0.9	
200		18.69	294.7	2.453	±.004	283.8	+ 0.7	+ 0.2	
400		17.99	281.0	2.448	±.004	280.5	- 2.6	- 0.9	
800		16.81	267.5	2.455	±.004	285.1	+ 2.0	+ 0.7	
Female means[1]		17.97	282.6						

[1]Geometric means

[2]Adjusted to the mean 60-day body weight

[3]Significance of the difference between adjusted means; 0-20r, 0-200r, etc.

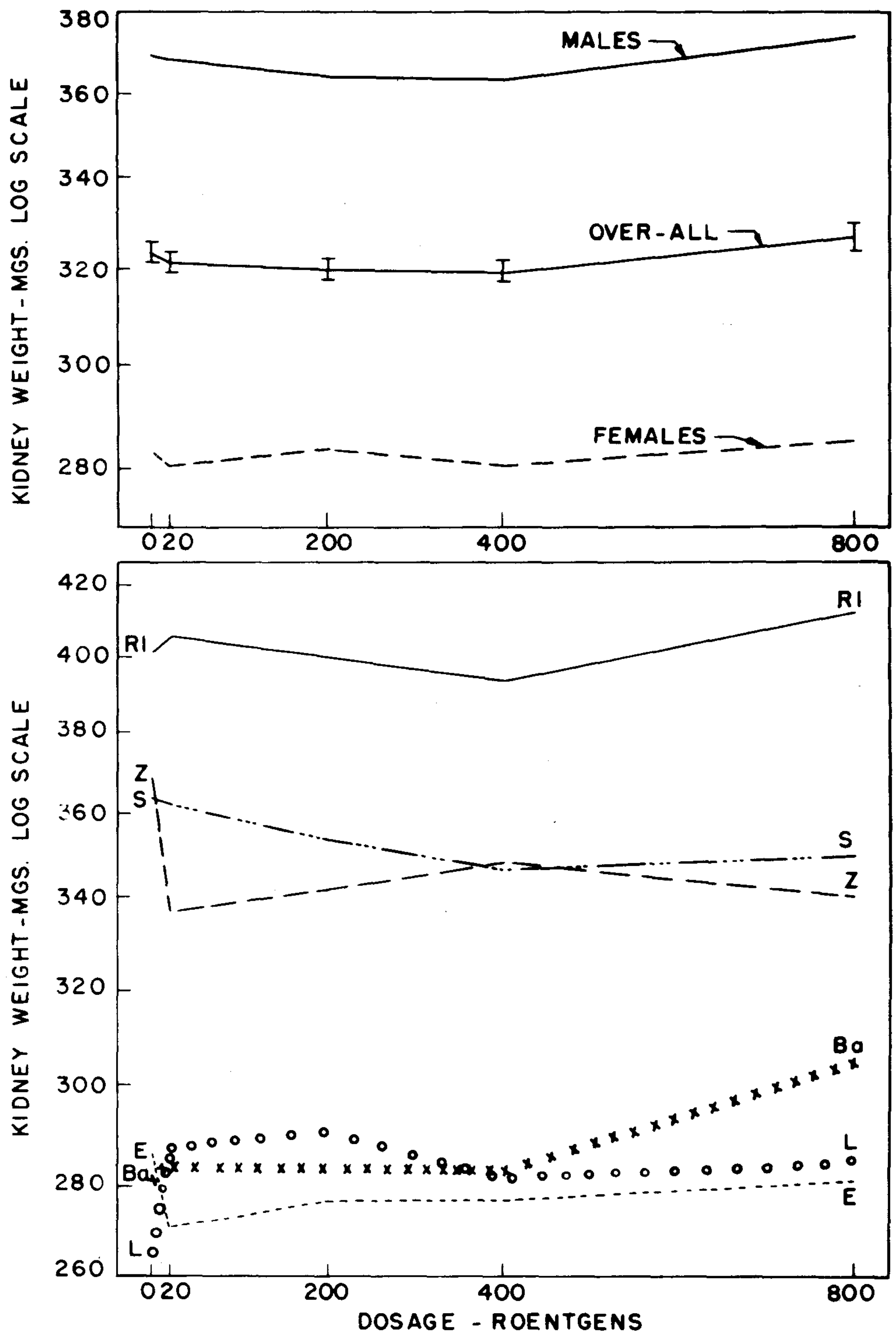

Figure 16. Kidney weight. Sex and strain means by dosage. Over-all means shown with ± one standard error. Each set of values adjusted to its respective constant 60-day body weight.

been shown in these mice previously (Grahn, 1950). This basic difference, however, does not alter the resistance of the kidneys in the two sexes.

Radiation response by strain

Tables 23 and 24 present the data on the different strains. Three strains, Z, S, and E, show consistent decreases in weight after exposure. The same strains showed a similar response in heart weight. These changes from the control value are highly significant in the Z mice at 20, 200, and 800r, and at 400r in the S strain.

The RI mice do not present a consistent reaction, while strains L and Ba have heavier kidneys at all irradiation levels. As noted in Table 24, the significance of the changes in the L mice at 20r and 200r are invalidated due to the appearance of hydro-nephrotic kidneys. Three such instances arose, two at 20r and one at 200r, always in the males and involving the right kidney. The right ureter was also affected, with an apparent point of stenosis of the ureter proximal to the bladder. The female litter-mate of one of the hydro-nephrotic males had an imperforate vagina, a frequently observed characteristic of the L mice. This may be more than coincidental and may indicate a genetically determined abnormal development of the uro-genital system. Since this last point cannot be proven, the hydro-nephrotic kidneys were left in the data, as it is not impossible for

Table 23. Kidney Weight and 60-day Body Weight Means; by Strain and Dosage

Dose r	Strain	Observed means[1] Body wt. grams	Observed means[1] K. wt. mgs.	Adj. means[2] Kidney wt. log	S.E.	Adj. means[1] Kidney wt. mgs.	Change from Or mgs.	Change from Or %	p[3] level
0	RI	24.35	400.5	2.604	±.008	401.8			at 38 df
20		24.74	411.7	2.608	±.008	405.5	+ 3.7	+ 0.9	
200		26.37	435.4	2.602	±.009	399.9	- 1.9	- 0.5	
400		23.47	377.2	2.595	±.008	393.6	- 8.2	- 2.0	
800		23.26	390.7	2.615	±.008	412.1	+10.3	+ 2.6	.40-.30
Strain means[1]		24.41	402.6						
0	Z	20.10	366.0	2.567	±.009	369.0			at 38 df
20		21.11	357.4	2.528	±.009	337.3	-31.7	- 8.6	.01-.001
200		19.25	320.4	2.534	±.009	342.0	-27.0	- 7.3	.02-.01
400		20.42	353.0	2.542	±.009	348.3	-20.7	- 5.6	.10-.05
800		20.26	341.7	2.532	±.009	340.4	-28.6	- 7.8	.01-.001
Strain means[1]		20.22	347.3						
0	S	19.81	377.1	2.561	±.006	363.9			at 38 df
20		19.12	360.6	2.559	±.006	362.2	- 1.7	- 0.5	
200		18.85	346.9	2.549	±.006	354.0	- 9.9	- 2.7	.20-.10
400		19.81	359.7	2.540	±.006	346.7	-17.2	- 4.7	.02-.01
800		18.37	332.9	2.544	±.006	349.9	-14.0	- 3.8	.10-.05
Strain means[1]		19.18	355.1						

[1]Geometric means

[2]Adjusted to the mean 60-day body weight

[3]Significance of the difference between adjusted means; 0-20r, 0-200r, etc.

Table 24. Kidney Weight and 60-day Body Weight Means; by Strain and Dosage

Dose r	Strain	Observed means[1] Body wt. grams	K. wt. mgs.	Adj. means[2] Kidney wt. log	S.E.	Adj. means[1] Kidney wt. mgs.	Change from Or mgs.	%	P[3] level
0	E	17.08	293.3	2.457	±.009	286.4			at 38 df
20		17.19	280.7	2.435	±.009	272.3	-14.1	- 4.9	.20-.10
200		17.31	287.5	2.443	±.010	277.3	- 9.1	- 3.2	
400		16.21	271.4	2.443	±.009	277.3	- 9.1	- 3.2	
800		15.42	262.8	2.449	±.010	281.2	- 5.2	- 1.8	
Strain means[1]		16.63	278.9						
0	L	19.30	284.8	2.427	±.010	267.3			at 38 df
20		19.05	301.0	2.458	±.010	287.1	+19.8	+ 7.4	No test*
200		17.84	282.3	2.463	±.010	290.4	+23.1	p 8.6	"
400		17.93	275.1	2.449	±.010	281.2	+13.9	+ 5.2	.20-.10
800		17.30	267.5	2.454	±.010	284.4	+17.1	+ 6.4	.10-.05
Strain means[1]		18.27	281.9						
0	Ba	19.57	304.0	2.447	±.007	279.9			at 38 df
20		18.98	298.1	2.453	±.007	283.8	+ 3.9	+ 1.4	
200		20.05	315.9	2.452	±.008	283.1	+ 3.2	+ 1.1	
400		18.91	295.5	2.451	±.007	282.5	+ 2.6	+ 0.9	
800		14.11	229.6	2.484	±.011	304.8	+24.9	+ 8.9	.02-.01
Strain means[1]		18.18	286.8						

[1]Geometric means

[2]Adjusted to the mean 60-day body weight

[3]Significance of the difference between adjusted means; 0-20r, 0-200r, etc.

*Includes hydro-nephrotic kidneys - see text a radiation induced concretion to have initiated the nephrotic condition.

The tendency for the kidney weight to be lower in some of the irradiated animals may be a reflection of an over-all growth inhibition. Increases in kidney weight are not explained.

The results of the component analysis are shown in Table 25. Here, as in the heart weight, the average radiation

Table 25. Kidney Weight - Component Analysis

Component of variation	Percentage of total variation	Absolute variance
S - Strain effect	31.8	.0007377
T - Treatment effect	0.0	.0
ST - Strain x treatment effect	3.8	.0000889
L - Between litter effect	11.6	.0002680
F - Sex effect	15.1	.0003492
FS - Sex x strain effect	1.8	.0000422
FT - Sex x treatment effect	0.2	.0000046
FST - Sex x strain x treatment	0.0	.0
E - Sex x litter effect	35.7	.0008290
		.0023196

response is zero, but a small strain differential in response (3.8 per cent) does exist. Sex and strain differences, both basically genetic, take out 47 per cent of the total variation, 15 per cent in the sex difference alone. Another 47 per cent is attributable to random fluctuation, with the E:L ratio being about 3:1, as compared to 2:1 in the heart.

Liver weight - over-all radiation response

At 20r and 200r, the liver weight is lighter than the controls, but a significant increase in weight occurs at 400r and 800r (Table 26 and Figure 17). The initial depression is very minor as compared to the increases in weight at the high doses. It should be noted that a change as small as 5 per cent of the control weight can become a very highly significant change. Simple observation of the unadjusted data would give no indication of this relative increase in weight.

Radiation response by sex

The two sexes do not reflect a completely parallel response in liver weight. The males show a slight increase at 20r, while the females decrease. A decrease at 200r occurs in the males, while the females begin a progressive increase that continues through 800r. Although the 20r and 200r shifts are not significant, those at 800r are significant. The females show both a greater absolute and relative increase at the high dose.

Radiation response by strain

With strain S excluded, all strains show an increase in liver weight at 800r. This change is significant in strains RI, L, and Ba (Tables 27 and 28). In these strains, the

Table 26. Liver Weight and 60-day Body Weight Means; by Dosage and by Sex and Dosage

Dose r	Sex	Observed means[1] Body wt. grams	Observed means[1] L. wt. mgs.	Adj. means[2] Liver wt. log	S.E.	Adj. means[1] Liver wt. mgs.	Change from 0r mgs.	Change from 0r %	P[3] level
0		19.92	1248	3.084	±.003	1213			at 238 df
20		19.90	1239	3.081	±.003	1205	- 8.0	- 0.7	
200		19.74	1235	3.083	±.003	1211	- 2.0	- 0.2	
400		19.33	1241	3.094	±.003	1242	+29.0	+ 2.4	.04
800		17.87	1183	3.106	±.004	1276	+63.0	+ 5.2	<.0001
Over-all means[1]		19.34	1229						
0	♂	21.84	1382	3.119	±.004	1315			at 118 df
20		21.73	1386	3.123	±.004	1327	+12.0	+ 0.9	
200		20.86	1293	3.111	±.004	1291	-24.0	- 1.8	
400		20.77	1333	3.126	±.004	1337	+22.0	+ 1.8	.30-.20
800		18.99	1255	3.139	±.004	1377	+62.0	+ 4.7	.001-.0001
Male means[1]		20.81	1329						
0	♀	18.18	1128	3.048	±.004	1117			at 118 df
20		18.22	1107	3.039	±.004	1094	-23.0	- 2.1	.20-.10
200		18.69	1180	3.056	±.004	1138	+21.0	+ 1.9	.20-.10
400		17.99	1154	3.062	±.004	1153	+36.0	+ 3.2	.05-.02
800		16.81	1116	3.074	±.004	1186	+69.0	+ 6.2	<.0001
Female means[1]		17.97	1137						

[1] Geometric means

[2] Adjusted to the mean 60-day body weight

[3] Significance of the difference between adjusted means; 0-20r, 0-200r, etc.

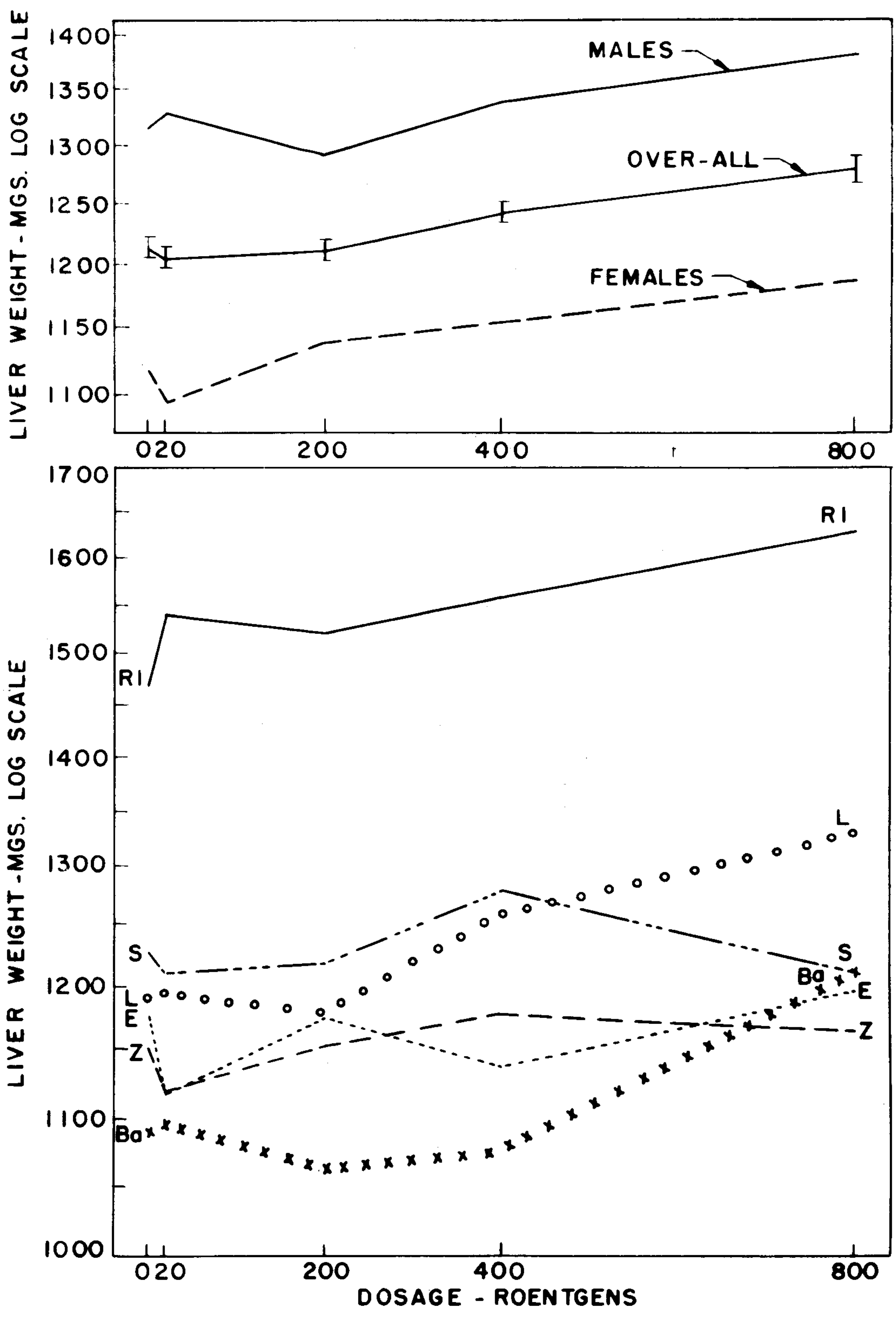

Figure 17. Liver weight. Sex and strain means by dosage. Over-all means shown with ± one standard error. Each set of values adjusted to its respective constant 60-day body weight.

Table 27. Liver Weight and 60-day Body Weight Means; by Strain and Dosage

Dose r	Strain	Observed means[1] Body wt. grams	Observed means[1] L. wt. mgs.	Adj. means[2] Liver wt. log	S.E.	Adj. means[1] Liver wt. mgs.	Change from 0r mgs.	Change from 0r %	P[3] level
0	RI	24.35	1464	3.166	±.007	1466			at 38 df
20		24.74	1555	3.187	±.007	1538	+72.0	+ 4.9	.05-.02
200		26.37	1619	3.182	±.008	1521	+55.0	+ 3.8	.20-.10
400		23.47	1509	3.192	±.007	1556	+90.0	+ 6.1	.02-.01
800		23.26	1564	3.211	±.007	1626	+160.0	+10.9	< .0001
Strain means[1]		24.41	1541						
0	Z	20.10	1147	3.062	±.007	1153			at 38 df
20		21.11	1174	3.049	±.007	1119	-34.0	- 2.9	.30-.20
200		19.25	1093	3.062	±.007	1153	0.0	0.0	
400		20.42	1189	3.071	±.007	1178	+25.0	+ 2.2	
800		20.26	1166	3.066	±.007	1164	+11.0	+ 1.0	
Strain means[1]		20.22	1153						
0	S	19.81	1263	3.089	±.007	1227			at 38 df
20		19.12	1207	3.083	±.007	1211	-16.0	- 1.3	
200		18.85	1201	3.086	±.007	1219	- 8.0	- 0.7	
400		19.81	1315	3.107	±.007	1279	+52.0	+ 4.2	.10-.05
800		18.37	1166	3.083	±.007	1211	-16.0	- 1.3	
Strain means[1]		19.18	1229						

[1] Geometric means

[2] Adjusted to the mean 60-day body weight

[3] Significance of the difference between adjusted means; 0-20r, 0-200r, etc.

Table 28. Liver Weight and 60-day Body Weight Means; by Strain and Dosage

Dose r	Strain	Observed means[1] Body wt. grams	Observed means[1] L. wt. mgs.	Adj. means[2] Liver wt. log	S.E.	Adj. means[1] Liver wt. mgs.	Change from 0r mgs.	Change from 0r %	P[3] level
0	E	17.08	1208	3.071	±.009	1178			at 38 df
20		17.19	1152	3.048	±.009	1117	-61.0	- 5.2	.10-.05
200		17.31	1221	3.070	±.009	1175	- 3.0	- 0.3	
400		16.21	1110	3.056	±.009	1138	-40.0	- 3.4	
800		15.42	1115	3.078	±.010	1197	+19.0	+ 1.6	
Strain means[1]		16.63	1160						
0	L	19.30	1251	3.076	±.012	1191			at 38 df
20		19.05	1240	3.077	±.011	1194	+ 3.0	+ 0.3	
200		17.84	1156	3.072	±.011	1180	-11.0	- 0.9	
400		17.93	1239	3.100	±.011	1259	+68.0	+ 5.7	.20-.10
800		17.30	1264	3.123	±.012	1327	+136.0	+11.4	.01-.001
Strain means[1]		18.27	1229						
0	Ba	19.57	1181	3.037	±.008	1089			at 38 df
20		18.98	1147	3.039	±.008	1094	+ 5.0	+ 0.5	
200		20.05	1185	3.027	±.008	1064	-25.0	- 2.3	
400		18.91	1123	3.032	±.008	1076	-13.0	- 1.2	
800		14.11	916	3.083	±.012	1211	+122.0	+11.2	.01-.001
Strain means[1]		18.18	1105						

[1]Geometric means

[2]Adjusted to the mean 60-day body weight

[3]Significance of the difference between adjusted means; 0-20r, 0-200r, etc.

increase over the controls is always more than 10 per cent. The reality of this weight change is substantiated in the RI and L mice by the fact that even the unadjusted liver weights are heavier at 800r, in spite of a decrease in body weight. Strains RI and L also show a liver weight increase at 400r, but only in the former strain is this significant.

The exact reason for the increase in liver weight is problematic. Histological examination revealed no evidence of ectopic hematopoiesis or fatty infiltration, factors that could have caused some weight increases. If an increased rate of growth had occurred, it was not evident by an increase in the number of mitotic figures. Since no sections were stained for glycogen, it cannot be stated as to what importance an increased glycogen storage might have played.

Other workers have seen indications of increases in liver weight, but not to the degree seen in this study. Brues, _et al._ (1946) did not consider as significant a relative increase in liver weight of rats exposed to chronic irradiation. The absolute weight of the liver was the same in the control and irradiated rats, although a 13 per cent drop in body weight occurred in the latter. Ludewig and Chanutin (1950) and Supplee and Entenman (1952) have observed an increase in liver weight between two and four days after exposure, but Ludewig and Chanutin noted the weight to be normal three weeks after exposure. The estimates of the present study are twenty days after exposure.

In view of the remarkable regenerative capacity of the liver (Maximow and Bloom, 1948), it is possible that this organ may be able to overcome the growth-inhibiting effect of irradiation more readily than other organs, leading to relative increases in liver weight.

Table 29 presents the component analysis of liver weight.

Table 29. Liver Weight - Component Analysis

Component of variation	Percentage of total variation	Absolute variance
S - Strain effect	39.4	.0007851
T - Treatment effect	2.3	.0000457
ST - Strain x treatment effect	3.7	.0000739
L - Between litter effect	20.2	.0004015
F - Sex effect	0.0	.0
FS - Sex x strain effect	1.7	.0000336
FT - Sex x treatment effect	2.4	.0000471
FST - Sex x strain x treatment	0.0	.0
E - Sex x litter effect	30.3	.0006040
		.0019909

The general radiation response appears as 2.3 per cent of the variation, while the strain and sex differential responses contribute 3.7 per cent and 2.4 per cent, respectively. There is no basic difference between the sexes in liver weight, but strain differences remove 39 per cent of the total variation. Uncontrollable variation takes out 50 per cent, with this being distributed between the E and L terms on a 3:2 basis.

Spleen weight - over-all radiation response

Splenic response to irradiation presents an interesting picture. As seen in Table 30 and Figure 18, there is a significant increase in spleen weight at 20r. A recession from this point occurs at 200r, followed by a progressive increase through 800r. The 800r increase is a very highly significant change.

Radiation response by sex

The sexes reiterate the reaction described above, although a slight divergence from parallelity occurs. The 20r response in the females is considerably less than in the males, and only the latter present a significant increase. The responses at the other doses are more exaggerated in the males, such that a rather broad divergence occurs at 800r. In the controls, the females have a slightly heavier spleen, but their weight terminates at a much lower level than in the males.

Radiation response by strain

The individual strain responses are given in Tables 31 and 32 and in Figure 19. At 20r, the strains react in a similar manner, with one exception. Strain E mice show a sharp depression in spleen weight at 20r, the loss being maintained through 400r. At 800r, the E spleens are above

Table 30. Spleen Weight and 60-day Body Weight Means; by Dosage and by Sex and Dosage

Dose r	Sex	Observed means[1] Body wt. grams	Observed means[1] S. wt. mgs.	Adj. means[2] Spleen wt. log	S.E.	Adj. means[1] Spleen wt. mgs.	Change from Or mgs.	Change from Or %	P[3] level
0		19.92	100.8	1.998	±.011	99.5			at 238 df
20		19.90	108.7	2.031	±.011	107.4	+ 7.9	+ 7.9	.04
200		19.74	98.9	1.991	±.011	98.0	- 1.5	- 1.5	
400		19.33	103.5	2.015	±.011	103.5	+ 4.0	+ 4.0	.30
800		17.87	134.3	2.143	±.012	139.0	+39.5	+39.7	< .0001
Over-all means[1]		19.34	108.5						
0	♂	21.84	101.4	1.991	±.014	98.0			at 118 df
20		21.73	112.7	2.038	±.014	109.1	+11.1	+11.3	.02-.01
200		20.86	97.2	1.987	±.014	97.1	- 0.9	- 0.9	
400		20.77	105.9	2.025	±.014	105.9	+ 7.9	+ 8.1	.10-.05
800		18.99	142.1	2.182	±.014	152.1	+54.1	+55.2	< .0001
Male means[1]		20.81	110.8						
0	♀	18.18	100.2	2.000	±.014	100.0			at 118 df
20		18.22	104.9	2.020	±.014	104.7	+ 4.7	+ 4.7	.40-.30
200		18.69	100.6	2.000	±.014	100.0	0.0	0.0	
400		17.99	101.2	2.005	±.014	101.2	+ 1.2	+ 1.2	
800		16.81	127.0	2.109	±.015	128.5	+28.5	+28.5	< .0001
Female means[1]		17.97	106.3						

[1] Geometric means

[2] Adjusted to the mean 60-day body weight

[3] Significance of the difference between adjusted means; 0-20r, 0-200r, etc.

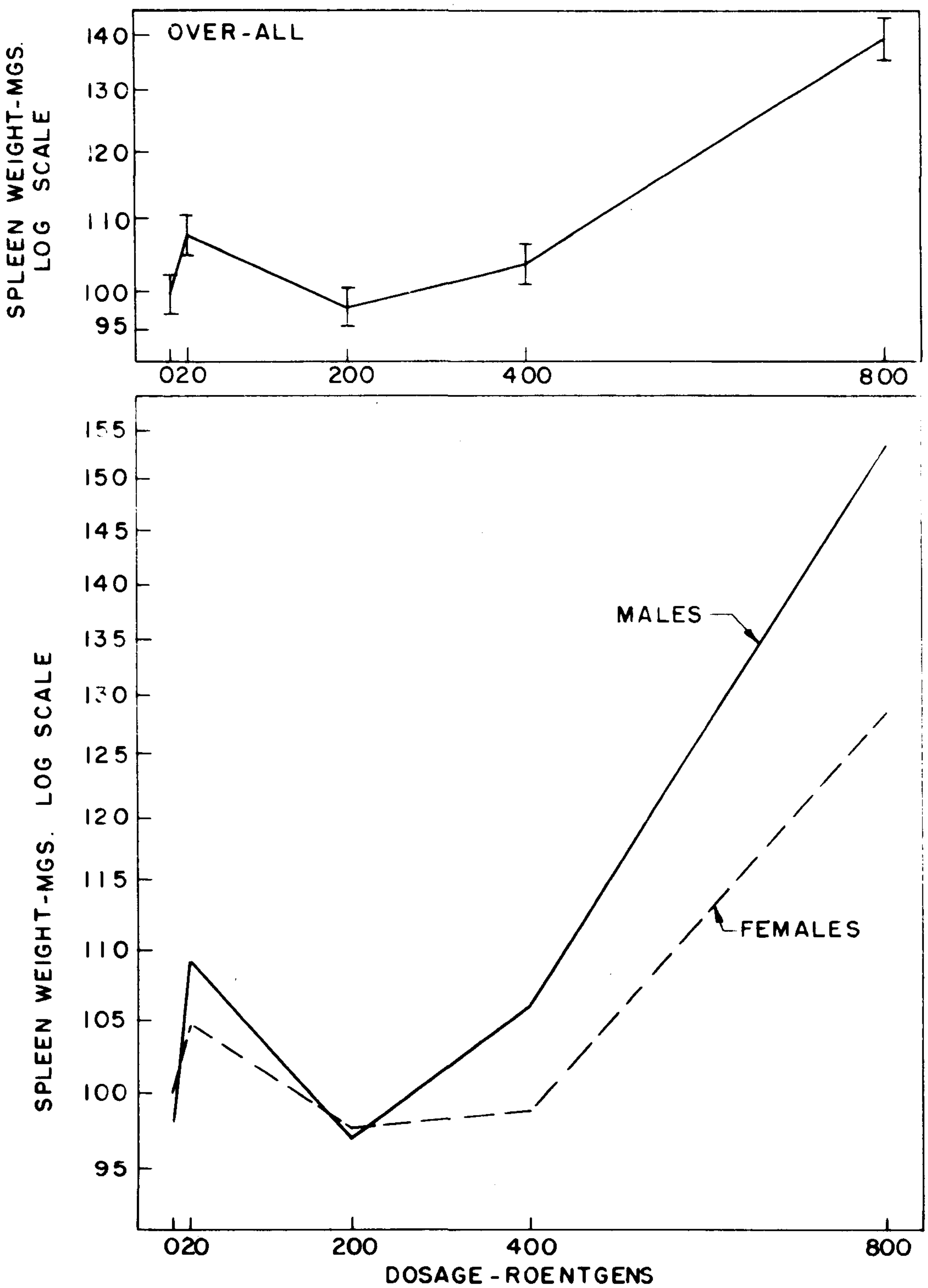

Figure 18. Spleen weight. Sex means by dosage. Over-all means shown with ± one standard error. Each set of values adjusted to its respective constant 60-day body weight.

Table 31. Spleen Weight and 60-day Body Weight Means; by Strain and Dosage

Dose r	Strain	Observed means[1] Body wt. grams	Observed means[1] S. wt. mgs.	Adj. means[2] Spleen wt. log	S.E.	Adj. means[1] Spleen wt. mgs.	Change from 0r mgs.	Change from 0r %	P[3] level
0	RI	24.35	94.9	1.977	±.031	94.8			at 38 df
20		24.74	123.0	2.092	±.031	123.6	+28.8	+30.4	.02-.01
200		26.37	112.0	2.060	±.034	114.8	+20.0	+21.1	.10-.05
400		23.47	115.5	2.057	±.032	114.0	+19.2	+20.3	.10-.05
800		23.26	144.0	2.151	±.032	141.6	+46.8	+49.4	<.0001
Strain means[1]		24.41	116.8						
0	Z	20.10	87.6	1.946	±.024	88.3			at 38 df
20		21.11	94.3	1.953	±.024	89.7	+ 1.4	+ 1.6	
200		19.25	83.1	1.944	±.024	87.9	- 0.4	- 0.5	
400		20.42	87.2	1.936	±.024	86.3	- 2.0	- 2.3	
800		20.26	112.0	2.048	±.024	111.7	+23.4	+26.5	.01-.001
Strain means[1]		20.22	92.3						
0	S	19.81	115.1	2.049	±.023	111.9			at 38 df
20		19.12	132.1	2.122	±.023	132.4	+20.5	+18.3	.05-.02
200		18.85	127.5	2.112	±.023	129.4	+17.5	+15.6	.10-.05
400		19.81	121.6	2.072	±.023	118.0	+ 6.1	+ 5.5	.50-.40
800		18.37	157.4	2.214	±.023	163.7	+51.8	+46.3	<.0001
Strain means[1]		19.18	130.0						

[1]Geometric means

[2]Adjusted to the mean 60-day body weight

[3]Significance of the difference between adjusted means; 0-20r, 0-200r, etc.

Table 32. Spleen Weight and 60-day Body Weight Means; by Strain and Dosage

Dose r	Strain	Observed means[1] Body wt. grams	S. wt. mgs.	Adj. means[2] Spleen wt. log	S.E.	Adj. means[1] Spleen wt. mgs.	Change from 0r mgs.	%	P[3] level
0	E	17.08	87.4	1.944	±.024	87.9			at 38 df
20		17.19	78.1	1.896	±.025	78.7	- 9.2	-10.5	.20-.10
200		17.31	78.5	1.899	±.025	79.3	- 8.6	- 9.8	.20-.10
400		16.21	82.7	1.915	±.024	82.2	- 5.7	- 6.5	.50-.40
800		15.42	106.8	2.021	±.026	105.0	+17.1	+19.5	.05-.02
Strain means[1]		16.63	86.1						
0	L	19.30	106.0	2.024	±.036	105.7			at 38 df
20		19.05	114.1	2.056	±.035	113.8	+ 8.1	+ 7.7	.60-.50
200		17.84	87.6	1.943	±.035	87.7	-18.0	-17.0	.20-.10
400		17.93	96.7	1.986	±.035	96.8	- 8.9	- 8.4	.50-.40
800		17.30	149.7	2.177	±.036	150.3	+44.6	+42.2	.01-.001
Strain means[1]		18.27	108.9						
0	Ba	19.57	118.3	2.045	±.024	110.9			at 38 df
20		18.98	121.0	2.066	±.023	116.4	+ 5.5	+ 5.0	.60-.50
200		20.05	114.7	2.022	±.024	105.2	- 5.7	- 5.1	
400		18.91	125.7	2.084	±.023	121.3	+10.4	+ 9.4	.30-.20
800		14.11	144.5	2.258	±.035	181.1	+70.2	+63.3	<.0001
Strain means[1]		18.18	124.4						

[1]Geometric means

[2]Adjusted to the mean 60-day body weight

[3]Significance of the difference between adjusted means; 0-20r, 0-200r, etc.

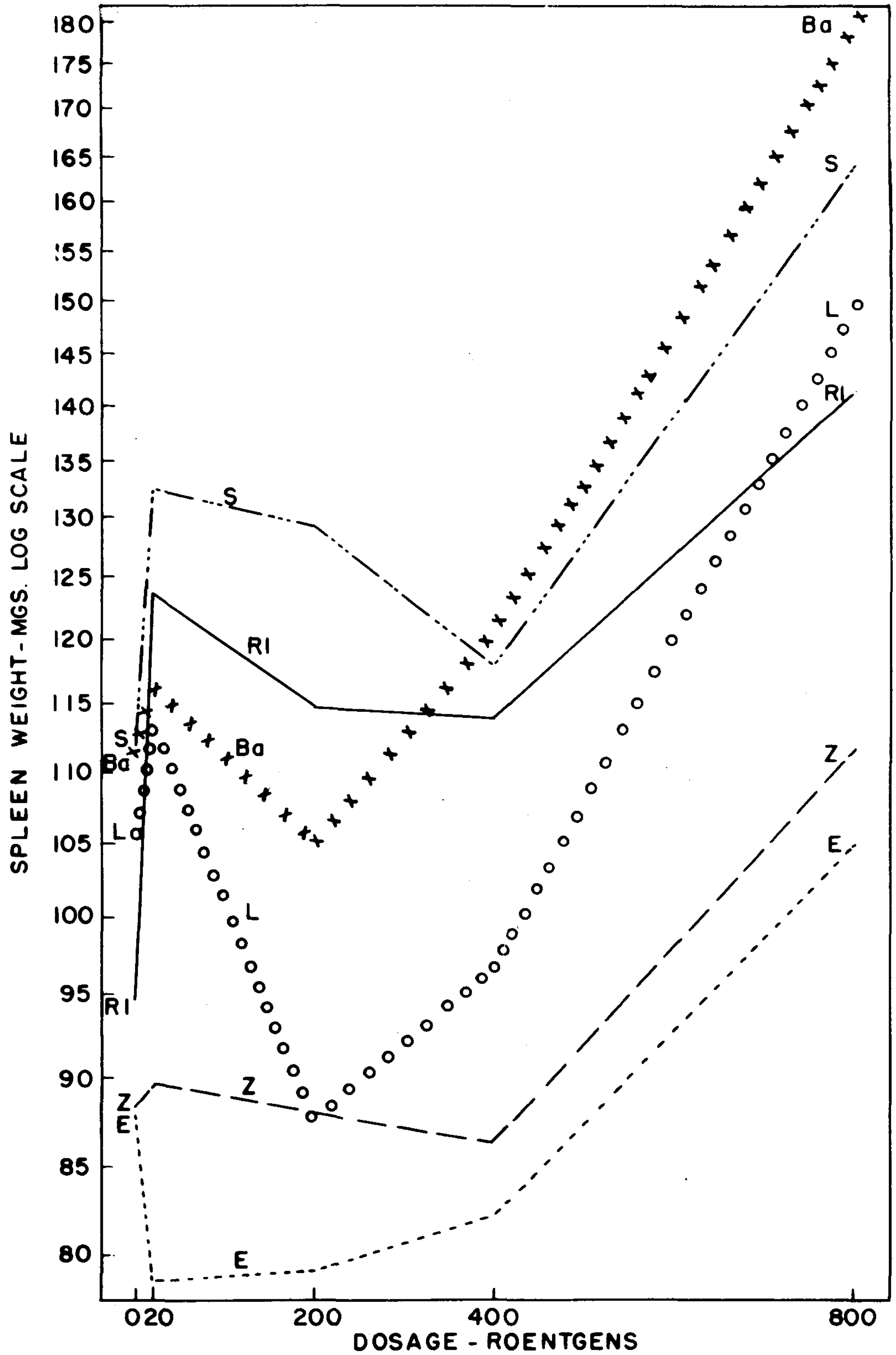

Figure 19. Spleen weight. Strain means by dosage. Each set of values adjusted to its respective constant 60-day body weight.

the controls, but less significantly than in the other strains.

The significant 20r increase is maintained throughout by strains RI and S, while only a minor increase and recession occurs in strain Z at the lower doses. Strains L and Ba show increases of 7.7 per cent and 5.0 per cent, respectively, at 20r, but these are not significant changes. Both strains show a recession to below the control weight at 200r, which is followed by a steady rise toward the 800r level. Although the increase in spleen weight at 20r is generally manifest, it is statistically significant in only two strains, RI and S, where increases of 30 per cent and 18 per cent have occurred.

Confirmation of the 20r reaction can be seen histologically. Investigations being carried out in this laboratory clearly indicate that, on the average, there is an increase in total white pulp at 20r, followed by a decrease at all other doses. In addition, a sharp increase in the amount of erythro- and myelo-poiesis occurs in the spleen after 20r, an increase that is maintained and developed further with increasing dose. Thus, there is an increased cellularity at 20r that would bolster the significance of the gross weight increase. The density of the tissue apparently decreases at 200r and 400r due to a partial loss of lymphoid tissue, while the gross hyperplasia at 800r is primarily due to increases in other hematopoietic tissue. Although the knowledge of spleen weight aids in the understanding of splenic reaction to irradiation, it would seem that knowledge of splenic volume, density, and linear dimensions would be necessary before the picture can be complete.

The 20r response observed in the study reported here is considered a secondary radiation response that rests on two factors. Primarily, the spleen is injured to only a very limited degree from this low dose, and, secondly, it fully retains its capacity to respond as it would to an inflammatory agent. A low grade toxemia is probably existing as a result of the total body exposure, and this persistent condition has acted to stimulate the normal defense mechanisms of the animal body. The result is a slight increase in spleen weight and productivity.

Increases in spleen weight at 400r and 800r are also considered as secondary radiation response mechanisms. Since these weight estimates are 20 days after exposure, it is felt that they reflect the animal's attempt to overcome the initial destructive effects of the radiation. At the higher doses, they represent the normally observed regeneration and over-compensation.

The component analysis findings are given in Table 33. Over-all radiation effects account for 15.5 per cent of the variation, while strain and sex differences in radiation response are nil. The basic strain differences in spleen weight contribute about 22 per cent to the total variation, while a sex difference is barely measured. Environmental variation takes out 68 per cent of the total, with the E:L ratio being 2:1 as in the heart weight.

The absence of a significant value for the ST component is interesting. In the spleen, where radiation effects are

Table 33. Spleen Weight - Component Analysis

Component of variation	Percentage of total variation	Absolute variance
S - Strain effect	21.8	.0042246
T - Treatment effect	15.5	.0030033
ST - Strain x treatment effect	0.3	.0000542
L - Between litter effect	19.3	.0037375
F - Sex effect	0.1	.0000220
FS - Sex x strain effect	2.3	.0004514
FT - Sex x treatment effect	0.9	.0001820
FST - Sex x strain x treatment	0.3	.0000643
E - Sex x litter effect	39.5	.0076590
		.0193983

important, strain differences in response appear unimportant, on a relative scale. The opposite is true for the heart and kidney weights. Actually, the absolute value of the ST component is nearly of the same magnitude for the heart, kidneys, liver, and spleen. However, while the absolute total variation of the first three organs is similar, it is ten times as great in the spleen. Consequently, the ST component of the spleen becomes about one-tenth as large as for the other organs when expressed on a percentage scale. As a result, the relative importance of the various components can only be ascertained on a within-analysis basis, since between-analysis comparisons can be very misleading. The small amount of strain differentials in response of the spleen may actually be of greater biological importance than any of the other strain differences.

Testes weight - over-all radiation response

The results of the study on testes weights are given in Table 34. The weight progressively decreases with increasing dosage. The drop at 20r is not significant, but all other decreases are unquestionably so. It should be noted that of the maximum loss of 59.4 milligrams at 800r, 74 per cent of this loss has occurred by exposure to only 25 per cent of that dose, and 95 per cent of the loss by 50 per cent of the dose.

Radiation response by strain

As seen in Tables 35 and 36 and in Figure 20, the six strains react in a nearly parallel manner and show a dosage relationship like that described above. Only in strain S does a notable difference exist, wherein the 800r testes weight is heavier than at 400r. The observed testes weight at 800r is a few milligrams lighter than at 400r, but the two gram difference in body weight, at these doses, is sufficient to bring the adjusted weight of the 800r group above the 400r mean weight. Whether this indicates that strain S is capable

Table 34. Testes Weight and 60-day Body Weight Means; by Dosage

Dose	Sex	Observed means[1]		Adj. means[2]	S.E.	Adj. means[1]	Change from 0r		P[3] level
r		Body wt. grams	T. wt. mgs.	Testes wt. log		Testes wt. mgs.	mgs.	%	
0	♂	21.84	137.8	2.113	±.008	129.7			at 118 df
20		21.73	130.7	2.092	±.008	123.6	-6.1	-4.7	.10-.05
200		20.86	86.2	1.934	±.008	85.9	-43.8	-33.8	<.0001
400		20.77	72.7	1.863	±.008	73.0	-56.7	-43.7	<.0001
800		18.99	62.6	1.847	±.008	70.3	-59.4	-45.8	<.0001
Male means[1]		20.81	93.3						

[1]Geometric means

[2]Adjusted to the mean 60-day body weight

[3]Significance of the difference between adjusted means; 0-20r, 0-200r, etc.

Table 35. Testes Weight and 60-day Body Weight Means; by Strain and Dosage

Dose r	Strain	Observed means[1] Body wt. grams	Observed means[1] T. wt. mgs.	Adj. means[2] Testes wt. log	S.E.	Adj. means[1] Testes wt. mgs.	Change from Or mgs.	Change from Or %	P[3] level
0	RI	26.45	133.9	2.119	±.016	131.5			at 18 df
20		26.58	124.3	2.084	±.016	121.3	-10.2	- 7.8	.20-.10
200		27.87	93.8	1.935	±.017	86.1	-45.4	-34.5	<.001
400		25.09	66.1	1.844	±.016	69.8	-61.7	-46.9	<.001
800		24.72	61.7	1.823	±.016	66.5	-65.0	-49.4	<.001
Strain means[1]		26.12	91.4						
0	Z	21.78	139.6	2.135	±.012	136.5			at 18 df
20		22.94	138.8	2.106	±.012	127.6	- 8.9	- 6.5	.20-.10
200		19.06	80.1	1.962	±.013	91.6	-44.9	-32.9	<.001
400		21.69	86.5	1.929	±.012	84.9	-51.6	-37.8	<.001
800		21.51	76.4	1.880	±.012	75.9	-60.6	-44.4	<.001
Strain means[1]		21.36	100.5						
0	S	22.02	189.0	2.254	±.014	179.5			at 18 df
20		21.34	169.1	2.222	±.013	166.7	-12.8	- 7.1	.20-.10
200		20.50	98.2	2.008	±.013	101.9	-77.6	-43.2	<.001
400		21.98	93.1	1.947	±.014	88.5	-91.0	-50.7	<.001
800		19.80	90.4	1.990	±.014	97.7	-81.8	-45.6	<.001
Strain means[1]		21.11	121.4						

[1] Geometric means

[2] Adjusted to the mean 60-day body weight

[3] Significance of the difference between adjusted means; 0-204, 0-200r, etc.

Table 36. Testes Weight and 60-day Body Weight Means; by Strain and Dosage

Dose r	Strain	Observed means[1] Body wt. grams	Observed means[1] T. wt. mgs.	Adj. means[2] Testes wt. log	S.E.	Adj. means[1] Testes wt. mgs.	Change from 0r mgs.	Change from 0r %	P[3] level
0	E	18.42	105.2	1.990	±.023	97.7			at 18 df
20		18.43	103.8	1.983	±.023	96.2	- 1.5	- 1.5	.90-.80
200		18.36	76.2	1.852	±.023	71.1	-26.6	-27.2	<.001
400		17.16	53.1	1.745	±.023	55.6	-42.1	-43.1	<.001
800		15.91	44.8	1.726	±.024	53.2	-44.5	-45.5	<.001
Strain means[1]		17.63	72.3						
0	L	21.53	115.2	2.013	±.031	103.0			at 18 df
20		21.31	102.1	1.967	±.031	92.7	-10.3	- 1.0	.30-.20
200		18.78	60.7	1.818	±.031	65.8	-37.2	-36.1	<.001
400		19.10	54.0	1.756	±.030	57.0	-46.0	-44.7	<.001
800		18.83	45.3	1.689	±.031	48.9	-54.1	-52.5	<.001
Strain means[1]		19.87	70.6						
0	Ba	21.56	160.1	2.173	±.012	148.9			at 18 df
20		20.63	161.1	2.191	±.012	155.2	+ 6.3	+ 4.2	.30-.20
200		21.93	119.7	2.040	±.012	109.6	-39.3	-26.4	<.001
400		20.48	96.7	1.972	±.012	93.8	-55.1	-37.0	<.001
800		14.38	69.4	1.940	±.017	87.1	-61.8	-41.5	<.001
Strain means[1]		19.71	115.7						

[1]Geometric means

[2]Adjusted to the mean 60-day body weight

[3]Significance of the difference between adjusted means; 0-20r, 0-200r, etc.

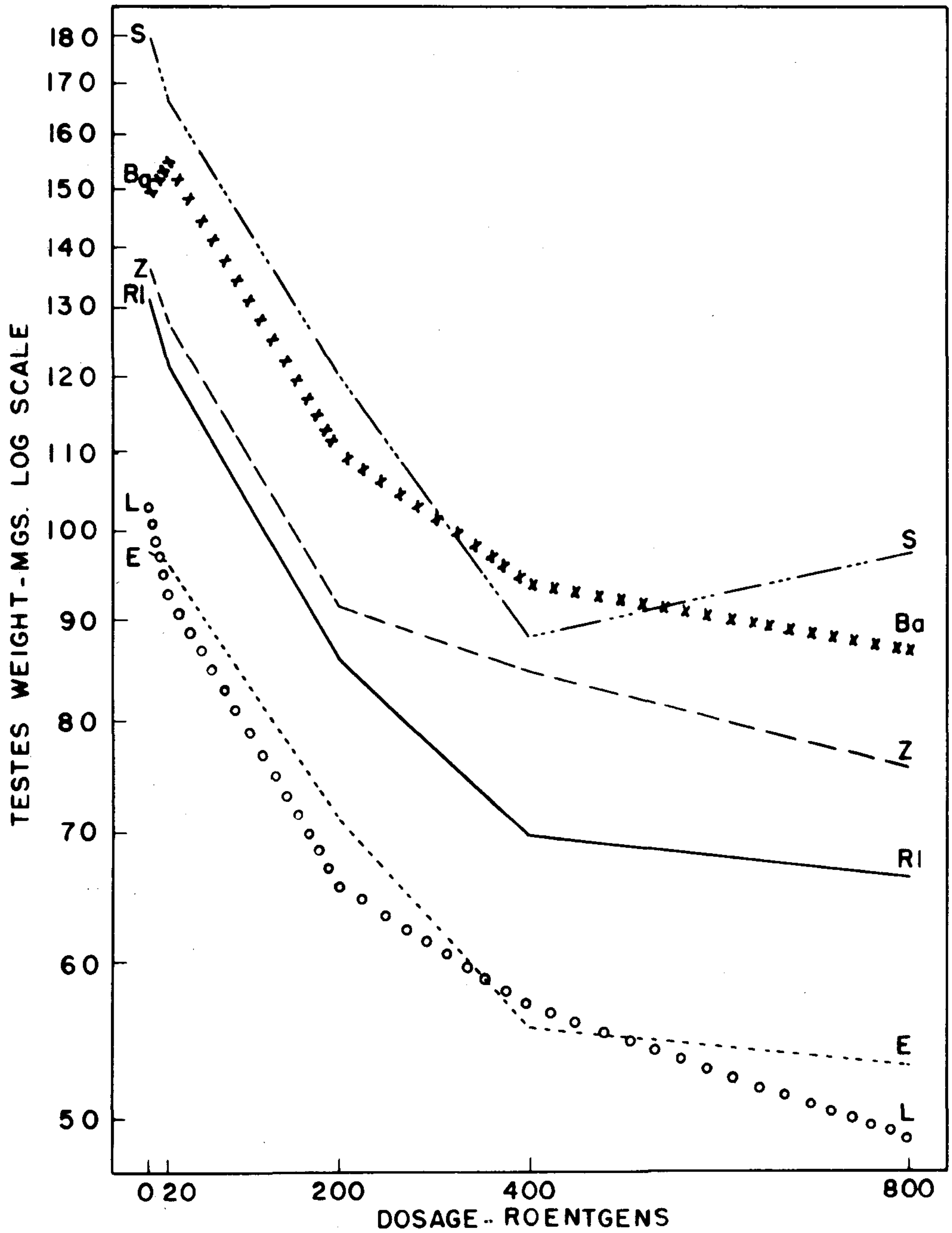

Figure 20. Testes weight. Strain means by dosage. Each set of values adjusted to its respective constant 60-day body weight.

of resisting further organ weight loss in spite of body weight loss cannot be stated with certainty.

The component analysis of testes weight, in Table 37, underlines the magnitude of the radiation effect and the similarity of the strains in their response. Less than 2 per cent of the variation is due to strain differences in response, while 50 per cent is due to the general effects of the radiation. A basic 35 per cent of the variation lies in strain differences in testes weight, and the remaining 13 per cent is attributed to random variation.

Table 37. Testes Weight - Component Analysis

Component of variation	Percentage of total variation	Absolute variance
S - Strain effect	35.2	.0097855
T - Treatment effect	50.0	.0139127
ST - Strain x treatment effect	1.8	.0004974
L - Between litter effect	13.1	.0036350
		.0278306

The weight loss of the testes following irradiation has been attributed to the cessation of spermatogenesis and progressive loss of the germinal elements (Eschenbrenner and Miller, 1950). They have shown that it is the spermatogonial cells which are affected by the radiation, the other germinal cells being resistant. Mature sperm continue to develop from the primary spermatocyte stage and on, but spermatogonia cease to produce primary spermatocytes. As well, these authors noted a high correlation of weight loss with dosage from 50r to 400r in mice and concluded that the testes are excellent material for quantitative radiobiological studies.

The rapidity of the loss, and its reverse multiplicative nature, is emphasized in Figure 21. In this graph, dosage has been transformed to a logarithmic scale, so that the weight and dose relation is now on a log-log basis. The linear relationship is obvious between 20r and 800r, but it cannot be integrated with the control weight.

The observed linearity of the dosage relationship has been used to determine the possible existence of strain differences in sensitivity, as measured by the value of the regression. The minor differences in slope that exist are not significant. This indicates a uniform sensitivity of the germinal tissue regardless of known differences in the involved genotypes. The weight loss is assumed to be a primary destructive response. The regressions, standard errors, and correlations are given in Table 38.

The decline of testes weight with increasing dosage can be made to fit a simple exponential curve. In order to do this, a constant weight must be removed from the mean testes weights. This constant, which differs for each strain, is approximately equal to the value toward which the weights are

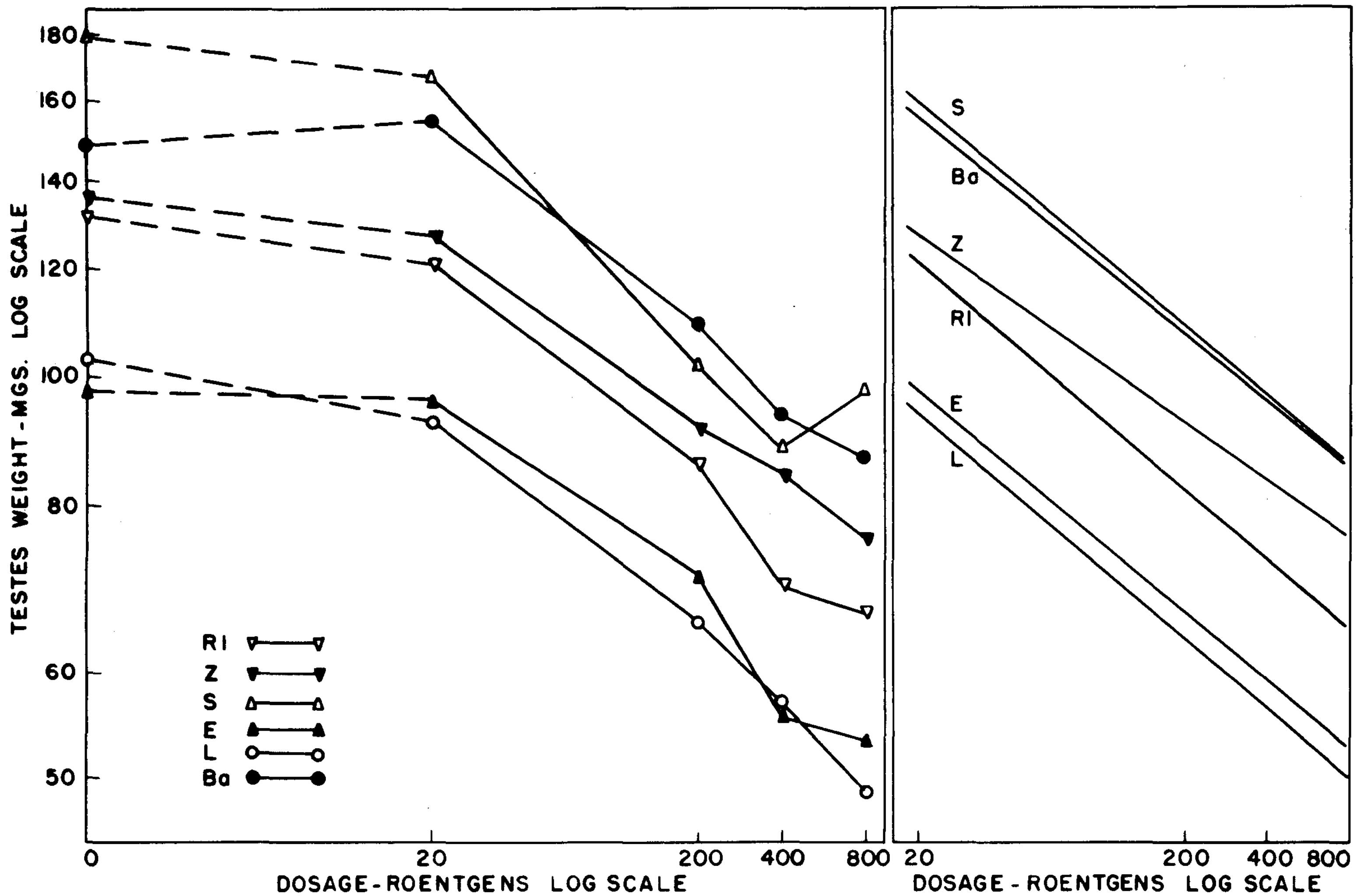

Figure 21. Relationship of testes weight to dosage (left); regression of weight on dosage: 20 to 800r (right).

asymptoting at 800r (see Figure 20). The adjusted testes weights are used in this procedure. The removal of a constant weight from each adjusted mean is consistent with the assumption of the existence of a constant quantity of testicular

Table 38. Regressions and Correlations of Testes Weight on Dosage. Logarithmic Scale.

Strain	Regression	S.E.	Correlation
RI	-.1694	±.0173	-.990
Z	-.1397	±.0040	-.999
S	-.1655	±.0440	-.936
E	-.1667	±.0241	-.980
L	-.1695	±.0120	-.995
Ba	-.1599	±.0090	-.997
Avg	-.1602	±.0140	-.992

tissue that either is not destroyed or is not susceptible to destruction at the given doses. This general procedure for correcting values to fit an exponential has been described by Price and Gowen (1937) in deriving exponential survival curves of tobacco mosaic virus after ultra-violet radiation.

The equation for the exponential curve is:

$$Y = ae^{-kD} + C,$$

where Y is the testes weight, a is the y intercept, C is the estimated constant removed for correction, k is the slope constant, D is dosage, and e is the basis for natural logarithms. The logarithm of the quantity (Y-C) is plotted against dosage on an arithmetic scale. When the best estimate of C is made, a nearly straight line results. These plots are given in Figure 22 and the resulting exponential equations are given in Table 39.

Table 39. Exponential Equations of Testes Weight Loss with Dosage; Derived from Corrected Weights.

Strain	Equation	Correlation
RI	$Y = 65.5e^{-.00679D} + 66.2$	- .998
Z	$Y = 58.8e^{-.00513D} + 75.0$	- .995
S*	$Y = 94.8e^{-.00866D} + 85.5$	-1.000
E	$Y = 51.3e^{-.00695D} + 53.0$	- .996
L	$Y = 50.9e^{-.00440D} + 47.4$	- .998
Ba	$Y = 73.3e^{-.00612D} + 86.6$	- .998
Avg.	$Y = 60.5e^{-.00721D} + 70.1$	- .999

*Derived from 0-400r data only.

The linearity of the fit is obvious from the consistently high correlations. The slope constants, ranging from -.00440 to -.00866, again indicate the similarity of response of the different strains. As the 800r value for strain S would not fit the curve, only the first four dosage means have been used for deriving the equation for this strain.

The value of C, on the average, is equal to 52 per cent of the control weight, ranging from 46 per cent to 58 per cent

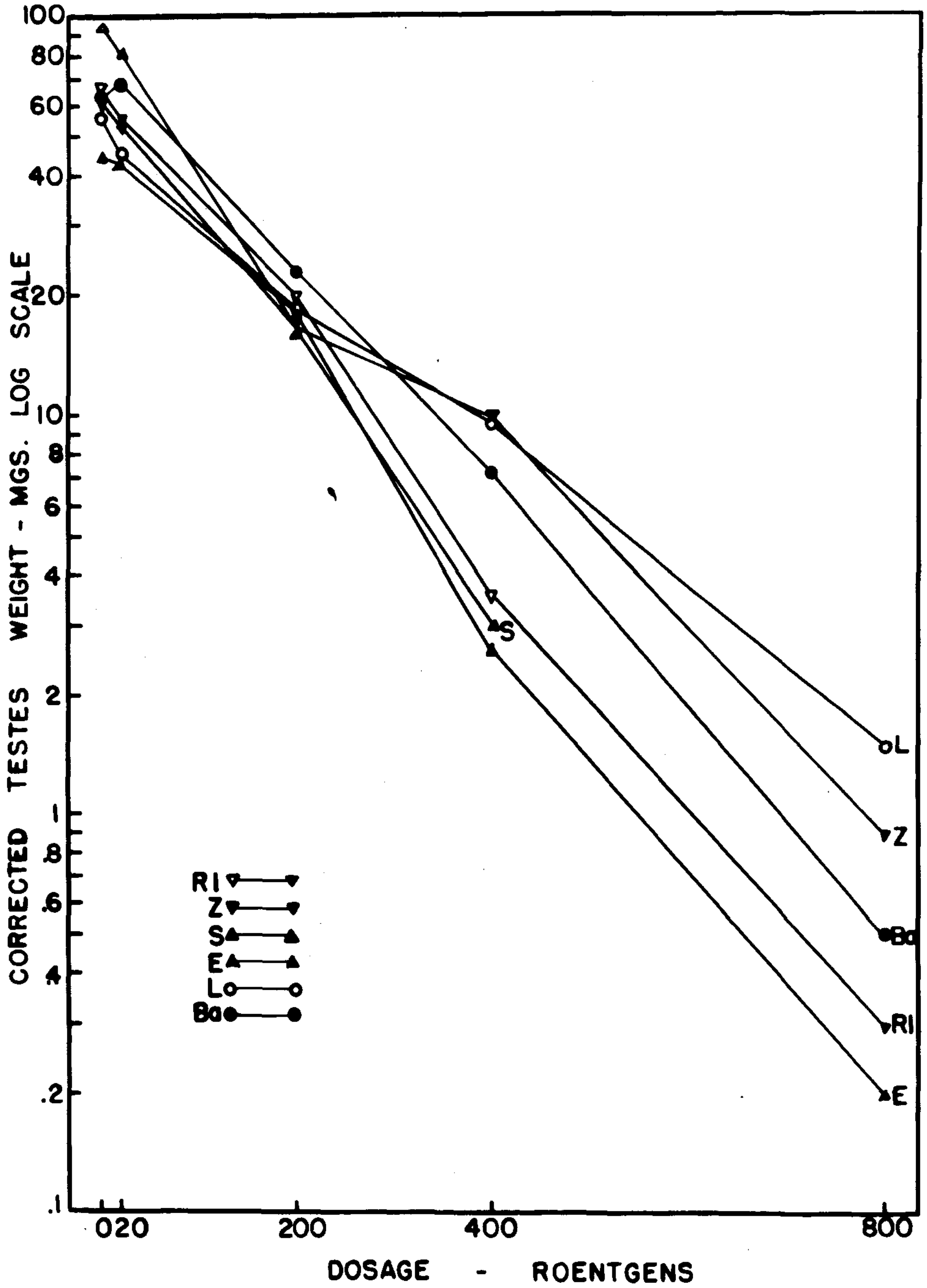

Figure 22. Exponential decline of testes weight with dosage. Weights corrected by removal of estimated lower asymptotic value.

for the six strains. Thus, twenty days after exposure, approximately 50 per cent of the testicular tissues remain either uninjured or incapable of being injured. The latter would include the interstitial and supporting tissues. Eschenbrenner, et al. (1948) have shown the interstitial tissue to be resistant, although it makes up only about 5 per cent of the normal testes weight. The remaining portion would be resistant connective tissues and uninjured germinal tissue. The exponential decline in weight clearly fits the single hit theory reviewed by Lea (1947). Apparently, the loss of germinal tissue is due to a constant relative rate of spermatogonial death with increasing dosage.

These same six strains of mice have been shown to respond to x-ray in an exponential manner on the basis of several other criteria. Gowen and Zelle (1945) observed an exponential reduction of survival from mouse typhoid after irradiation. Gowen (1948) had indicated that the total leucocyte count is exponentially reduced by x-irradiation. The slope constants derived from these different responses are considerably lower than those for the testes weight. However, since different time factors are involved, straight comparison cannot be made.

Integration of organ weight response to irradiation

A single sample of the organ weights leaves unanswered the most essential clues to relative importance; the rates, times, and magnitudes of organ weight loss and recovery. An attempt to overcome this deficiency was made by exposing an additional group of the most susceptible mice (strain Ba) to 800r. Four unirradiated litter-pairs of one male and one female were killed at 40 days of age as controls. At the ages of 42, 45, 50, and 55 days, four irradiated litter-pairs were killed, exposure having been made at the age of 40 days. The results are given in Figure 23.

The percentage change in body weight is measured from the observed initial weight, while organ weight changes have been determined from a calculated expected initial weight. This was accomplished by determining the organ:body weight ratios in the 40-day controls and then estimating the 40-day organ weights of the irradiated mice by equating the control ratio to the term: x/observed 40-day body weight. The 60-day points are estimated on the basis of the full study results, but they are no more reliable than the others since the 40-day estimate is the controlling factor.

The data of Figure 23 show that the heart and kidneys lose proportionately less weight than the whole body from the second post-irradiation day and beyond. The liver fluctuates with the body weight loss. The weight of the testes declines very slowly at first but is apparently in a continued phase of loss throughout the 20-day interval. The spleen is strikingly reduced in weight to 21 per cent of its initial weight in two days and to 17 per cent in five days. True

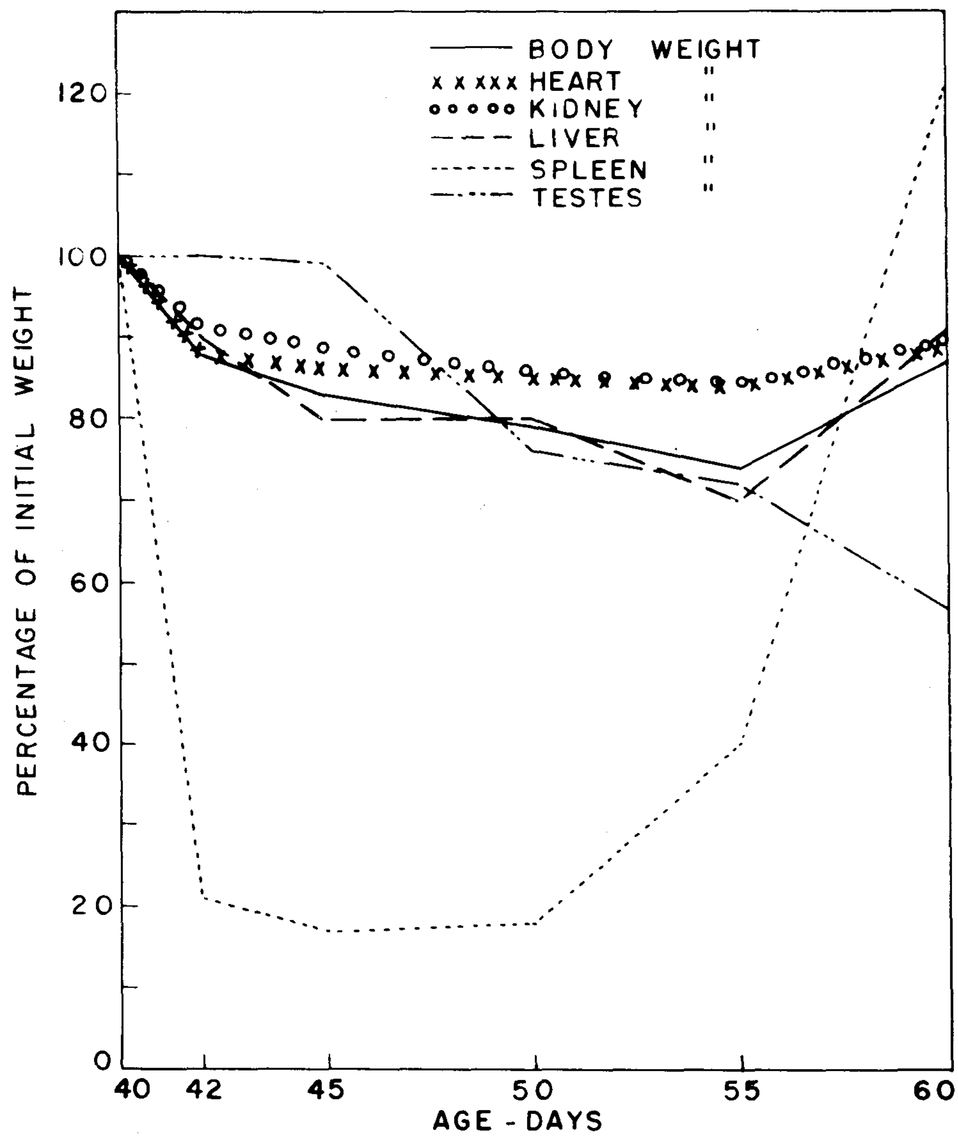

Figure 23. Sequential organ and body weight changes in strain Ba at 800r. Body weight changes from observed initial weight, organ weight changes from expected initial weight.

recovery does not start until at least the tenth post-irradiation day. The recovery is rapid in the last five days, and a 20 per cent over-compensation occurs.

Since loss and recovery of weight of the heart, kidneys, and liver are concomitant to the body weight response, some of the strain differences may result from a varying resistance to this inanitional type of loss, or to a greater ability to return to normal. Specific responses, such as a cardiac hypertrophy, would be super-imposed on the above reactions. Unfortunately, this brief study throws little light upon the problem of increased liver size 20 days after irradiation. The testes response confirms the assumption that this organ is still in a primary effect phase, the expression of which is apparently independent of genetic factors. A study of the recovery of testes weight, however, would permit genetic differences in regenerative capacity to become expressed.

Thus, only the spleen has gone through a series of changes that can permit clear expression of genetic differences in response. Although the maximum loss and recovery rate factors are not known, the stage of recovery and regeneration is reflected in the data. Genetic differences observed in splenic response are probably of the greatest importance and should be elucidated over a complete range of dosages, ages, and time intervals. The importance of the spleen in radiation response and resistance is emphasized by the post-irradiation therapy studies of Cronkite, Brecher, and Chapman (1951b) and the spleen-shielding studies reviewed by Jacobson (1952).

Although one of the original purposes of the investigation was to study the organ:body weight regressions and correlations, these have provided nothing of substantial or unequivocable biological value. Similarly, the inter-organ partial correlations gave no definite indication of organ changes not otherwise observable. These regressions and correlations are given in Appendix A.

In Figure 24, the adjusted means, at each dosage level, are averaged for the three resistant (RI, Z, S) and three susceptible (E, L, Ba) strains. Resistance and susceptibility are based on the body weight response previously described.

The most obvious difference between these two groups of mice lies in the basic body weight difference. The resistant mice are initially, and throughout, heavier than the susceptible mice. Between 400r and 800r, the susceptible mice lose a greater amount of weight than the resistant mice, but below 400r the reactions of the two groups are similar.

The heart, kidney, and testes weights run in an essentially parallel manner in both groups. The consistent difference between the organ weights of the two groups is merely a reflection of the average body weight difference and does not reflect a response difference. The liver weight of the susceptible mice shows a greater average increase at 800r, but they are parallel to the resistant mice from 0r to 400r.

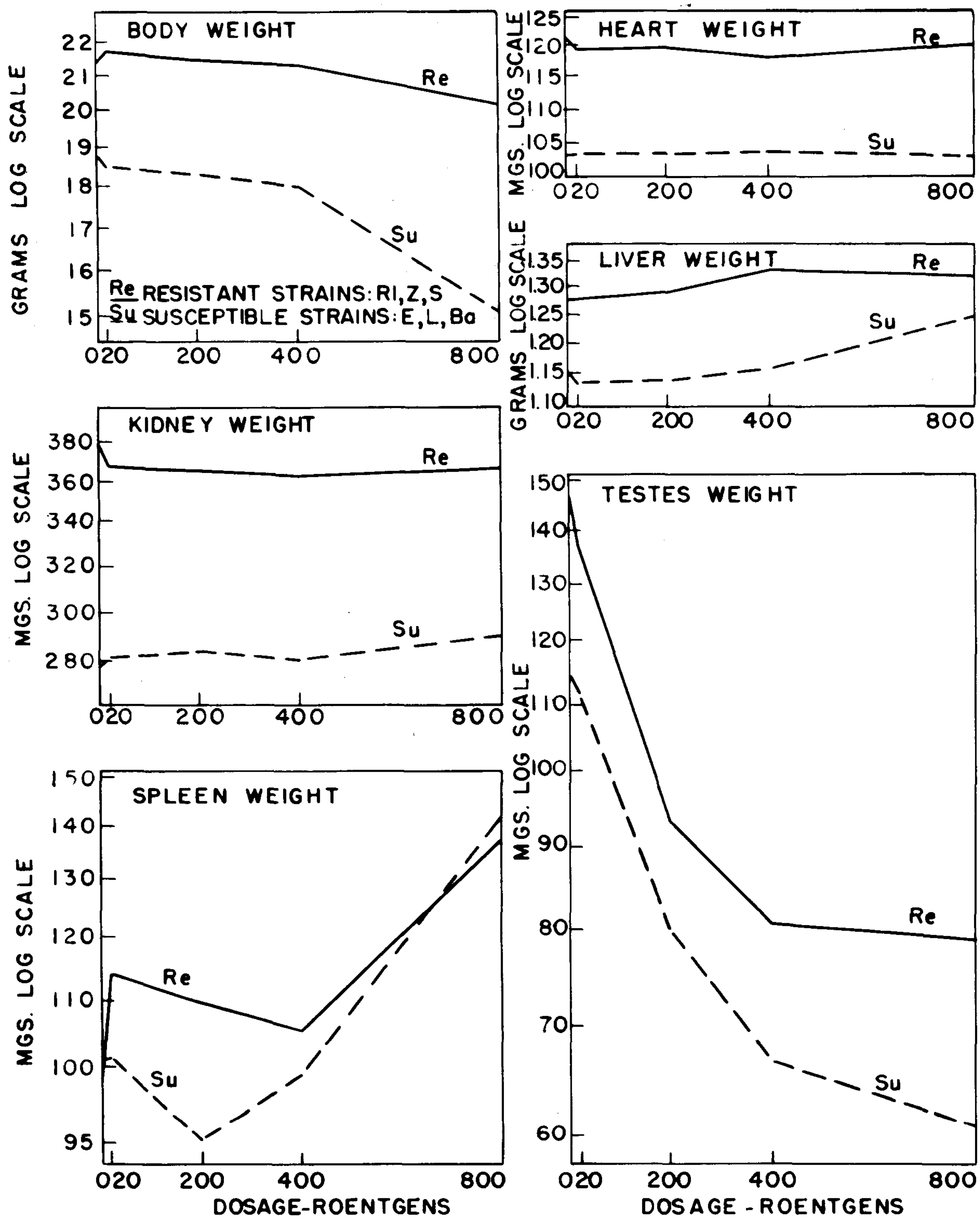

Figure 24. Summary of differences in body and organ weight reactions in the resistant (RI, Z, S) and susceptible (E, L, Ba) strains.

In the controls, the spleens of the susceptible mice are a little heavier than those of the resistant mice, indicating a considerable difference in relative weight. In spite of this initial advantage, the susceptibles are much less capable of favorably responding at 20r, possibly indicating that their normal defense mechanisms are not able to respond as actively to stress. At 200r, the susceptibles are below their control weight, while the resistant mice are maintaining the 20r increase. Between 200r and 400r, the susceptible mice increase as the resistants decrease to a slight degree. The latter are still above their control weight, while the susceptibles have not yet regained their control weight. The 800r response is greater in the susceptible mice, and they again become heavier than the resistant mice. At 200r and 400r, the susceptible mice apparently show a poorer degree of regeneration, while at 800r genetic differences are lost. This latter point is illustrated by the perfectly parallel lines that would connect the 0r and 800r weights of the two groups.

The necropsy records that were obtained were not sufficient to show whether strain differences existed in the incidence of characteristic lesions. Neither was it always possible to determine the immediate cause of death. The most frequent gross lesion was a pulmonary hemorrhage with a pleural effusion. The sternal and costal marrow cavities were sharply defined, due to either early congestion, subsequent hyperplasia, or both. The spleens appeared atrophic, while the livers were occasionally reduced in size, sometimes to nearly one-half normal size. The hearts and kidneys were usually unaffected. The mesenteric, superficial inguinal, and auxillary lymph nodes appeared atrophic and were occasionally hemorrhagic. Grossly, the appearance of the small intestine varied from an anemic through normal to a hyperemic state. Peyer's patches appeared hemorrhagic and atrophic. Petechial hemorrhages sometimes were seen in the dorsal integument, the cerebrum, cerebellum, and medulla. Suffuse hemorrhage was occasionally seen following the lines of the folds of the gastric mucosa. Massive hemorrhage was seen on only one occasion when death clearly occurred from an intestinal perforation and hemorrhagic peritonitis.

The presented data on body and organ weights have clearly indicated that genetic differences in radiation response do exist. For the most part, these are quantitative differences, though qualitative differences in response have been pointed out. It is felt that the observed differences are important enough to cause an extremely variable response to irradiation if a tight control is not placed upon the genetic quality of the experimental animals.

DISCUSSION

The body weight data of this investigation are of sufficient continuity and reliability to permit conception of certain theoretical considerations. Since these data are of a gross nature, the questions of the physiological or cellular basis of the genetic differences cannot be discussed in positive terms. Rather, it is hoped that the biological area of these differences can be outlined, and that an integrated theory of the biological basis of the radiation response can be put forth.

The body weight itself has been considered a factor in resistance, although this rests on contradictory evidence. Quastler (1945) and Quastler, et al. (1951) showed that the heavier mice had a greater survival time than the lighter mice after x-irradiation. Abrams (1951) denied a weight effect upon survival rate that could be considered independent of age. He did not mention survival time, however. All of these studies involved sufficient data to give reliable results, but in the study by Abrams, the weight range in the age groups of mice x-rayed was narrow. For example, his 45-day-old mice ranged from 16-21 grams, the 60-day group from 18.5-22.5 grams. This narrow range may have accounted for the absence of weight effect.

Hagen, *et al.* (1944) demonstrated a greater resistance of heavier rabbits to the lethal effects of x-rays. Ely and Ross (1947), studying rats exposed to neutrons, showed that heavy rats were more resistant than light rats, when both groups were of the same age. Naiman (1949) has also shown that heavier rats resist the lethal effects of x-ray in the dose range of 300r to 500r.

Several features of the present investigation confirm the hypothesis of greater resistance with greater weight. It has been pointed out that the three resistant strains are heavier mice on the average than the three susceptibles. The correlation between the estimated resistance levels and the observed initial weights of these six strains is +.201. In other words, about 4 per cent of the genetic variation in body weight response is related to initial genetic variation in body weight.

Further substantiation lies in the between-strain regressions and correlations of weight change on initial weight, within each age and dosage level. These are given in Table 40. At 0r, 20r, and 200r, these regressions and correlations are always negative, that is, the heavy strains have a lower gain than the light strains. At 200r, where definite weight losses initially occur, the heavier strains are losing more weight than the others.

At 400r and 800r, the reverse is true. Over the first ten days, the heavier strains are actually losing less or gaining more than the light ones. This condition is maintained throughout the 20-day period at 800r, while the approach to full recovery at 400r is keynoted by a return to a normal negative interrelationship of gain and weight. These positive

Table 40. Between-Strain Regressions and Correlations of Weight Change on Initial Weight

Dose		Weight change interval (days)					
		40-41	40-42	40-45	40-50	40-55	40-60
0r	b	-.006	-.002	-.055	-.053	-.142	-.227
	r	-.069	-.020	-.438	-.399	-.662	-.703
20r	b	-.008	-.031	-.045	-.051	-.088	-.037
	r	-.174	-.355	-.299	-.291	-.376	-.153
200r	b	-.024	-.039	-.038	-.094	-.148	-.142
	r	-.370	-.524	-.285	-.465	-.624	-.582
400r	b	+.024	+.029	+.043	+.030	-.023	-.067
	r	+.357	+.379	+.289	+.133	-.078	-.223
800r	b	+.059	+.003	+.116	+.095	+.136	+.161
	r	+.532	+.024	+.300	+.149	+.138	+.182

values, at the higher doses, emphasize the ability of the genetically heavier strains to resist weight loss and enter a phase of weight recovery to a greater degree than the lighter strains.

Evidence that, within the strains, heavier nice tend to be more resistant is provided by the average within-strain between-litter regressions and correlations, given in Table 41.

The regressions and correlations, at each age level, from 0r to 400r are noticeably similar. Thus, in normal growth and under the effects of x-ray up to a dose of 400r, the heavier mice in a strain can be expected to gain less or lose more

Table 41. Between-Litter Regressions and Correlations of Weight Change on Initial Weight

Dose		Weight change interval (days)					
		40-41	40-42	40-45	40-50	40-55	40-60
0r	b	-.079	-.094	-.220	-.359	-.443	-.580
	r	-.434	-.369	-.679	-.814	-.872	-.907
20r	b	-.081	-.123	-.277	-.376	-.457	-.541
	r	-.475	-.488	-.760	-.820	-.812	-.832
200r	b	-.072	-.074	-.181	-.195	-.268	-.363
	r	-.389	-.340	-.569	-.438	-.488	-.595
400r	b	-.098	-.105	-.204	-.320	-.395	-.489
	r	-.484	-.496	-.567	-.747	-.784	-.827
800r	b	-.061	-.045	+.004	-.063	-.224	-.313
	r	-.274	-.171	+.011	-.143	-.365	-.465

weight. However, at 800r, the regressions are consistently lower, and five days after exposure it becomes slightly positive, indicating that during the early period of recovery, the heavy mice are showing a greater gain or lesser loss than the light mice.

Since nearly all the strains, at 400r and 800r, have entered a phase of weight recovery between the second and fifth post-irradiation days, this interval should be a critical one for determining the ability of heavy mice to respond more favorably. The between-litter regressions are: for 400r, -.099; for 800r, +.049. The respective correlations are -.414 and +.175. Thus, at this turning point age interval, the heavy mice of a strain are definitely recovering more adequately at 800r.

There seems to be no clear-cut reason for this capacity of larger mice to respond less severely to irradiation. Since this situation exists within a homogeneous group of mice, it may be that environmental features which enabled the mouse to attain a greater weight at a given age may be reflected in the mouse's ability to withstand injury to a greater degree. The greater weight may also reflect a more complete state of maturity, in spite of chronological age similarity. The more mature mice are known to be more resistant. Quastler (1945) and Abrams (1951) both agree on this point.

However, since heavier strains also show greater resistance, the point of environmental factors becomes inadequate, as environmental fluctuations should be the same within all strains. Whether or not, at a given age, the greater weight of a strain reflects a higher state of maturity cannot be positively maintained, since the breeding behavior of the heaviest strain, RI, would not support this contention.

This leaves two postulations. It can be logically assumed that heavier mice, whether within a strain or as a strain in themselves, due to this greater weight, have a greater tissue reserve. If a given dosage of radiant energy must destroy a given proportion of the total tissue, the larger animals may be better able to spare this tissue with less serious effects. This would be particularly true if the heavier animals had proportionately greater muscle mass and fat deposition, which, through depreciation, could provide the energy for physiological maintenance during the acute period of radiation response.

Secondly, it can be postulated that a certain degree of unanimity exists in the genetic factors controlling growth, body weight, and a resistance to irradiation. Obviously, and unfortunately, these postulates cannot be extrapolated to other species, since existing data indicates that heavier and larger species are generally more susceptible to external x-irradiation.

The characteristic weight response has been the subject of investigation by others in an effort to determine its physiological basis. A decreased food intake always parallels the weight losses. Prosser (1947) and Kirschner, Prosse, and Quastler (1949) reported that greater losses occurred in irradiated dogs than in those kept on a food allowance equivalent to what the irradiated animals consumed. An increased rate of protein catabolism was considered to make up the difference.

Hagen, et al. (1944) believed that decreased food intake of x-rayed rabbits accounted for the weight loss, but offered no control data for comparison. Ely and Ross (1947), in neutron irradiated rats, found that the weight loss was the same in unirradiated and irradiated animals, when the food intake of the former was limited to that of the irradiated rats. Recovery was complete only in the unirradiated group, however.

If unirradiated rats are fasted, then the weight loss is equivalent to full-fed, irradiated animals (Smith, D. E., et al., 1951), but fasted mice may lose more weight more rapidly than irradiated mice at doses in the lethal range (Smith, W. W., et al., 1952). In addition, Smith, D. E., et al. showed that combined starvation and irradiation caused no greater weight loss than irradiation alone. It would seem, then, that whatever food is consumed is virtually unutilized to combat weight loss. Apparently, irradiated animals are in a transient period of complete starvation.

There is complete agreement between many investigators on the existence of a short period of increased gastric retention following irradiation. This has been seen by Leitch (1947) and Ely and Ross (1947) in neutron irradiated rats, and it was stated to last for two or three days after exposure. Bennett, et al. (1951) observed an increased retention in mice at 600r of x-ray, as did Smith, W. W., et al. (1952) in the same species at the same dose. The latter authors noted that the gastric contents were static for the first three days after exposure. Goodman, Lewis, and Schuck (1952), in a study on rats exposed to 450r of x-ray, demonstrated that the maximum retention occurred 48 hours after exposure, then slowly returned to normal.

It is obvious that the periods of gastric retention and weight loss are coincident. It is likely that this retention creates the condition of starvation, even when food is being consumed. Since force-feeding was shown to be of no help, and was even detrimental (Smith, W. W., et al., 1952), the decreased food intake that follows irradiation is probably the animal's expression of diminished desire to consume food. Because of the progressive nature of the reaction, it is undoubtedly a secondary effect resulting from neural or humoral stimuli. Variation in the time, degree, and extent of occurrence of this retention may be responsible for some of the genetic differences in weight response. Strains that recover quickly may show a minimum degree of retention that is rapidly overcome.

Conard (1951) has demonstrated an increased motility of the small intestine of rats exposed to x-rays soon after exposure. By the third hour, however, the propulsive motility is reduced to below normal, remaining there for about three days. The increase in motility was shown to be due to a stimulation of the parasympathetic nerves at the level of the enteric ganglia. Goodman, et al. (1952), however, found intestinal motility unaffected, and assumed that a decrease in intestinal contents was a reflection of the gastric retention. Bennett, et al. (1951) could not demonstrate any change of absorptive ability of the small intestine with respect to protein, although Curtis (1951) reported a complete inhibition of glucose absorption in the rat four hours after exposure to 50r. Variation in alterations of intestinal motility and absorption ability may also be basic to genetic differences in response, but these may be of lesser importance.

Jennings (1949) observed a sharp reduction in the $LD_{50/30}$ of rats on a low protein diet. Strain differences in response could exist, if unavoidable dietary deficiencies occurred in strains with excessive requirements that are not being met by the standard feeds.

X-irradiation can also create a state of partial physiological hypophysectomy, as shown by Denniston (1949). He created a definite growth retardation in rats by local irradiation of the pituitary gland. Selye (1946), whose General Adaptation Syndrome can be loosely applied to irradiation effects, considered that a stressor-induced increased production of adreno-corticotropic hormones from the anterior pituitary occurs at the expense of other hormone production. This includes a decreased output of growth hormones. Ellinger (1948) assumed that the adrenal gland is vital in radiation resistance, and that adrenal-cortical reactions may be responsible for many radiation responses. If an adrenal insufficiency resulted, death followed. Edelmann (1951) was able to increase survival of rats, at 800r, from 10 per cent to 65 per cent by lead-shielding the adrenals, indicating that direct effects of radiation are also important in this organ. Some genetic variation in growth and body weight response may arise from intrinsic differences in hormonal reactions that result from indirect radiation effects.

The six strains employed in the investigation have been studied in some detail with respect to their resistance to mouse typhoid (Gowen and Calhoun, 1943; Oakberg, 1946; Weir, 1949). Their twenty-one-day survival values, after intraperitoneal inoculation of 200,000 live organisms of *Salmonella typhimurium* for all strains, are summarized by Thompson (1951) on data collected in the period 1940-1950. The correlation between the typhoid survival values and the estimated radiation resistance to weight change is +.843. In addition, Jacobson and Marks (1947) reported that National Institute of Health LAF_1 mice, which are considered as radiation resistant, are also resistant to mouse typhoid and pneumonia.

Genetic differences in the reaction to typhoid, at the cellular level, may be basic to the correlation of radiation and disease resistance. Oakberg's (1946) histological observations indicated that the livers of resistant strains are better able to wall off typhoid lesions, while the uninjured cells retain their functional integrity for normal glycogen storage. The susceptible mice showed diffuse degenerative changes of the hepatic cells. This indicates that a cellular resistance to the bacterial toxins and degradation products of necrotic tissue is an important factor. The toxic effects of irradiation are at least similar to those from phosphorous poisoning (Ellinger, 1945) and may be similar to those of infectious diseases. The combined resistances to irradiation and bacterial infection may find its genetic basis in intrinsic cellular capacities to resist a toxic environment and maintain a normal state of metabolism.

In summary, the body weight response has been shown to depend, to a small degree, upon the initial weight of the animal. The weight loss is considered primarily a function of decreased food intake which is reflecting a gastric stasis. The absorptive ability of the small intestine is probably not severely impaired, but the gastric retention is preventing the normal movement of nutrition to the absorbing surfaces. Some effect may result from altered assimilation processes and from the basic nutritional state at the time of exposure. Endocrine factors may also be entering, as well as cellular differences in resistance to degenerative changes. The rate, time, and completeness of weight recovery, as they differ from strain to strain, may reflect underlying differences in the strain's ability and capacity to overcome known physiological and cellular changes. These considerations assume that the primary effects of irradiation are nearly constant for all strains. However, induced primary changes, through death or abnormal metabolism of the containing cell, may alter an uninjured cell's ability to maintain its status quo.

In conclusion, genetic variation in radiation response is assumed to be expressive in the secondary or indirect effects of the radiation. At the cellular level, the variation in response will lie in the genetically determined capacity of a cell to resist induced detrimental environmental influences so as to regain its normal metabolic activity and/or turn to regenerative processes.

SUMMARY AND CONCLUSIONS

Six genetically differentiated inbred strains of mice have been exposed to total body x-irradiation at an age of 40 ± 3 days. Equal numbers of mice of each sex and strain were exposed to 0r, 20r, 200r, 400r, and 800r. Body weights of all mice have been obtained throughout a 20-day post-irradiation period. At the end of this period, the weights of the heart, kidneys, liver, spleen, and testes were obtained. The results of this investigation permit the following conclusions.

1. There are positive genetic differences in the body weight response of mice subjected to total body x-irradiation.

2. When considering the entire population of mice employed, the genetic differences in response become maximum 15 days after exposure. At the maximum, this genetic variation amounts to 17 per cent of the total variation.

These differences arise, primarily, in the time and rate of recovery of weight loss, and, also, in the maximum loss itself. Very little genetic variation in response is seen two to five days after exposure, when the over-all effect of the radiation is maximum.

3. Qualitative strain differences in body weight response were not observed.

4. A sex difference in body weight response, although consistently favoring the female as the more resistant, does

not contribute significantly to the over-all variation.

5. The pre-irradiation initial body weight is found to be an important variable that must be controlled for accurate estimation of the variation in response. Evidence has also been presented to indicate that initially heavier strains, and heavier mice within strains, tend to be more resistant to irradiation.

6. A high degree of correlation between the weight change from initial weight and the incident dosage is noted. The resulting regressions have been utilized in an empirical procedure for scaling the relative resistance, of these strains, to alteration of the normal growth pattern. The scaling procedure has yielded the following resistance levels for the six strains; RI: 68.1 per cent; Z: 64.8 per cent; S: 64.1 per cent; E: 52.7 per cent; L: 42.5 per cent; Ba: 0 per cent.

7. The heart and kidney weights are resistant to irradiation, although they reflect an inanitional loss concomitant to losses in body weight.

8. The liver, in strains RI and L, shows significant absolute and relative increases in weight at 800r. No apparent reason for this change is available.

9. The spleen, at 20r, increases in weight in five of the six strains, with only strain E showing a decrease. The weight increase is considered a secondary defense reaction to the small, but definite, destructive effects of the x-ray.

At 200r and 400r, the spleen weight tends to be above normal in resistant strains RI, Z, and S, and below normal in susceptible strains E, L, and Ba. A uniform over-compensating increase in spleen weight is seen in all strains at 800r. Qualitative and quantitative strain differences in splenic response do occur and are considered to be based upon intrinsic differences in regenerative time and rate.

10. A parallel decrease in testes weight, with increasing dose, is seen in all strains. These changes are assumed to be due to direct destructive effects of the radiation upon the germinal tissue. The testes weight loss has also been shown to fit a simple exponential curve.

11. The genetic differences in response are postulated to be expressive in the indirect or secondary effects of irradiation. Primary effects are assumed constant for all strains.

12. Theoretical consideration of the body weight response leads to the assumption that certain known physiological and cellular disturbances that follow irradiation are basic to the measured weight changes. Genetic variation in body weight change may rest on a varying expression of these physiological alterations.

13. The cellular basis of genetic variation in response is postulated as due to intrinsic genetic differences in the capacities of cells to overcome the indirect noxious effects of radiation and to enter a phase of regeneration or return to normal metabolism.

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APPENDICES

APPENDIX A

Table 42. Between-strain Organ:Body Weight[1] and Inter-Organ[2] Correlations for Each Dosage Level

Correlated weights	Dosage - roentgens 0	20	200	400	800
Body:Heart	+.814*	+.902*	+.952**	+.834*	+.965**
:Kidneys	+.756	+.892*	+.935**	+.900*	+.967**
:Liver	+.756	+.855*	+.866*	+.821*	+.875*
:Spleen	+.046	+.420	+.486	+.501	+.087
:Testes	+.355	+.156	+.534	+.478	+.275
Heart:Kidneys	+.680	+.499	+.478	+.259	+.132
:Liver	+.554	+.798	+.833	+.671	+.840
:Spleen	-.328	+.023	+.285	-.178	+.203
:Testes	+.291	-.012	-.239	-.402	-.306
Kidneys:Liver	-.155	-.067	+.137	-.028	-.382
:Spleen	-.243	+.284	+.502	-.156	-.099
:Testes	+.458	+.571	+.370	+.447	+.538
Liver:Spleen	-.061	+.102	-.096	+.030	+.161
:Testes	-.289	-.463	-.319	-.625	-.841
Spleen:Testes	+.580	+.435	+.669	+.601	+.125

*P = .05 - .01

**P < .01

[1] Standard correlations at 4 degrees of freedom

[2] Partial correlations at 3 degrees of freedom

Table 43. Between-litter Organ:Body Weight[1] and Inter-Organ[2] Correlations for Each Dosage Level

Correlated weights	Dosage - roentgens 0	20	200	400	800
Body:Heart	+.673**	+.831**	+.895**	+.732**	+.769**
:Kidneys	+.771**	+.834**	+.939**	+.832**	+.872**
:Liver	+.605**	+.798**	+.881**	+.865**	+.866**
:Spleen	+.027	+.250	+.403**	+.162	+.071
:Testes	+.599**	+.612**	+.849**	+.672**	+.742**
Heart:Kidneys	+.701**	+.410**	+.362**	+.608**	+.513**
:Liver	+.331*	+.065	+.088	-.036	+.219
:Spleen	+.096	+.045	+.140	+.020	+.333*
Kidneys:Liver	+.098	-.053	+.336*	+.145	+.171
:Spleen	-.110	+.108	+.237	+.119	+.385**
Liver:Spleen	+.467**	+.296*	+.335*	+.242	+.322*

*P = .05-.01 **P < .01

[1]Standard correlations at 53 degrees of freedom

[2]Partial correlations at 52 degrees of freedom

Table 44. Between-litter Regressions of Organ Weight on Body Weight. Logarithmic Scale.

Dose	Heart	Kidneys	Liver	Spleen	Testes
Avg.	+.728	+1.121	+ .964	+.432	+1.267
0r	+.572	+ .922	+ .650	+.072	+1.182
20r	+.779	+1.173	+ .915	+.500	+ .995
200r	+.783	+1.232	+ .982	+.759	+1.338
400r	+.710	+1.081	+1.237	+.392	+1.492
800r	+.705	+1.061	+ .924	+.165	+1.161

APPENDIX B

In the following tables, all of the original observations are presented. The paired male and female observations constitute the litter-mate pairs that were irradiated at the same time. The 60-day body weight immediately precedes the organ weights that were obtained from that mouse at that age.

STRAIN RI: Or

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
93846	M	20.4	19.8	21.2	21.9	24.3	25.3	26.3	145	445	1631	101	149	8
93845	F	19.0	19.7	18.8	20.1	20.7	21.7	22.9	129	347	1395	107		
93823	M	18.2	18.8	19.8	21.0	20.4	21.1	23.6	127	418	1394	139	118	9
93822	F	14.6	15.7	16.6	18.0	20.1	21.4	21.8	133	339	1373	124		
99291	M	17.8	18.5	19.5	20.7	23.8	25.5	26.1	151	488	1846	90	132	8
99290	F	18.7	19.8	19.4	20.1	21.6	22.2	23.4	141	398	1466	82		
100438	M	19.0	19.4	19.5	21.2	22.7	23.7	24.3	141	434	1534	108	125	8
100436	F	11.8	12.3	12.5	15.6	18.1	18.8	19.1	114	288	1190	111		
103932	M	22.6	22.3	22.8	23.3	25.3	25.9	27.2	151	476	1660	101	102	8
103931	F	21.4	22.1	21.6	21.1	22.3	23.5	23.3	131	332	1322	73		
104165	M	23.9	24.3	24.4	25.6	27.6	28.7	28.3	149	493	1519	93	153	9
104164	F	20.8	20.9	20.8	21.3	21.7	23.7	22.8	123	347	1228	86		
105479	M	23.7	23.8	24.1	24.8	26.5	27.7	28.6	156	508	1630	90	147	8
105478	F	19.2	19.2	20.1	20.7	23.1	23.2	22.8	126	366	1358	90		
105483	M	21.7	21.5	22.1	25.0	26.7	28.5	27.4	150	499	1677	90	140	6
105482	F	20.7	21.0	21.7	22.0	23.7	24.7	23.4	114	358	1320	103		
105492	M	23.4	23.7	25.4	26.3	27.9	28.3	27.9	144	499	1742	105	159	7
105491	F	21.4	21.1	21.6	22.9	24.5	24.8	23.6	132	371	1362	100		
105537	M	18.4	19.1	19.4	20.3	23.1	24.1	25.2	136	404	1518	67	125	9
105536	F	18.3	18.7	18.9	19.2	19.6	20.5	21.5	116	318	1316	69		

STRAIN RI: 20 F

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
93840	M	23.3	23.2	23.3	25.7	27.3	28.2	28.9	138	508	1794	148	138	9
93839	F	19.4	19.2	19.0	20.8	20.9	23.0	23.0	130	353	1488	113		
95400	M	22.7	21.8	22.1	23.2	24.3	26.1	26.0	141	463	1630	95	147	9
95399	F	20.4	20.2	20.1	21.5	22.3	24.4	23.9	131	402	1600	148		
99299	M	18.6	18.0	18.8	20.0	23.1	24.5	25.6	152	490	1722	110	104	11
99298	F	17.8	17.8	18.6	19.3	22.2	22.6	23.7	129	353	1485	115		
100322	M	23.9	23.8	23.4	24.7	25.8	25.8	26.8	153	551	1671	102	129	8
100321	F	21.9	21.6	21.6	21.7	24.3	24.4	24.4	137	400	1385	84		
103985	M	17.9	18.2	18.5	19.7	21.3	23.3	24.5	141	359	1548	112	118	9
103984	F	12.4	13.0	13.4	14.9	17.0	18.5	19.4	112	285	1228	97		
103995	M	23.3	22.5	21.9	24.5	27.2	27.6	30.2	164	503	1823	150	128	4
103994	F	20.6	20.1	20.6	21.6	22.6	24.1	24.0	124	356	1490	101		
105675	M	23.5	23.5	23.2	25.3	26.9	27.7	26.9	150	485	1581	149	146	8
105674	F	21.1	21.1	20.8	22.2	23.2	23.5	23.7	125	345	1269	128		
105817	M	16.2	17.1	17.8	20.0	22.1	24.2	25.9	139	448	1804	196	116	9
105813	F	17.4	17.5	17.2	18.9	19.7	21.4	21.7	126	342	1420	182		
108369	M	25.4	25.1	26.1	25.7	26.3	27.3	27.8	145	479	1670	77	152	8
108368	F	22.0	22.6	23.2	24.0	24.3	24.5	24.9	134	382	1571	136		
108707	M	12.6	13.6	13.5	15.3	19.1	21.1	23.8	145	457	1628	137	83	7
108706	F	14.9	13.4	15.8	17.8	20.0	21.6	22.1	138	391	1472	154		

STRAIN RI: 200 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
93872	M	17.9	18.6	18.8	20.3	21.7	23.5	24.8	138	441	1600	122	82	9
93871	F	19.8	19.6	19.7	21.2	21.0	22.9	23.6	137	372	1595	113		
98734	M	27.0	27.0	27.2	27.5	29.8	31.4	31.2	167	541	1732	88	101	4
98733	F	24.6	23.8	23.2	24.2	26.1	25.7	25.7	148	413	1582	97		
99302	M	22.0	21.1	21.5	23.0	26.1	26.3	27.0	152	496	1692	74	91	7
99301	F	20.1	19.1	19.5	22.0	23.2	24.0	25.4	144	388	1583	91		
100544	M	23.9	22.9	22.7	25.0	26.3	27.8	28.1	154	498	1608	109	92	4
100543	F	21.6	21.4	20.6	22.4	23.3	23.9	23.7	125	349	1394	115		
101427	M	24.3	23.3	23.1	24.4	25.8	27.2	28.5	150	586	1860	101	93	9
101426	F	21.4	21.5	21.3	22.8	23.7	24.6	25.3	140	402	1715	117		
105734	M	24.5	24.1	23.6	25.8	27.0	28.7	28.6	155	449	1620	145	92	6
105733	F	20.3	20.2	20.3	22.4	22.9	23.2	23.5	127	335	1256	115		
107662	M	23.6	23.1	23.5	24.3	26.2	27.1	27.1	152	485	1702	139	87	10
107661	F	22.6	22.3	22.4	24.3	25.3	25.7	27.4	147	429	1739	157		
108376	M	28.3	28.2	29.5	29.4	30.2	31.5	31.4	161	510	1877	69	108	12
108375	F	23.7	24.1	25.3	25.1	26.6	26.9	27.8	142	419	1990	166		
108380	M	24.5	23.7	25.0	26.5	27.5	28.4	28.5	136	479	1628	100	94	7
108379	F	23.7	21.9	22.2	24.2	25.7	25.7	24.6	143	388	1445	118		
108709	M	17.3	18.3	17.7	20.2	21.7	24.0	24.4	140	431	1472	82	101	6
108708	F	18.3	17.1	18.0	19.7	20.5	22.3	22.9	134	385	1463	203		

STRAIN RI: 400 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
93830	M	23.3	23.3	23.2	23.9	25.0	26.8	27.4	153	491	1580	120	80	11
93829	F	20.5	19.5	19.6	19.0	21.5	22.4	22.5	120	343	1566	108		
95391	M	24.0	24.2	23.3	23.7	25.7	26.9	26.8	157	508	1528	73	91	8
95390	F	20.4	19.7	19.8	19.7	22.3	23.6	23.6	136	354	1607	112		
98739	M	21.2	20.2	20.1	21.4	24.0	27.1	26.0	150	451	1696	78	77	9
98378	F	18.7	18.3	18.5	18.8	21.2	22.2	22.3	125	344	1369	93		
100315	M	17.1	17.9	18.0	19.3	21.9	24.0	24.9	143	444	1602	88	61	8
100314	F	18.3	17.0	16.3	18.7	20.9	22.8	24.0	125	361	1704	93		
102469	M	12.5	12.4	12.6	13.7	16.0	17.1	18.5	103	299	1265	104	36	8
102468	F	9.1	9.8	9.7	10.7	13.9	16.3	16.4	98	247	1047	111		
103998	M	16.2	16.2	16.4	17.7	20.6	22.1	23.4	141	358	1561	109	55	9
103996	F	17.1	17.1	16.7	19.1	20.7	21.2	21.4	127	309	1338	80		
105833	M	21.4	21.0	21.4	22.5	22.7	24.4	25.3	138	402	1597	170	68	11
105832	F	19.3	19.8	19.0	20.6	21.7	22.8	24.1	132	326	1378	170		
105842	M	21.8	21.4	21.3	22.2	24.7	26.7	25.9	141	435	1662	158	70	12
105841	F	19.3	18.9	18.4	19.6	21.0	21.4	21.9	110	329	1490	182		
108007	M	22.9	21.8	21.8	23.0	24.8	26.9	27.4	156	488	1775	188	75	11
108006	F	19.1	18.4	17.8	18.7	20.0	21.3	21.6	129	341	1461	148		
108586	M	21.2	20.9	20.6	21.9	25.5	26.4	26.8	146	470	1658	85	66	8
108585	F	19.5	18.6	18.4	21.0	22.2	23.2	22.9	139	377	1509	144		

STRAIN RI: 800 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
93864	M	20.5	19.6	19.3	18.7	20.4	22.5	24.5	143	417	1561	108	61	10
93863	F	18.7	17.7	17.5	17.9	18.7	20.7	21.7	109	291	1592	100		
95386	M	21.0	19.7	18.8	20.2	22.4	24.4	26.1	149	461	1709	117	69	11
95385	F	19.0	18.6	17.7	19.0	20.1	22.4	22.4	131	355	1447	125		
99480	M	22.0	21.6	21.1	21.3	23.3	24.7	27.0	154	509	1689	147	66	8
99478	F	19.0	19.1	18.5	18.7	20.7	22.0	23.0	137	354	1536	110		
100548	M	24.1	23.5	22.6	23.6	24.4	25.4	25.3	131	439	1643	180	65	5
100545	F	23.0	21.8	20.7	22.7	23.0	23.7	24.0	131	357	1427	137		
101071	M	24.4	23.1	21.7	22.5	25.1	25.7	27.0	154	541	1787	136	65	9
101070	F	21.0	20.4	19.4	20.1	23.3	24.6	24.9	141	386	1738	128		
103991	M	17.2	17.3	15.4	17.6	20.2	22.5	23.8	143	415	1687	128	54	10
103989	F	14.4	15.2	13.5	12.4	15.1	17.6	20.0	120	283	1228	73		
105854	M	16.6	17.1	16.5	17.1	18.9	19.4	19.9	131	348	1429	180	51	13
105853	F	17.4	17.9	17.2	17.8	18.7	19.6	20.5	125	297	1390	170		
107672	M	22.9	22.3	22.6	22.0	23.4	25.1	25.9	163	497	1807	222	59	8
107671	F	21.0	20.5	20.5	20.8	21.4	23.2	23.1	142	365	1597	167		
108438	M	18.7	18.6	17.5	18.2	18.6	20.9	22.3	115	400	1418	121	62	11
108437	F	20.8	20.1	19.3	20.1	22.4	21.5	22.1	155	383	1672	243		
109295	M	20.3	21.0	20.0	22.2	23.7	24.8	26.4	146	457	1607	163	68	8
109294	F	18.9	18.1	18.2	18.9	16.3	15.8	18.0	143	379	1471	264		

STRAIN Z: Or

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
94851	M	20.2	20.5	21.6	22.9	22.4	23.0	22.5	126	464	1224	79	170	6
94850	F	17.2	17.2	18.0	17.1	16.8	18.3	17.3	108	343	947	83		
95933	M	19.2	19.2	18.6	20.1	21.4	21.3	20.9	122	415	1237	77	133	10
95932	F	15.7	15.4	15.3	15.7	16.8	17.9	18.2	98	288	1008	87		
95944	M	18.6	20.2	20.6	21.2	22.6	23.0	23.2	121	449	1447	109	118	8
95943	F	15.9	16.7	16.4	17.0	18.7	19.4	19.1	108	285	1097	109		
98907	M	13.1	13.7	13.8	14.9	17.1	19.2	19.6	111	395	1225	93	116	11
98906	F	12.6	12.9	13.2	14.0	15.9	16.3	18.1	101	294	1109	94		
98975	M	21.8	21.8	22.7	22.9	23.1	22.4	21.5	125	437	1164	62	148	7
98974	F	17.0	17.2	17.4	17.8	19.9	20.1	19.7	115	330	1159	88		
98984	M	16.1	16.6	16.8	17.2	19.7	21.2	21.3	119	423	1209	81	146	9
98983	F	12.2	12.7	12.9	13.2	15.0	15.3	16.3	86	249	866	74		
98991	M	17.1	17.3	17.8	18.8	20.7	21.4	20.8	116	413	1141	66	137	7
98990	F	15.3	15.6	15.5	16.2	18.4	18.2	19.4	105	321	1023	92		
98916	M	20.2	21.6	22.4	22.1	21.8	21.7	23.0	120	408	1343	103	148	4
98915	F	18.3	19.7	20.2	20.3	20.4	21.0	21.5	109	331	1384	128		
99205	M	15.6	17.2	16.9	19.0	21.0	21.4	22.3	122	475	1278	83	137	9
99204	F	13.8	14.5	13.9	14.4	16.3	16.0	17.3	92	285	913	83		
99213	M	19.7	21.3	21.1	22.7	23.8	23.2	23.0	132	553	1343	87	151	7
99212	F	16.5	17.4	16.2	17.2	19.0	18.4	19.2	116	321	1043	99		

STRAIN Z: 20 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
94698	M	16.5	16.6	16.9	18.2	19.9	21.6	21.4	115	360	1294	97	133	8
94697	F	15.9	15.8	16.1	16.3	17.6	19.1	19.1	99	306	1087	95		
94637	M	21.2	20.4	21.3	21.8	22.2	23.5	22.5	114	423	1278	90	145	7
94636	F	17.1	16.4	16.5	17.0	17.8	18.2	18.9	121	288	941	92		
94935	M	21.7	21.6	19.7	20.3	23.1	22.9	24.0	129	495	1488	100	153	6
94934	F	19.0	18.6	19.0	19.5	21.0	22.9	22.4	121	342	1254	114		
95959	M	16.8	17.4	17.6	19.2	21.7	23.8	22.6	120	410	1308	88	135	9
95958	F	14.6	14.7	14.9	15.2	17.1	18.3	18.6	103	277	955	99		
97280	M	20.2	20.1	20.4	21.3	22.4	22.9	23.2	120	403	1225	77	149	9
97279	F	17.3	17.4	17.4	17.5	18.5	19.0	19.6	116	348	1070	75		
97389	M	19.6	19.2	19.6	20.9	22.2	23.1	22.9	120	432	1235	75	142	9
97388	F	17.9	17.0	16.5	17.8	19.5	20.2	19.8	105	316	1007	88		
97264	M	18.6	19.1	19.1	19.3	21.2	22.1	21.9	115	391	1290	94	134	11
97262	F	14.6	15.2	15.1	16.2	16.9	18.3	18.1	99	290	1040	100		
97321	M	20.7	19.1	20.3	21.8	23.3	23.7	23.4	129	494	1275	85	139	6
97320	F	17.2	17.9	18.0	18.0	19.4	20.0	19.7	101	318	1119	120		
97243	M	20.6	22.0	22.7	24.2	24.7	26.2	26.7	132	480	1537	115	149	8
97242	F	17.9	18.7	18.8	19.4	19.9	20.7	20.6	110	301	1097	92		
97477	M	14.4	14.8	15.0	16.4	18.4	21.0	21.3	105	355	1188	111	114	8
97476	F	14.2	14.0	14.4	15.0	15.8	17.4	17.8	96	255	1002	95		

STRAIN Z: 200 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
94652	M	20.9	20.1	20.1	20.5	22.6	24.7	24.2	137	442	1353	91	106	7
94651	F	17.8	17.1	16.4	17.9	18.8	20.4	19.9	107	325	1113	83		
94669	M	9.3	9.7	9.9	10.9	9.2	9.2	9.6	66	148	504	41	35	9
94667	F	15.2	14.7	14.6	15.2	16.7	17.3	17.5	101	251	1055	95		
94688	M	15.1	15.1	15.6	16.4	18.9	20.4	20.2	111	365	1166	75	100	10
94687	F	14.9	15.0	15.1	15.5	17.1	18.0	18.7	102	292	1014	86		
94956	M	15.4	15.1	15.3	16.3	18.8	21.5	21.1	111	350	1158	78	89	11
94955	F	14.8	13.7	13.7	14.3	16.6	18.0	17.6	97	280	1162	107		
95971	M	17.5	17.1	17.1	17.7	20.5	22.5	21.6	117	390	1159	86	98	10
95970	F	14.9	14.2	14.3	14.5	16.4	18.1	18.3	103	286	998	87		
97415	M	11.7	11.7	12.0	11.7	10.6	10.8	10.4	58	161	561	25	38	8
97414	F	18.9	17.7	17.6	18.6	20.1	20.2	20.7	107	352	1135	81		
97272	M	20.5	20.2	21.4	22.2	22.4	21.8	22.6	127	458	1410	134	108	9
97271	F	15.4	16.8	17.1	17.1	18.3	20.1	19.8	100	343	1182	110		
97294	M	22.5	20.4	20.1	21.8	23.5	26.0	24.5	130	487	1436	99	95	7
97293	F	17.8	16.5	17.4	18.7	21.3	22.5	22.6	113	366	1289	123		
97335	M	19.7	20.0	19.6	21.9	23.3	24.2	22.7	118	404	1235	71	93	6
97334	F	18.3	17.8	17.4	17.8	19.9	21.1	20.5	111	308	1119	98		
97474	M	16.4	15.0	16.0	17.8	21.0	22.8	22.7	115	383	1431	92	93	12
97470	F	16.4	16.1	15.9	17.0	17.8	20.0	19.2	97	276	1037	88		

STRAIN Z: 400 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
94673	M	22.6	20.3	21.7	23.6	23.7	25.3	24.1	129	499	1418	90	102	4
94672	F	19.2	18.1	19.2	19.7	20.4	21.8	21.1	120	361	1164	94		
94974	M	17.5	17.2	16.8	18.0	20.6	22.1	21.6	108	394	1327	128	86	10
94973	F	15.8	15.6	15.3	15.4	16.9	17.9	18.9	99	276	1046	99		
95032	M	22.7	21.9	21.6	21.5	23.0	23.8	24.1	140	532	1636	99	91	6
95031	F	19.4	18.8	18.1	18.7	20.0	21.4	21.3	125	378	1377	109		
95020	M	18.0	17.0	17.5	19.9	19.7	22.1	20.6	115	356	1154	73	87	6
95019	F	19.0	17.5	18.2	18.9	19.3	19.7	19.9	114	333	1007	78		
97426	M	20.6	20.7	20.7	20.4	21.3	21.9	21.6	124	484	1272	55	98	11
97425	F	17.4	17.1	17.0	17.2	18.7	19.3	19.3	109	326	1042	57		
97519	M	12.7	12.6	12.7	14.4	17.0	18.4	20.0	103	361	1218	82	60	10
97518	F	15.2	14.3	13.9	14.9	16.4	18.3	19.6	103	329	1093	83		
97501	M	17.4	17.0	18.2	19.0	21.3	20.4	21.3	111	380	1218	107	90	9
97500	F	15.9	15.1	15.2	15.1	15.4	17.4	18.3	93	294	1081	77		
97371	M	17.2	17.1	16.5	17.4	19.3	21.6	21.6	115	366	1385	111	88	9
97370	F	16.0	15.7	15.1	15.8	16.6	18.7	18.8	106	291	1084	90		
97249	M	16.9	17.2	16.9	18.4	19.6	21.0	21.4	105	360	1162	69	91	8
97248	F	15.3	14.8	15.4	15.2	15.7	17.2	18.1	86	243	956	73		
98340	M	15.0	15.0	15.3	16.1	17.9	19.7	20.9	106	366	1335	104	79	10
98339	F	13.4	12.5	12.5	13.0	14.5	16.7	17.3	93	269	1028	107		

STRAIN Z: 800 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
94707	M	17.1	15.5	15.8	15.1	16.6	18.2	19.3	101	295	1009	90	69	10
94706	F	13.8	13.5	13.7	13.5	13.4	16.0	16.7	94	245	960	96		
94859	M	21.8	20.5	21.4	21.0	21.6	23.0	21.9	121	422	1130	91	79	10
94858	F	17.3	16.6	16.6	16.9	17.2	17.5	18.4	110	281	1017	104		
95049	M	19.4	19.5	19.3	20.0	21.7	22.5	22.3	119	405	1355	107	82	9
95048	F	17.4	17.8	17.0	16.8	16.5	19.0	19.8	109	289	1189	120		
95038	M	15.5	15.6	15.1	17.0	16.4	19.1	19.8	102	341	1211	101	69	9
95037	F	17.0	15.5	15.6	15.6	14.8	16.9	18.6	97	297	1086	119		
95025	M	19.9	19.0	18.6	19.5	20.1	21.1	21.9	121	442	1232	96	71	7
95024	F	18.2	17.5	17.4	17.5	18.9	19.6	19.7	110	329	1122	105		
97303	M	20.4	20.4	20.0	20.2	20.5	22.5	23.0	115	457	1327	141	83	5
97302	F	17.3	17.4	16.4	17.5	17.7	19.9	19.8	110	325	1168	107		
97438	M	21.5	21.6	20.2	21.6	20.9	23.2	23.0	124	407	1459	147	90	5
97437	F	18.2	18.0	17.2	18.1	17.8	17.6	18.9	101	362	1262	284		
97314	M	18.6	17.7	16.6	15.5	16.4	18.7	19.3	101	316	1124	93	68	7
97313	F	18.7	17.8	17.6	17.2	18.1	19.1	20.5	115	353	1171	134		
97466	M	21.5	21.7	21.3	21.8	23.2	24.0	22.5	118	432	1246	95	85	6
97465	F	19.3	18.7	18.2	18.1	19.7	19.9	20.2	111	317	1035	108		
97492	M	19.0	18.1	17.9	18.2	18.9	21.4	22.6	117	372	1329	112	72	11
97491	F	17.0	16.0	15.4	16.2	16.5	18.1	18.4	91	254	1018	85		

STRAIN S: Or

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
95109	M	17.5	16.5	15.5	17.2	18.3	19.8	19.3	129	420	1119	71	210	8
95108	F	15.7	14.8	14.3	15.3	16.6	17.9	17.6	114	332	1108	86		
95214	M	15.8	15.6	16.4	18.2	19.9	20.8	22.1	130	435	1388	176	208	8
95213	F	15.3	15.4	16.5	17.1	18.2	19.8	19.7	107	358	1161	112		
95167	M	17.3	17.3	17.5	18.3	19.8	21.2	21.7	129	416	1357	102	186	10
95166	F	14.1	14.4	14.6	16.0	16.8	17.4	18.1	108	330	1196	109		
95588	M	17.4	18.2	18.2	19.9	21.6	23.1	22.6	141	468	1456	109	189	8
95587	F	15.0	14.7	15.0	15.4	16.6	17.6	17.7	100	332	1061	126		
95984	M	18.6	19.1	19.9	20.6	22.2	22.9	23.2	139	467	1636	170	175	7
95983	F	15.7	16.0	16.4	16.9	17.2	18.2	18.0	106	332	1222	137		
95990	M	17.4	17.9	18.5	19.8	21.2	22.4	21.4	122	416	1486	156	174	9
95989	F	15.3	16.3	16.0	16.7	17.5	18.5	17.3	105	292	1029	94		
96246	M	16.4	16.3	16.7	18.0	18.9	20.6	20.0	129	417	1342	89	163	11
96245	F	13.7	14.0	14.7	15.4	16.0	16.1	16.4	102	309	1064	108		
96251	M	19.0	19.1	19.6	20.7	22.0	24.1	23.5	137	470	1512	95	194	5
96250	F	16.0	16.0	16.4	16.8	17.2	18.6	18.3	108	308	1054	93		
98356	M	18.8	18.8	18.5	20.1	21.8	24.2	23.6	148	484	1614	160	209	8
98355	F	16.2	16.0	15.9	16.9	17.6	18.8	17.4	113	323	1107	115		
98408	M	19.4	19.3	20.0	20.7	22.5	24.3	23.3	133	433	1488	137	188	8
98407	F	15.1	15.0	15.0	15.6	16.6	18.1	17.7	107	306	1145	125		

STRAIN S: 20 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
95093	M	21.2	20.6	21.7	21.8	23.4	24.9	25.2	146	498	1794	148	187	6
95092	F	16.8	16.6	17.1	17.3	18.1	18.8	19.5	117	382	1176	143		
95532	M	12.7	13.6	13.8	15.6	17.1	19.0	19.0	129	377	1299	144	155	8
95531	F	12.0	11.8	11.4	13.2	15.3	15.8	15.7	93	280	997	73		
95522	M	21.9	21.4	22.2	23.1	24.7	25.7	25.7	158	594	1680	131	204	4
95521	F	16.7	16.1	16.3	16.7	18.2	19.2	19.2	121	370	1245	135		
95609	M	18.9	18.6	18.9	19.7	21.6	23.4	23.2	140	457	1658	160	181	5
95608	F	15.1	14.8	14.9	15.9	16.4	17.9	17.4	98	291	1085	116		
95574	M	18.8	18.9	18.7	20.2	21.7	22.5	21.1	135	451	1347	153	171	6
95573	F	15.2	15.1	15.6	15.6	16.8	17.7	17.0	110	286	978	138		
96554	M	13.6	13.9	14.4	16.7	18.2	20.1	20.7	121	384	1364	135	157	12
96553	F	13.2	13.0	13.7	14.6	14.9	16.6	16.4	95	281	1058	108		
96625	M	18.2	18.4	18.6	19.3	21.0	22.3	22.2	126	412	1195	113	185	7
96624	F	14.6	15.2	15.5	16.1	17.7	18.3	18.1	103	324	1048	160		
96548	M	13.3	13.6	13.9	16.2	16.9	19.5	19.8	114	381	1250	152	141	9
96547	F	11.7	12.0	10.8	13.8	14.3	15.5	17.7	97	281	948	116		
98370	M	11.9	12.7	13.7	15.3	16.6	17.9	18.7	112	378	1253	157	151	7
98368	F	9.9	10.9	11.3	12.6	13.6	15.2	14.7	88	257	1027	132		
98227	M	15.8	15.9	15.9	17.0	18.6	20.2	19.1	121	400	1187	123	169	9
98226	F	14.1	14.2	14.3	15.1	15.8	16.6	16.2	102	304	974	144		

STRAIN S: 200 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
95188	M	16.1	15.8	16.3	16.7	18.7	20.8	20.9	127	398	1337	128	106	8
95187	F	12.0	12.5	12.3	14.0	16.4	17.4	17.3	110	305	1082	90		
95148	M	17.3	17.3	17.4	18.5	20.1	21.2	21.1	129	418	1308	107	113	8
95147	F	14.4	13.9	14.3	15.2	16.7	17.4	17.7	101	301	1059	113		
95130	M	20.1	19.0	18.9	20.6	22.7	23.6	23.4	139	474	1569	163	126	8
95129	F	13.7	13.2	13.3	14.4	16.3	17.6	17.5	105	308	1195	154		
95540	M	14.6	14.0	14.3	16.1	17.7	19.2	19.4	123	387	1234	155	88	12
95539	F	13.9	13.3	13.8	14.6	15.8	17.1	17.0	112	334	1158	113		
95615	M	16.8	16.9	17.2	18.8	20.5	22.2	21.7	139	412	1335	156	95	7
95614	F	15.3	15.8	15.9	17.1	18.7	19.3	18.6	108	308	1161	117		
95598	M	13.7	13.3	13.1	13.7	16.1	18.2	17.9	110	372	1188	141	93	10
95596	F	14.3	13.9	13.6	13.7	15.3	15.4	16.5	107	286	966	213		
96540	M	11.3	12.5	11.8	14.5	16.6	18.3	19.1	121	346	1311	97	87	12
96539	F	12.5	12.3	12.9	14.1	15.4	16.1	17.2	98	296	1169	111		
96560	M	21.3	20.7	21.1	21.4	24.2	24.0	24.1	135	485	1451	130	116	7
96559	F	17.6	17.3	17.4	18.1	19.2	19.9	19.6	121	344	1164	112		
96564	M	16.2	16.1	16.0	17.6	19.0	20.7	21.2	113	366	1277	164	95	9
96563	F	14.2	14.5	14.4	15.7	16.5	17.7	17.8	106	351	1161	148		
96572	M	11.8	12.1	12.5	13.6	15.3	17.1	17.3	94	317	1085	111	74	6
96571	F	10.3	10.8	11.1	12.1	13.4	14.2	14.6	85	234	976	92		

STRAIN S: 400 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
95205	M	18.2	17.2	17.3	18.1	19.9	21.9	22.3	121	411	1554	120	93	7
95204	F	18.5	18.0	18.6	18.3	19.2	20.5	20.9	115	379	1447	105		
95176	M	18.0	16.3	16.8	18.7	21.0	22.4	22.3	140	430	1570	126	91	4
95175	F	14.2	13.7	14.0	14.3	16.2	17.8	18.4	101	297	1208	150		
95178	M	21.4	20.1	20.3	20.1	22.6	24.6	24.2	139	510	1586	177	105	2
95177	F	16.6	15.4	15.3	16.2	17.5	19.0	18.3	110	324	1106	107		
95136	M	16.6	16.2	16.5	17.5	19.3	21.3	21.0	137	399	1369	110	86	9
95135	F	11.2	11.1	10.3	11.6	14.8	15.4	16.2	109	294	1089	109		
95557	M	19.0	18.8	18.1	19.2	20.7	22.2	22.4	131	442	1573	127	96	7
95556	F	16.0	15.6	15.2	15.9	16.4	18.2	18.4	102	302	1386	168		
96583	M	12.6	12.6	13.1	14.5	16.8	18.3	18.9	113	360	1353	111	73	9
96582	F	13.6	13.7	13.9	14.6	15.4	16.0	16.3	94	285	1063	108		
96611	M	12.8	14.6	15.0	16.2	18.2	20.3	20.5	119	410	1324	102	74	10
96610	F	11.6	12.0	11.7	13.3	14.0	14.5	15.2	79	244	999	83		
96648	M	20.7	19.1	18.9	18.7	21.4	22.5	23.4	132	464	1507	114	111	7
96647	F	14.2	13.9	13.9	13.4	16.2	17.2	16.9	107	314	1111	85		
96592	M	20.3	20.0	20.2	20.5	22.0	24.0	23.9	129	410	1492	152	112	6
96591	F	18.3	17.8	17.8	18.2	19.9	20.5	20.3	103	340	1270	127		
98372	M	17.7	17.4	17.5	18.0	20.1	21.3	21.5	123	384	1351	155	99	7
98371	F	15.6	15.3	15.2	15.7	16.7	18.6	18.3	108	318	1211	147		

STRAIN S: 800 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
95103	M	19.8	18.8	18.4	19.3	20.7	21.0	21.4	119	401	1226	187	98	6
95102	F	17.0	16.1	16.6	16.5	17.5	18.5	18.9	106	317	1216	177		
95182	M	19.9	18.9	18.6	19.5	20.1	21.5	21.9	131	416	1299	197	113	6
95181	F	18.2	16.6	16.6	16.7	18.0	18.9	18.9	111	346	1017	119		
95087	M	17.8	16.8	17.0	16.9	17.5	18.5	19.3	109	387	1201	126	90	8
95086	F	16.6	15.9	15.4	15.4	15.8	18.0	17.8	103	305	1190	163		
95161	M	16.6	15.7	15.7	15.8	17.0	19.0	20.6	123	386	1254	189	82	8
95160	F	13.4	12.6	12.3	12.5	13.2	14.9	15.7	93	267	964	111		
95564	M	16.4	15.7	15.4	15.1	16.6	18.0	19.4	120	354	1295	180	77	9
95563	F	11.9	11.6	12.0	12.3	13.1	13.1	14.8	92	249	978	118		
96652	M	20.2	19.8	20.1	20.8	21.7	22.0	21.7	147	421	1396	280	131	6
96651	F	19.1	18.2	18.0	17.3	18.6	19.2	19.3	104	345	1333	235		
96618	M	17.5	18.4	17.7	18.5	19.5	20.6	21.4	129	452	1446	171	106	6
96617	F	16.0	15.7	15.1	15.5	16.7	17.4	17.9	110	315	1162	129		
96602	M	16.1	15.9	16.1	16.4	17.1	16.6	17.9	120	348	1292	192	80	10
96601	F	14.0	14.1	14.5	14.7	14.4	15.5	16.4	107	281	1061	141		
96642	M	13.5	13.1	12.9	12.8	14.5	15.7	17.2	97	309	1136	186	66	10
96639	F	10.9	10.7	10.4	10.9	11.6	13.2	14.1	82	224	920	111		
98425	M	17.8	17.8	15.2	17.9	18.8	19.3	17.9	95	327	1064	106	79	8
98424	F	14.5	14.3	14.2	13.8	15.2	16.3	17.4	103	311	1056	143		

STRAIN E: Or

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
93683	M	15.0	15.0	15.6	17.1	19.1	20.2	19.3	104	295	1208	80	110	5
93682	F	16.9	16.6	16.1	17.5	17.9	18.8	18.4	111	261	1189	102		
93690	M	15.0	17.4	17.3	19.1	18.1	18.8	19.5	116	354	1365	118	102	7
93689	F	11.9	11.7	12.2	13.3	14.8	15.9	14.5	91	236	964	71		
95410	M	17.0	17.0	16.9	17.2	18.1	19.8	20.6	118	380	1305	56	135	9
95409	F	13.5	13.4	13.1	14.1	14.8	15.3	15.4	101	259	1102	88		
95416	M	11.7	11.9	12.2	13.3	16.2	16.1	17.8	120	330	1310	91	98	8
95415	F	14.1	13.7	13.6	14.4	15.0	16.3	16.9	108	281	1236	80		
99311	M	12.7	12.9	12.9	14.1	16.2	18.2	19.5	119	335	1325	91	120	7
99310	F	11.8	12.2	11.9	12.8	14.1	14.9	16.6	104	269	1119	87		
96216	M	10.2	10.5	11.2	12.5	14.1	16.7	17.7	119	343	1425	96	95	8
96214	F	10.8	11.0	11.9	12.4	13.5	15.3	15.6	107	249	1150	64		
96224	M	15.1	15.0	16.2	17.1	17.7	19.0	18.8	120	392	1317	60	127	7
96223	F	12.0	11.9	12.9	13.4	14.1	15.3	15.7	117	287	1130	71		
98729	M	9.2	9.8	10.1	11.2	12.2	13.4	15.1	98	257	1090	84	75	8
98728	F	14.4	14.1	14.4	15.3	13.8	15.3	16.8	99	257	1339	94		
99190	M	13.7	13.9	13.7	14.8	16.1	17.5	19.0	124	372	1363	104	108	6
99189	F	12.4	12.7	12.6	13.4	14.8	15.9	17.3	119	279	1236	149		
99354	M	10.8	11.9	11.8	12.6	14.0	15.8	17.5	114	306	1336	98	96	7
99351	F	7.6	8.3	8.2	9.0	10.1	10.5	12.1	84	207	838	110		

STRAIN E: 20 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
93741	M	14.6	14.2	14.7	15.2	14.0	14.6	15.2	94	248	948	80	72	8
93740	F	13.6	13.0	13.7	14.2	14.9	15.1	14.3	97	235	865	55		
95374	M	15.2	15.0	14.9	16.4	18.7	20.7	19.5	121	319	1295	76	127	8
95373	F	15.2	14.4	14.8	16.0	16.8	18.5	18.2	109	295	1133	62		
95459	M	14.8	15.3	15.4	16.2	18.9	20.1	20.4	122	358	1447	84	111	7
95458	F	13.5	13.0	12.8	13.6	14.6	14.9	14.6	89	224	1053	74		
95426	M	15.3	15.0	15.3	16.2	18.4	19.6	19.5	109	383	1353	71	137	8
95425	F	14.3	14.3	14.4	14.4	16.2	17.5	17.0	103	292	1091	76		
96501	M	15.4	15.4	15.3	15.9	17.3	18.6	20.0	123	365	1234	90	116	6
96500	F	14.1	13.8	14.0	14.6	15.4	15.9	16.1	121	268	953	83		
96506	M	17.8	17.7	18.1	18.6	19.9	21.5	20.1	116	320	1332	87	128	10
96505	F	13.6	13.4	14.2	15.4	16.0	17.5	17.6	102	264	1211	90		
98266	M	12.1	12.5	12.6	13.7	15.5	16.8	17.3	109	275	1299	71	69	10
98264	F	11.4	11.7	12.2	13.5	14.7	15.3	15.1	91	221	1072	78		
98254	M	11.4	11.9	12.3	13.9	14.4	15.4	15.9	98	249	1097	60	89	11
98253	F	10.2	10.2	10.5	11.9	13.2	14.3	15.0	99	234	1108	60		
98283	M	14.2	14.6	15.3	16.6	18.2	19.4	19.2	121	344	1428	95	100	9
98282	F	14.0	14.7	15.2	15.6	16.7	17.3	17.2	110	262	1131	86		
99334	M	13.3	13.6	13.5	14.7	16.5	17.0	18.1	98	304	1163	84	114	7
99333	F	11.7	10.7	10.7	11.3	13.2	14.2	15.7	88	235	1034	129		

STRAIN E: 200 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
93710	M	13.9	14.0	14.7	16.1	16.9	19.5	19.1	118	320	1366	83	91	8
93709	F	13.4	12.9	12.9	12.0	13.7	15.3	15.8	85	246	1064	73		
93764	M	14.9	14.1	14.6	15.4	16.4	18.6	18.0	112	281	1069	95	78	8
93763	F	13.7	13.2	13.8	14.0	15.1	16.2	15.9	94	238	1050	67		
95367	M	11.6	12.3	12.6	14.1	16.4	18.4	19.8	116	324	1473	84	89	8
95366	F	11.2	10.9	11.4	12.7	13.5	12.6	13.2	79	215	1021	54		
95382	M	16.0	15.2	15.9	16.8	17.3	19.0	18.5	107	344	1209	90	97	5
95381	F	15.1	14.5	14.7	15.8	16.7	17.7	17.1	106	281	1140	57		
96512	M	16.1	16.4	16.5	17.6	15.7	17.0	19.0	117	410	1309	111	90	7
96511	F	15.4	15.0	15.1	16.2	15.9	16.8	17.1	104	283	1399	110		
96496	M	13.6	14.1	14.1	14.8	16.2	17.9	20.3	125	393	1376	82	71	7
96493	F	15.0	14.3	14.7	14.3	15.6	16.8	17.1	108	281	1328	62		
98157	M	9.8	10.0	9.7	10.9	12.3	13.9	14.5	91	222	1055	100	39	9
98156	F	9.2	9.7	9.8	10.6	12.1	14.6	15.3	98	240	1112	97		
98173	M	15.8	15.5	15.7	16.8	17.4	14.4	15.6	83	259	1121	77	69	6
98172	F	14.0	14.1	14.0	16.3	17.7	18.4	17.0	103	272	1327	81		
98278	M	16.6	16.4	16.8	17.8	18.7	20.3	19.5	116	297	1351	86	74	6
98277	F	13.0	13.1	13.1	14.1	16.0	17.6	17.1	108	272	1265	73		
98326	M	17.6	17.2	17.5	17.9	19.0	20.3	20.3	112	361	1291	56	85	6
98325	F	14.3	14.3	14.9	15.5	17.3	17.6	18.2	109	298	1238	66		

STRAIN E: 400 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
93754	M	12.2	11.5	11.7	12.4	12.3	13.9	15.2	123	282	902	100	57	9
93753	F	11.5	10.7	10.7	11.6	12.9	14.2	15.0	106	226	979	54		
93716	M	10.8	11.1	11.5	12.0	13.4	15.7	15.1	104	251	936	62	50	9
93715	F	13.5	13.0	12.6	13.0	14.9	16.0	15.8	110	231	1123	61		
95433	M	14.7	13.7	14.2	15.0	17.6	18.3	18.2	112	304	1147	78	69	8
95432	F	13.9	13.0	13.4	13.2	13.3	13.3	13.4	86	235	936	86		
95439	M	13.8	13.6	13.3	13.4	14.9	16.7	18.8	109	341	1636	126	60	5
95437	F	15.0	14.5	14.3	15.2	16.5	17.3	17.5	114	277	1330	55		
95883	M	9.3	9.3	9.7	11.0	12.3	13.6	14.2	100	230	1015	104	27	8
95881	F	10.5	10.1	10.0	10.4	11.3	12.5	13.9	93	224	937	97		
97077	M	14.4	13.9	14.0	15.5	17.2	19.5	19.8	114	344	1398	104	66	7
97076	F	14.3	13.7	13.6	14.3	15.6	17.3	17.5	112	276	1260	61		
98289	M	14.7	14.4	14.5	15.4	16.9	18.6	19.0	118	301	1338	68	54	9
98288	F	12.7	12.6	12.7	13.3	15.1	16.5	16.2	94	233	1141	70		
98296	M	16.3	15.3	14.5	15.6	17.6	18.7	18.8	118	368	1148	111	66	7
98295	F	14.0	13.6	13.4	13.8	14.9	16.0	16.0	104	269	1201	91		
99319	M	11.6	11.4	10.5	10.1	11.7	13.7	14.5	111	276	873	106	31	8
99318	F	11.8	11.9	11.6	11.3	12.1	12.9	13.2	93	260	808	113		
99329	M	14.1	14.6	14.3	14.9	17.6	18.8	19.4	106	309	1291	70	77	7
99327	F	12.2	12.0	11.9	12.9	14.1	15.2	15.3	99	249	1166	92		

STRAIN E: 800 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
93785	M	16.1	15.5	15.2	15.6	16.4	16.9	17.1	106	300	1163	172	57	8
93784	F	14.9	13.7	13.6	13.9	14.8	16.0	16.5	113	278	1142	123		
95380	M	13.0	12.9	12.8	12.6	13.3	14.6	16.0	95	288	1155	115	39	2
95379	F	12.2	11.5	11.6	10.9	11.8	12.2	11.9	70	222	975	86		
93795	M	15.7	14.7	14.1	14.0	15.3	14.6	15.0	101	305	1015	174	61	8
93794	F	15.2	14.2	13.1	13.0	14.7	12.9	13.2	88	239	955	87		
95447	M	13.4	12.6	12.3	11.4	12.7	15.1	15.7	104	240	1212	102	41	9
95444	F	13.0	12.4	11.7	11.7	12.0	14.1	14.2	96	228	1124	77		
96529	M	12.3	12.2	12.0	11.5	12.8	14.2	14.6	96	248	1045	72	41	7
96528	F	12.1	11.6	11.6	11.3	12.7	13.7	14.4	92	239	1027	115		
96525	M	17.1	17.4	17.0	17.5	17.4	19.2	20.9	117	416	1539	99	55	3
96524	F	14.5	14.4	14.1	14.4	15.7	16.4	17.2	89	243	1201	73		
98182	M	14.8	14.5	14.3	14.5	15.8	16.6	16.8	101	295	1189	137	53	7
98178	F	14.4	13.6	13.5	13.9	15.4	17.0	16.4	103	257	1081	101		
98533	M	15.0	14.4	14.5	14.8	15.9	17.4	18.4	111	303	1273	134	48	5
98532	F	16.3	15.6	15.3	15.5	16.7	17.8	18.6	108	270	1342	75		
98313	M	14.3	13.9	14.2	13.9	13.2	13.9	14.3	83	267	976	143	39	10
98312	F	12.5	11.6	11.4	11.4	12.6	14.6	15.1	92	224	1011	78		
98537	M	10.8	10.7	10.9	10.9	11.7	13.3	12.0	84	229	988	135	26	7
98536	F	10.1	9.8	9.9	10.2	11.3	12.1	13.1	90	228	1042	120		

STRAIN L: Or

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
94552	M	19.0	18.7	19.4	20.8	21.9	21.6	22.5	116	332	1471	106	115	6
94551	F	15.6	15.6	16.0	16.5	17.4	18.1	18.2	95	274	1153	74		
94571	M	18.8	18.4	18.8	20.6	20.7	22.1	22.4	115	339	1502	117	136	5
94570	F	14.0	14.3	14.1	15.1	15.9	16.7	16.2	81	206	995	64		
94630	M	18.1	18.5	17.3	18.4	19.2	19.8	19.9	105	323	1348	124	127	5
94629	F	12.8	13.1	13.2	13.9	14.9	16.2	15.6	89	228	1123	98		
100410	M	18.8	18.9	19.1	20.0	20.9	21.6	21.4	108	329	1227	103	115	4
100409	F	15.9	15.8	15.6	15.8	17.2	18.1	17.5	105	241	997	103		
100413	M	11.7	11.8	11.7	14.0	16.3	18.2	18.9	117	310	1426	126	82	6
100412	F	9.8	10.0	9.9	10.1	12.0	12.6	12.6	87	187	954	137		
101988	M	15.6	15.1	15.4	16.7	18.6	19.6	20.7	115	335	1593	157	98	4
101987	F	14.6	15.0	15.2	15.8	17.5	18.1	18.7	102	265	1389	173		
104215	M	18.8	18.7	18.9	19.8	22.0	23.4	23.0	109	344	1324	104	125	7
104214	F	14.6	15.5	15.2	15.4	16.6	17.8	17.7	94	227	1079	82		
104220	M	18.7	18.8	19.1	20.1	21.8	22.9	23.2	117	340	1474	111	110	5
104219	F	15.9	16.7	16.3	16.6	18.0	18.9	19.1	108	287	1270	140		
104249	M	19.9	20.4	20.4	20.9	22.0	23.0	22.5	119	354	1323	89	116	5
104248	F	17.7	17.7	17.5	17.9	18.7	19.5	19.2	99	292	1091	83		
104231	M	17.0	17.2	17.6	18.6	20.0	20.4	21.2	108	313	1416	93	140	3
104230	F	16.8	16.6	17.0	17.8	19.0	19.7	19.6	106	262	1141	100		

STRAIN L: 20 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
94548	M	19.0	18.4	18.5	19.9	21.5	22.6	22.2	116	337	1264	85	108	6
94547	F	16.4	15.9	16.1	16.9	17.2	18.0	17.5	99	255	971	72		
95668	M	17.8	18.2	18.8	19.7	20.3	22.2	21.8	124	368	1390	178	105	4
95667	F	12.7	12.0	12.6	13.6	14.8	14.5	14.8	99	239	951	143		
97549	M	16.4	15.7	16.4	17.4	18.9	22.0	22.2	119	345	1472	106	98	12
97548	F	16.2	16.4	16.9	17.2	18.6	19.1	17.5	97	245	951	91		
97554	M	17.2	17.5	17.8	19.3	20.3	20.8	21.4	119	346	1572	120	129	6
97553	F	14.7	15.7	16.0	15.5	16.0	16.9	16.7	101	243	1078	77		
98939	M	14.8	14.7	15.7	16.3	18.0	20.0	20.5	122	318	1360	99	88	7
98938	F	14.6	14.6	15.1	15.5	17.0	17.5	17.6	110	266	1036	90		
99493	M	17.2	16.4	17.2	18.4	19.9	20.7	21.1	123	408	1502	141	125	8
99492	F	15.1	15.3	15.4	14.5	15.8	18.0	17.7	102	281	1109	88		
100383	M	12.6	13.1	13.4	14.6	16.8	19.3	20.3	123	307	1372	118	98	7
100382	F	13.0	12.5	13.1	14.2	15.5	16.7	17.2	102	244	1163	98		
100401	M	16.8	16.6	16.7	18.5	20.2	22.2	22.0	130	376	1510	196	122	5
100400	F	10.6	10.9	11.1	13.0	14.3	15.1	15.0	98	224	1156	173		
102808	M	17.3	18.5	18.6	19.3	20.5	21.1	21.0	122	664	1366	175	90	6
102807	F	14.9	14.9	15.7	16.2	17.1	18.4	19.0	98	257	1102	103		
103902	M	13.0	13.6	14.6	16.3	18.0	20.4	20.7	111	295	1550	121	73	6
103901	F	14.4	14.9	15.3	16.2	17.4	17.6	17.7	94	225	1269	107		

STRAIN L: 200 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
94602	M	14.0	13.7	13.6	15.0	16.3	18.1	18.2	108	285	1078	74	67	7
94601	F	12.7	12.2	12.5	13.9	15.1	15.4	15.5	94	234	932	62		
95673	M	18.7	18.5	18.6	19.4	20.7	22.7	21.5	123	350	1409	72	81	5
95672	F	16.0	15.6	15.9	16.9	17.6	17.5	17.6	111	262	934	57		
97580	M	19.1	19.1	19.7	20.0	21.0	22.2	21.3	121	322	1418	78	93	8
97579	F	16.4	16.2	16.1	16.6	17.8	18.9	18.9	108	287	1245	79		
98459	M	12.0	11.7	12.2	12.7	12.4	11.3	12.1	80	152	659	26	20	7
98458	F	13.6	13.5	13.5	13.8	12.1	15.1	13.6	90	221	1071	118		
98944	M	19.0	18.0	18.3	19.2	20.3	21.7	22.0	119	464	1351	96	78	4
98943	F	17.1	16.5	16.3	16.5	18.0	18.0	18.6	109	269	1121	98		
99486	M	12.5	12.4	12.9	13.8	15.4	16.1	17.1	111	276	1309	169	59	8
99485	F	15.4	14.3	15.7	16.2	17.7	18.1	18.3	109	300	1280	130		
100388	M	16.1	15.2	15.6	15.3	14.9	16.3	18.1	105	308	1249	120	81	4
100387	F	15.7	15.3	14.5	14.8	16.6	18.0	18.1	109	265	1156	93		
100417	M	16.9	16.9	17.2	18.0	20.5	21.1	20.5	102	340	1368	98	72	5
100416	F	14.1	13.9	14.0	14.7	15.7	16.9	17.6	97	266	1200	97		
101999	M	12.9	12.1	12.1	14.1	14.7	15.7	17.2	102	297	1213	93	45	10
101998	F	12.5	11.9	12.2	12.9	14.3	14.8	15.1	96	228	1053	76		
102828	M	15.2	15.7	15.6	17.2	19.6	21.6	22.5	136	411	1400	106	56	8
102827	F	13.0	13.3	13.9	15.2	16.2	16.9	16.9	103	255	1022	120		

STRAIN L: 400 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
94606	M	15.1	14.5	14.0	15.6	16.3	17.4	17.7	104	261	1120	82	63	6
94605	F	13.6	13.2	13.1	13.6	14.8	15.1	15.4	98	217	917	76		
94612	M	15.6	14.4	14.4	14.9	16.7	18.4	21.0	113	331	1569	90	67	9
94611	F	14.6	14.0	13.8	14.1	14.8	15.5	16.6	100	263	1240	101		
97567	M	13.0	13.4	13.5	13.1	14.4	15.6	15.7	90	251	1023	78	49	3
97566	F	14.8	13.9	13.3	14.3	15.4	16.5	17.3	98	249	1251	84		
98450	M	16.5	15.4	15.5	16.8	18.9	21.0	22.1	124	339	1656	80	59	7
98449	F	14.8	13.4	14.1	15.9	17.8	19.8	19.8	115	295	1656	161		
99518	M	16.8	17.1	16.4	17.5	19.2	20.9	20.9	110	344	1394	93	61	5
99517	F	14.9	14.5	14.1	14.9	16.4	16.5	17.1	92	246	1093	104		
100392	M	16.4	16.0	16.3	16.7	18.5	19.8	21.4	123	374	1468	121	63	5
100391	F	14.5	13.8	13.5	14.1	15.6	17.0	17.3	106	274	1151	82		
100406	M	13.0	12.6	12.5	13.7	14.1	14.9	15.0	83	227	975	103	44	3
100405	F	13.4	12.8	12.7	13.4	14.5	15.5	15.0	95	211	892	71		
100423	M	17.9	17.6	17.7	18.2	19.7	19.8	18.8	94	293	1276	80	76	7
100422	F	14.4	14.0	14.1	14.3	16.3	16.9	17.2	100	246	1181	78		
101397	M	14.1	13.8	14.0	15.4	17.1	19.2	19.7	119	372	1555	96	43	6
101395	F	13.2	12.7	12.4	12.9	13.8	14.2	15.7	96	240	1241	234		
103919	M	17.3	16.9	16.7	16.8	17.8	17.4	20.2	108	316	1524	109	31	5
103918	F	15.6	14.9	14.6	15.0	15.8	16.9	17.3	90	236	1044	99		

STRAIN L: 800 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
94510	M	21.6	19.8	19.6	19.4	20.4	21.6	21.1	114	340	1543	213	36	6
94509	F	16.5	15.6	16.4	16.4	16.6	17.6	16.9	95	234	1148	115		
94625	M	15.5	15.1	14.3	13.9	15.4	15.2	15.8	95	258	1341	171	32	7
94623	F	15.8	15.0	14.6	14.7	15.9	16.5	17.5	104	261	1350	126		
97598	M	19.7	19.1	18.4	18.4	19.0	18.9	19.7	105	328	1437	139	63	6
97599	F	15.4	14.6	13.7	13.3	12.7	12.4	13.0	81	186	848	162		
98454	M	18.1	17.9	17.9	17.8	17.6	19.5	20.5	106	350	1577	148	53	4
98453	F	16.3	15.7	15.8	15.6	15.9	17.0	16.4	105	226	1124	104		
99308	M	18.2	16.2	17.1	16.4	17.2	17.2	17.4	100	268	1297	107	48	6
99307	F	15.8	14.5	14.5	14.5	15.1	15.1	16.1	98	256	1247	167		
99500	M	16.8	15.8	15.6	15.5	16.5	18.6	18.3	136	319	1310	210	49	6
99499	F	15.2	14.4	14.1	14.3	15.2	16.1	16.1	109	278	1183	182		
102009	M	15.4	14.4	13.8	13.6	13.4	14.3	15.6	97	243	1077	124	32	4
102008	F	12.9	12.4	12.4	12.4	13.1	13.5	13.7	86	183	952	128		
102784	M	19.9	19.2	19.0	19.7	20.9	22.4	22.9	128	407	1647	127	53	5
102783	F	15.9	14.9	14.7	16.1	16.7	16.8	17.3	105	266	1213	98		
102834	M	20.6	19.1	19.5	19.9	21.1	22.1	21.1	105	311	1591	130	50	5
102833	F	16.4	16.2	16.4	17.2	18.2	18.9	19.0	108	277	1349	132		
106051	M	16.7	16.5	15.6	16.8	17.4	16.3	17.3	112	259	1389	358	48	9
106050	F	15.1	14.2	13.7	14.1	14.2	13.3	13.9	81	206	1023	212		

STRAIN Ba: Or

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
94445	M	19.3	19.6	19.5	20.8	22.1	23.3	23.2	131	406	1454	100	180	8
94444	F	15.2	15.8	15.6	16.6	18.1	19.0	19.3	103	303	1120	126		
94399	M	16.8	17.1	17.6	18.6	19.8	20.6	20.2	110	343	1081	124	158	9
94398	F	14.4	14.6	15.3	15.6	16.2	16.7	16.6	90	240	915	105		
94187	M	18.2	19.0	19.8	20.4	21.5	22.1	21.8	114	336	1263	162	145	9
94186	F	14.8	15.4	16.1	16.0	17.0	17.7	17.4	98	259	985	128		
95496	M	18.1	18.2	18.6	19.6	20.9	22.0	22.2	118	362	1366	109	182	8
95495	F	15.1	15.1	15.3	15.9	17.4	18.1	17.8	103	262	1028	118		
95505	M	15.1	15.1	15.7	16.7	18.6	20.6	21.3	119	337	1291	112	158	9
95504	F	14.5	14.6	14.8	15.4	16.1	18.0	18.1	100	269	1154	148		
95473	M	14.9	15.5	16.0	17.7	19.9	20.8	21.7	121	346	1362	133	172	8
95472	F	14.5	14.6	15.2	15.8	16.4	17.4	18.0	105	268	1195	149		
98492	M	18.7	18.8	19.2	20.2	20.4	21.7	21.8	111	351	1305	104	169	9
98491	F	17.0	17.1	17.2	17.8	18.1	19.3	18.7	104	284	1154	111		
98482	M	16.8	17.0	18.1	19.7	21.3	23.0	22.5	115	374	1416	129	155	10
98481	F	14.4	14.8	15.1	16.4	17.9	18.5	18.1	96	244	1045	119		
98518	M	12.1	12.6	13.5	15.2	17.1	19.0	18.7	104	283	1202	107	119	11
98516	F	10.5	11.3	11.6	13.2	14.1	15.6	14.8	82	211	975	94		
98523	M	19.8	19.6	20.0	20.3	22.1	23.4	22.5	126	416	1388	104	174	8
98522	F	16.8	17.0	17.1	17.8	19.6	19.9	19.3	104	287	1131	109		

STRAIN Ba: 20 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
94466	M	13.7	13.7	13.6	13.4	14.5	14.0	13.7	81	222	838	83	136	3
94464	F	9.9	9.7	9.4	10.2	11.2	11.8	12.0	68	170	679	76		
94284	M	19.9	20.2	19.9	20.9	22.4	23.0	22.1	124	419	1302	149	180	7
94283	F	18.6	18.1	18.5	18.9	19.8	21.2	21.0	121	334	1190	104		
94223	M	13.7	14.2	14.8	16.2	17.6	19.2	20.3	110	335	1262	116	144	10
94222	F	11.4	11.7	12.3	13.7	15.7	16.5	16.4	97	251	955	129		
94048	M	18.3	18.0	18.8	19.6	21.0	22.6	22.5	127	394	1437	133	181	10
94047	F	15.1	14.5	15.2	15.3	15.8	16.6	17.0	89	256	948	121		
94292	M	18.1	17.8	18.5	19.1	20.8	21.4	21.2	121	364	1322	115	165	8
94290	F	15.3	15.1	15.7	15.9	16.7	17.3	18.4	103	275	1076	110		
96879	M	16.5	16.6	16.4	17.5	18.8	20.6	21.4	111	367	1349	131	162	11
96878	F	14.7	14.8	14.6	16.0	16.7	17.4	17.8	90	268	1093	110		
96763	M	14.9	15.2	15.9	17.5	17.9	18.9	19.9	112	317	1283	139	151	9
96762	F	13.5	13.4	13.6	15.0	15.4	16.1	16.7	90	256	1055	125		
96839	M	17.8	17.7	17.7	18.4	20.7	21.9	22.1	122	376	1569	108	168	9
96838	F	16.8	17.1	17.0	17.3	18.9	19.2	19.3	96	271	1173	119		
96684	M	20.0	20.6	21.2	21.6	22.4	24.0	23.3	123	403	1503	189	164	7
96683	F	15.8	15.5	15.7	16.5	17.5	18.4	18.1	94	233	1032	137		
98473	M	19.1	19.4	17.3	19.6	20.2	21.3	21.7	110	333	1233	112	166	9
98472	F	18.8	17.8	17.1	18.4	19.3	20.2	19.7	100	271	1065	162		

STRAIN Ba: 200 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
94194	M	18.2	17.5	17.7	18.2	18.5	19.3	19.6	100	295	999	94	111	6
94193	F	17.7	17.1	17.3	17.7	18.5	19.1	18.7	95	266	1021	102		
94144	M	18.7	18.0	18.8	19.2	20.9	22.0	21.4	113	343	1154	129	116	10
94143	F	15.3	14.6	15.0	15.7	16.2	17.0	17.2	98	256	1002	145		
94170	M	17.7	17.6	17.1	17.6	19.8	20.6	20.0	124	364	1234	135	118	6
94169	F	16.4	15.6	16.1	15.9	17.0	18.2	18.7	116	284	1084	100		
94119	M	22.4	21.5	22.1	22.9	23.6	25.1	24.9	134	458	1485	124	133	5
94118	F	18.6	17.4	17.9	18.5	19.6	20.4	19.8	112	295	1135	99		
95502	M	18.5	17.9	16.3	18.6	19.4	19.4	20.9	119	384	1277	96	117	9
95501	F	15.6	14.8	15.4	15.6	16.9	17.0	17.7	99	262	1018	121		
95487	M	19.0	18.7	18.5	19.5	21.2	23.0	23.3	122	373	1480	128	114	7
95486	F	17.1	16.6	16.6	17.0	18.4	19.2	19.3	108	276	1202	117		
96958	M	18.6	18.0	17.7	19.0	21.1	22.6	22.5	130	419	1499	111	121	9
96957	F	12.5	12.2	12.7	13.2	14.8	16.8	18.0	94	276	1146	100		
96810	M	16.9	16.4	17.2	18.7	19.7	21.7	22.5	116	342	1212	142	125	9
96809	F	14.5	13.9	13.5	15.1	16.3	16.8	17.3	96	251	1005	95		
96691	M	18.2	18.2	18.2	18.8	20.1	21.3	20.8	100	331	1184	135	119	10
96690	F	15.6	15.2	15.4	16.3	16.5	17.4	17.1	93	238	1038	95		
96888	M	20.3	20.1	20.3	21.5	23.2	24.2	24.1	133	425	1559	119	124	9
96887	F	17.5	16.9	16.9	17.2	18.3	19.6	19.8	107	296	1207	132		

STRAIN Ba: 400 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
94365	M	19.4	18.0	18.8	19.9	21.0	21.6	21.1	109	335	1162	134	94	10
94363	F	15.5	14.8	15.1	15.7	15.5	17.1	17.2	96	270	998	133		
94343	M	18.9	17.4	16.9	17.1	19.1	20.6	19.9	120	381	1211	126	99	10
94342	F	15.5	14.6	14.3	14.6	16.3	17.8	18.1	103	275	1092	99		
94470	M	18.6	18.1	17.7	18.8	20.3	21.1	21.6	111	339	1288	112	102	7
94469	F	16.0	15.6	15.5	16.6	17.5	18.5	19.1	97	259	1043	108		
94209	M	17.0	15.7	15.3	14.3	17.0	18.7	18.5	104	301	1085	137	95	7
94208	F	14.9	14.1	14.4	13.9	15.1	15.7	16.1	93	231	808	95		
94045	M	19.4	18.7	18.2	18.2	19.9	20.8	20.0	113	365	1157	131	99	8
94044	F	16.0	15.4	15.3	15.8	17.5	18.0	17.6	108	266	1006	101		
94261	M	14.7	14.4	14.9	15.4	18.0	18.7	18.9	99	286	1116	75	83	8
94260	F	14.9	14.5	14.9	14.7	15.9	16.8	17.1	94	259	1122	121		
97092	M	16.8	16.8	16.5	17.0	18.8	20.9	22.0	112	369	1384	150	96	8
97091	F	14.0	14.0	13.8	14.2	15.0	16.0	16.6	90	245	1107	149		
96667	M	19.5	19.5	19.9	20.8	21.7	20.0	20.3	119	361	1307	233	108	9
96665	F	14.8	15.2	14.8	15.4	16.0	17.0	16.6	97	258	998	137		
97186	M	17.9	17.2	17.0	18.1	18.7	20.1	21.5	112	332	1283	155	102	7
97185	F	15.8	15.5	14.8	15.0	15.9	15.3	16.2	88	245	1034	100		
96971	M	19.0	17.9	17.3	17.7	20.1	21.3	21.3	107	336	1159	129	61	9
96970	F	17.1	16.6	16.4	16.6	18.2	19.6	20.3	100	269	1266	163		

STRAIN Ba: 800 r

Mouse No.	Sex	Grams of body weight at days of age: 40	41	42	45	50	55	60	Milligrams of organ weight: Heart	Kidneys	Liver	Spleen	Testes	Litter size
94246	M	17.5	16.6	16.3	16.2	14.5	12.3	12.6	85	216	795	174	63	10
94245	F	15.2	14.2	14.1	13.3	13.2	13.5	15.3	89	250	1093	127		
94270	M	16.1	15.5	15.2	13.6	13.0	12.6	12.3	75	225	748	134	50	8
94269	F	15.4	14.6	13.4	12.8	12.7	12.6	13.0	73	216	731	173		
94349	M	17.4	16.9	16.0	14.9	15.4	13.8	14.5	90	242	852	131	76	7
94348	F	15.8	14.4	13.7	13.2	13.2	12.2	14.0	77	227	953	143		
94163	M	16.8	15.8	15.9	15.5	15.5	14.3	16.6	99	283	1163	176	82	8
94162	F	15.2	13.9	14.1	13.8	13.0	12.0	14.0	85	218	968	98		
94476	M	19.3	18.2	17.2	16.5	15.7	14.4	16.3	91	259	1014	221	83	9
94475	F	15.7	14.7	13.6	13.2	12.6	11.8	12.5	78	201	836	256		
94216	M	19.7	18.3	18.4	17.9	16.4	14.4	18.2	97	302	1229	186	76	8
94215	F	17.3	15.9	15.4	14.3	13.5	13.6	15.3	84	252	999	99		
96677	M	16.0	15.9	14.8	13.6	14.1	14.5	15.4	103	273	1057	170	77	10
96676	F	15.6	15.1	14.6	13.6	12.0	11.4	12.6	82	202	849	151		
98465	M	15.5	15.0	14.8	13.8	12.0	11.4	11.7	60	168	692	72	47	7
98464	F	15.2	14.5	13.7	13.0	1.17	11.1	12.1	67	174	834	178		
98650	M	17.7	16.6	15.6	13.0	13.6	14.3	13.8	84	234	958	97	68	9
98649	F	13.9	13.2	12.3	10.6	11.9	11.9	10.6	73	158	600	79		
99888	M	17.8	17.3	16.4	15.9	17.9	18.0	19.4	103	334	1235	216	85	9
99887	F	14.1	13.8	13.5	12.9	14.0	14.1	15.2	84	235	1027	167		