SELECTION FOR SERUM CHOLESTEROL, VOLUNTARY PHYSICAL ACTIVITY, 56-DAY BODY WEIGHT AND FEED INTAKE IN ALBINO MICE

by

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This dissertation is dedicated to the author's husband, , and to her mother.

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INTRODUCTION

Elevated circulating cholesterol (CC) levels almost certainly contribute to the development of atherosclerosis (Kritchevsky, 1958; Reiser, 1973). The incidence of this vascular disease appears to be increasing in humans. A detailed understanding of factors influencing the levels of CC is essential before effective treatment and preventive measures for the control of atherosclerosis can be determined. Both genetic and environmental factors which influence CC need to be thoroughly investigated.

The literature dealing with interrelationships among serum cholesterol (SC), activity, body weight and feed intake is quite contradictory and studies have usually been done on a within-generation basis. Very few estimates of the genetic parameters of SC and activity in laboratory mice have been reported. By developing lines of mice selected for extreme values of the various traits, this study will allow evaluation of direct responses to selection. Also, the correlated responses obtained after several generations of selection will be more reliable than those from single generation studies.

Although the ultimate goal of the study of CC levels is to relate results to atherosclerosis in humans, much of the research concerning the modes of inheritance and environmental influences on CC has involved species other than humans (e.g., mice, rats, chickens, squirrel monkeys).

Even though some results may not be directly applicable to human populations, there are several definite advantages to using species other than humans in developing a basic understanding of the genetics, biosynthesis, metabolism and other phenomena related to SC. Some of these advantages are: (1) adaptability to laboratory environments, (2) ease of controlling food intake and activity, (3) relatively short generation intervals and (4) comparatively inexpensive maintenance costs.

The objectives of this experiment were to evaluate the direct effects of selection for maximum and minimum values of SC, voluntary physical activity, 56-day body weight and feed intake and correlated responses among these traits as well as reproductive and other physiological traits. Also, general trends in body weight and SC as the mice advanced in age were observed.

REVIEW OF LITERATURE

Genetic Control of SC

The genetic aspects of circulating (serum or plasma) cholesterol levels have been studied in several species. Bruell et al. (1962) determined that significant differences occurred in SC of mice from five inbred strains. He also found a significantly higher SC in males than in females across all lines. In a later study, Bruell (1963) reported that the mode of inheritance of SC in mice was intermediate (i.e., neither dominant nor recessive) and additive. This conclusion was reached by performing a diallel cross with five inbred strains of mice and comparing the SC of the F_1 progeny with the midparent SC values. The correlation between theoretical (midparent) and observed values was 0.837, indicating that the F_1 progeny values came very close to the midparent values. When the results of reciprocal crosses were pooled, the correlation was even higher.

Similarly, Yamamoto et al. (1963) reported that the genetic factors which control plasma lipid concentration (total lipids, cholesterol plus cholesterol esters and phospholipids) in rats were additive in nature and were influenced by many loci. Three inbred parental strains, their F_1 reciprocal hybrids, backcrosses with the parental lines and reciprocal F_2 crosses from the F_1 lines were employed in the study. Considerable variation in plasma lipid concentration was found among the paren-

tal strains. Within litter variances and coefficients of variation were greater in the F_2 crosses than in the F_1 crosses, indicating genetic control. The mean values of total plasma lipid concentration suggested to the researchers that the genetic variation was additive.

During the development of lines of mice selected for high and low plasma cholesterol (PC) for five generations, Weibust (1973) estimated the realized heritability of PC to be 0.51 ± 0.05 in males and 0.50 ± 0.03 in females. The mice from this study originated from eight unrelated inbred strains which were crossed to produce all possible combinations, resulting in a heterogeneous base population upon which selection for high and low PC was performed. After only one generation of selection, both male and female means among the high, control and low lines were significantly different.

Eapen et al. (1971) reported heritability of SC for male mice to be 0.73 ± 0.47 but did not estimate the value in females due to large sampling errors. Paternal half-sib as well as full-sib family groups were tested for their relative SC in this experiment.

Dunnington et al. (1977b) reported the heritability of SC in unselected, random-bred ICR mice to be 0.31 ± 0.07, estimated at 62 days of age by a sire-son regression. In order to be used in the analysis, each male had to sire at least two litters from which groups of two or more full brothers survived. Every sire's record was repeated for each of his sons and a total of 466 sire-son pairs were used in the analysis.

Although little other information is available on the heritability of cholesterol levels in mice, results have been reported for several

other species. Reported estimates of the heritability of SC in chickens ranged from -0.04 to 0.34 (Cherms et al., 1960; Wilcox et al., 1963; and Estep et al., 1969). An estimate of heritability of total SC in beef cattle calculated from paternal half-sibs was 0.80 (Stufflebean and Lasley, 1969). Dairy heifers (2 to 20 months of age) were found to have SC heritability of 0.19 ± 0.08 and dairy cows to have SC heritability of 0.51 ± 0.18 (Arave et al., 1975). Rothschild and Chapman (1976) reported SC heritabilities in swine of 0.22 ± 0.05 (realized), 0.10 ± 0.04 (paternal half-sib analysis) and 0.26 ± 0.07, 0.27 ± 0.08 and 0.24 ± 0.08 (regression of offspring on sire, dam and midparent, respectively). Clarkson et al. (1971) found squirrel monkeys had a realized PC heritability of 0.92.

The estimates of heritability of CC in the literature at present indicate that additive gene action influences the trait. The moderate heritabilities suggest that unintentional selection for elevated CC in human populations may result in cardio-vascular problems in offspring. The knowledge that heredity plays a sizable part in such a situation allows preventative measures or early treatment to avoid such conditions.

Genetic Control of Voluntary Physical Activity

Several reports in the literature have indicated that genetic control of voluntary physical activity or exploratory behavior exists in animals. Employing five inbred lines of mice, Thompson (1956) observed significant differences in levels of exploratory behavior among the lines. Two types of apparati, a grid platform and a Y-maze, were used to

determine the relative exploratory tendencies of the mice over 10-minute intervals. When activity was graphed as a function of time, there was only one case of overlap between two of the lines. Except for that one instance, each strain maintained activity scores absolutely apart from the other strains, indicating that hereditary factors definitely influenced the exploratory behavior of mice. Goodrick (1975) measured the activity of two inbred strains of mice in exercise wheels and found statistically significant differences between the lines, again indicating genetic control of activity.

Using a grid apparatus similar to the one mentioned above, McClearn (1961) measured the activity of two inbred strains, their F_1 progeny, backcrosses with the parental strains and F_2 progeny. An increase found in the F_1 mean over the midparent mean was interpreted by the author to indicate the existence of dominance. The data obtained from the F_2 generation led McClearn to estimate that approximately one-half of the F_2 variance in activity was determined by genetic factors.

Bruell (1964) reported the mode of inheritance of spontaneous wheel-running to be of a heterotic nature. Over a two-year period, 4,000 mice from 13 inbred strains and 31 F_1 populations (randomly chosen) were tested for their willingness to exercise in activity wheels. A significant number of F_1 hybrids in this study had activity scores which exceeded the score of their more active parent. Thus, the tendency of these animals to exercise showed "behavior hybrid vigor" which Bruell attributed either to a dominant or an over-dominant mode of expression.

Dunnington et al. (1977b) reported the heritabilities of spontaneous

wheelrunning in mice of 0.31 ± 0.12, 0.50 ± 0.11 and 0.27 ± 0.14 at 28, 49 and 70 days of age, respectively. Activity was measured in exercise wheels for a 22-hour period at each of these ages. An earlier study (Dunnington et al., 1977a) had resulted in significant, positive correlations among eight activity periods and indicated that three activity measurements would provide an adequate evaluation of each mouse's willingness to exercise. The heritability estimates were obtained from sire-son regressions using a total of 466 sire-son pairs.

Genetic Control of Postweaning Body Weight and of Feed Consumption

Genetic control of postweaning body weight in mice has been well documented. Falconer (1953) reported considerable divergence in body weight of lines of mice selected for maximum and minimum 42-day body weight. Realized heritabilities of 42-day body weight were estimated to be 0.20 ± 0.04, 0.50 ± 0.04 and 0.34 ± 0.02 in the large line, small line and pooled data, respectively. Other workers have reported similar heritability estimates for 42- and 56-day body weights. Estimates of heritability of 42-day body weight were 0.16 (Miller et al., 1963), 0.55 ± 0.21 (Vinson et al., 1969) and 0.33 ± 0.13 (Jara-Almonte and White, 1973). Heritability estimates for 56-day body weight obtained by Vinson et al. (1969) and Jara-Almonte and White (1973) were 0.49 ± 0.19 and 0.29 ± 0.13, respectively.

A trait closely related to postweaning body weight is the amount of feed consumed by an individual. Research has shown that feed consumption is a moderately heritable trait in mice. Sutherland et al. (1970) re-

ported a realized heritability of 0.20 ± 0.57 and a heritability calculated from paternal half-sib correlations pooled over generations, lines and sexes of 0.08 ± 0.10. Jara-Almonte and White (1973) reported post-weaning feed intake heritabilities of 0.05 ± 0.06 and 0.31 ± 0.10 for 21 to 42 and 42 to 56 days of age, respectively.

Correlated Responses

Artificial selection for a particular character often results in alteration of the means of other traits. The four characters which were used as criteria of selection in this selection study (SC, voluntary physical activity, 56-day body weight and feed consumption) were chosen for two reasons. First, as the preceding review of literature had indicated, a reasonable amount of progress should be achieved by short-term artificial selection for maximum and minimum values of each trait. That is, each of the traits is under moderate genetic control. Second, previous studies have indicated that the four traits are, to some degree, phenotypically and genetically interrelated. The comparisons of major interest in this study concern how SC fluctuates with activity and how varying levels of SC and activity are associated with other physiological traits, such as body weight, feed consumption, percentage of body moisture and reproductive fitness. The following review summarizes studies in the literature concerning these interrelationships.

Much of the literature exploring the effects of activity on SC levels, intake and body weight in laboratory animals has actually dealt with systematic physical training (or exercise) rather than voluntary

activity. The evidence concerning the effects of exercise on circulating cholesterol include opposing conclusions that exercise increases SC, has no effect on SC and decreases SC.

While subjecting rats to a strenuous program of swimming exercise, Papadopoulos et al, (1969) found that plasma cholesterol decreased gradually. The training regime consisted of a four-hour period of swimming daily for four weeks. Since trained rats consistently had lower PC than the unexercised control animals, it was concluded that a continuous program of strenuous training resulted in a reduction of PC in rats.

Lewis et al. (1961) reported the effects of exercise on serum lipids in rats which were fed various high fat diets. The form of exercise used was automatically revolving drums in which the rats spent eight hours daily. An interaction was found between exercise and level of fat in the diet. Exercise successfully reduced the level of serum lipids in rats which had suffered elevated serum lipid levels due to a high fat intake.

The relationships between SC, exercise and food restriction in rats was examined by Jones et al. (1964). Exercise by swimming was found to be effective in preventing an increase in SC as the animals aged. The authors speculated that exercise might have influenced the correlation between fatness and cholesterol by lowering both.

In another study concerning diet, forced exercise and SC in rats, Hanson et al. (1967) reported that SC was elevated in animals whose caloric intake was restricted as compared to those fed ad libitum and was higher in exercised animals than in sedentary ones. An interaction

($P<.01$) between calorie restriction and exercise occurred. The group of exercised animals for which intake was restricted had the highest SC, indicating a different relationship between SC and exercise than the preceding studies.

Similarly, Brainard (1959) reported that rabbits undergoing forced exercise in revolving drums experienced higher SC levels than did the sedentary controls. A significant interaction occurred between high levels of cholesterol in the diet and intense levels of exercise.

Dunnington et al. (1977a,b) reported on the association between SC, voluntary physical activity (as opposed to forced exercise), and body weight. In studying unselected random-bred mice, Dunnington et al. (1977b) reported phenotypic and genetic correlations between SC and activity which were not significantly different from zero. An interesting trend occurred in comparing activity scores with body weight at certain ages, however. The body weight at 21 days of age was significantly, positively correlated ($P<.05$) with all activity scores. Weight at 44 and 67 days of age were positively (but not significantly) correlated with activity at 28 days of age. However, weights at 44 and 67 days of age were negatively correlated with the remaining activity scores (at 49 and 70 days of age and with total activity). These results agreed with those obtained by Thye (1973) indicating that mice must reach a certain, minimum weight by their first activity period in order to be successful in turning the exercise wheel effectively. Thye found that the initial activity scores of mice selected for minimum 21- to 42-day gain were less than those of mice selected for maximum 21- to 42-day gain, pre-

sumably because the low line mice did not have the weight and/or stamina necessary to turn the exercise wheels. After this initial period, however, the low line mice obtained much higher activity scores than did those from the high line. The significant positive correlation between weight at 21 days of age and all activity scores reported by Dunnington et al. (1977b) suggested that the mice which weighed comparatively more at 21 days of age were more active than those of lesser body weight. However, the negative trend in the correlations of weights at 44 and 67 days of age indicated that heavier weight at these ages were associated with lower activity scores (i.e., heavier individuals after 44 days of age were less inclined to exercise).

In a study using mice that had been selected for 22 generations for maximum and minimum postweaning gain, Dunnington et al. (1977a) found significant, negative phenotypic correlations between activity and SC at five weeks of age and between activity and SC at 10 weeks of age in the mice selected for maximum postweaning gain. Also, a significant negative phenotypic correlation between activity and SC at five weeks of age occurred in the mice selected for minimum postweaning gain.

In measuring feed intake from three to 10 weeks of age in these two divergent selected lines of mice, Dunnington et al. (1977a) reported highly significant, negative phenotypic correlations between total intake and SC (both at five and at 10 weeks of age) in the maximum gain line, but no significant correlations for either the low gain line or the random-bred control.

The evidence presented above provides reasonable indication that

there are various interactions among SC, activity, body weight and intake but these interrelationships were not fully clarified by the one- or two-generation studies referenced. One of the major purposes of the present study was to afford a clear picture of these interrelationships by measuring correlated responses in all the developed lines after five generations of selection.

SC and Body Weight During Aging

The long-term trends of SC and of body weight during aging are of considerable interest in humans since the occurrence of atherosclerosis (a possible result of high levels of SC and weight) is more frequent as age increases (Kritchevsky, 1958). Trends in body weight and, to a lesser extent SC, have been studied in laboratory animals in order to clarify the basic aspects of their occurrence.

Several reports have indicated that change in body weight of mice is greatly dependent on the population which is being measured. Roberts (1961) recorded body weight of male mice at four-week intervals from time of first mating (56 days) until natural death of the animals. These mice originated from lines that had been selected for maximum 56-day weight (high lines), minimum 56-day weight (low lines), an unselected control, and various crosses of the high and low lines. One high line and one high x high crossed line revealed growth patterns in which maximum body weight was reached at a relatively early age and then decreased rather sharply. In contrast, the remaining lines achieved maximum body weight later in life than the two lines mentioned above,

but remained essentially at maximum body weight until death. These results indicated to the author that the mice selected for maximum 56-day weight laid down a comparatively large quantity of fat as mature animals which was gradually reduced by further aging.

Based on the results reported by Roberts (1961), the expectation of trend in body weight during aging in the present study was a steady increase in weight to a maximum and then general plateauing (maintenance of maximum weight) until death since an unselected population of individuals was used.

A similar increase and then plateauing was expected for levels of SC during aging. Dunnington et al. (1977a) tested mice for SC at five and 10 weeks of age and found a significant increase in levels of SC with maturation. Bruell et al. (1962) reported no differences in SC of mice at two and 12 months of age. Although other workers have measured cholesterol levels of aged mice (e.g., Weibust and Schlager, 1968), they did not indicate the levels of SC in those animals early in life. Since SC is highly dependent on the strain of mice being measured (Dunnington et al, 1977a; Bruell et al., 1962), the values of SC given for aged mice could not be used as a mean value to which other data might be compared.

Sexual Dimorphism

Most of the traits measured in this study are expressed in different magnitudes by males and females. Generally, males have higher SC values than females at all ages (Kritchevsky, 1958; Bruell et al., 1962;

Weibust and Schlager, 1968). Physical activity measured in activity wheels was considerably higher in female rats than in male rats (Brody, 1950). Bruell (1964) reported a highly significant sex difference in wheelrunning in mice with males scoring higher than females in 38 of the 44 genotypes tested. Higher postweaning body weight in male mice as compared to female mice has been well documented (Falconer, 1953; Eisen and Legates, 1966).

Since significant differences in the traits measured were expected for males and females, the analyses of the data in the present study were performed separately for the two sexes. Although methods are available for correcting for sex effects (e.g., Falconer and King, 1953), a sufficient number of animals was available in each within-sex subclass to yield reasonable magnitudes of error for the various analyses, and the differing expression of measured traits in the two sexes (due to different hormonal levels, etc.) was of interest.

EXPERIMENTAL PROCEDURES

General Husbandry

The mice in this study were from an ICR albino stock originally from the Institute of Cancer Research, Philadelphia. All the animals were maintained in a controlled environment laboratory with temperature of 22°C, relative humidity of 50-60% and alternating 12-hour periods of light and dark. Housing consisted of translucent polypropylene cages approximately 27 cm x 17 cm x 13 cm, with metal cage tops which served as feed hoppers and held water bottles. Purina Lab Chow was fed at all times except during breeding and lactation when Purina Mouse Chow was fed for additional energy. Feed and water were available *ad libitum* at all times.

Standard procedures in rearing the mice were practiced. These procedures included recording litters at birth, standardizing litters to eight pups (four males and four females) at five days, obtaining litter weights and permanently identifying pups by toe-notching at 12 days, weaning at 21 days, obtaining individual body weights at 21, 42 and 56 days and breeding at approximately 80 days of age. Litter size at birth and the percentage of females littering (the proportion of those females exposed to males which actually littered) were routinely obtained in all lines throughout the study.

Selection Study

The selection experiment was conducted with ICR albino mice produced by the reciprocal crossing of two lines of unselected, random-bred animals which had been maintained in this lab as control lines for 28 generation. After the initial crossing of the two lines (generation 1), 30 males and 30 females were randomly assigned to each of nine lines and randomly pair-mated within lines for one more generation (generation 2). Generation 2 and each subsequent selected generation, in each line, consisted of 25 males and 25 females along with five extras of each sex. Single paired matings were made at random within the selected groups with the avoidance of sibbing.

The traits for which individual selection was practiced were SC, voluntary physical activity and 56-day body weight. Selection for feed intake was on a within-sex, full-sib family selection basis.

SC selection. Three randomly chosen lines served as the base populations for SC selection. After establishing the high, control and low lines, male and female breeders were selected each generation solely on the basis of maximum SC (line CH) and minimum SC (line CL). A cholesterol control line (line CC) was maintained by random selection of breeders. Serum cholesterol for each animal was determined from a blood sample taken between 57 and 62 days of age.

The range in age of sexual maturity for these mice is approximately 35 to 42 days. The age range of 57 to 62 days was chosen for SC testing since, at that time, the mice were sexually mature, young adults.

Dunnington et al. (1977a) reported a significantly lower SC in five-week old mice as compared to SC of the same mice at 10 weeks of age. Bruell et al. (1962) found no difference in SC of two- and 12-month-old mice. These results indicated an increase in SC during the period of sexual maturity followed by plateauing of SC levels in mature adult mice. Therefore, SC in this study was determined approximately two to three weeks after sexual maturity in order to obtain a relatively constant, adult SC value.

The serum cholesterol level of the mice was determined from approximately 0.5 ml of blood, removed by sinus orbital puncture (Riley, 1960). The total SC concentration was obtained by gas chromatography (Driscoll et al., 1971). In this method of cholesterol determination, the blood sample was centrifuged for 30 minutes. The cleared serum was then siphoned off and mixed with one ml of ethanol and one ml of alcoholic potassium hydroxide (6 ml of 33% potassium hydroxide were diluted to 100 ml with ethyl alcohol) on a Vortex mixer. Saponification was allowed to occur for three hours in a 37^{o}C water bath. One-half ml of heptane was added to the sample and mixed, then one ml of water was added and mixed. The heptane fraction was immediately drawn off and injected into an F & M model 400 gas chromatograph. The sample cholesterol peaks were compared with peaks from a pure cholesterol standard which was injected after every second sample. Duplicates were analyzed on any sample which contained a sufficient amount of blood.

Activity selection. Voluntary physical activity was measured in

three of the lines. Activity was measured in exercise cages for a period of 22 hours when the mice were 28 and 49 days of age. Each cage consisted of a small sedentary space (5 cm x 5 cm x 9 cm) where feed and water were available, and an adjoining wheel approximately 15 cm in diameter and 6 cm wide which revolved freely. The number of revolutions turned by each individual during an activity period of 22 hours was recorded by a mechanical counter and served as the activity score for that period. The sum of the activity scores obtained during the two measurements (total activity score) served as the criterion of selection for the maximum activity line (AH) and the minimum activity line (AL). An unselected activity control line (AC) was maintained.

In earlier mouse studies using the same exercise cages for measurement of voluntary physical activity (Dunnington et al., 1977a,b), activity was measured for a 22-hour period every six days in a seven-week study and at three-week intervals in a six-week study. The high positive correlation among activity scores at different ages resulting from these projects indicated that activity scores recorded at 28 and 49 days of age would provide a total activity socre as reliable as could be expected from more extensive measurements. Therefore, the total activity score was chosen as the criterion of selection for the activity lines in this study.

Body weight selection. The remaining three lines of the original nine were selected on the basis of 56-day body weight. Line WH was selected for maximum 56-day body weight, line WL for minimum 56-day body

weight and line WC was an unselected control line. Selection for increased and decreased 56-day body weight was expected to result in considerable divergence in body weight (Falconer, 1953) and in obesity. Lang and Legates (1969) observed that male mice increased fat deposition from six to eight weeks of age and that females reached essentially the same level of body fat composition at eight weeks of age although their period of greatest fat deposition was from four to six weeks. White (1974) reported a definite increase in body fat from seven to 10 weeks of age for both sexes with females having higher percentage of fat than males at all ages. Thus, selection for maximum and minimum 56-day body weight should significantly alter the body weight and composition of the mice in this study.

Feed intake selection. After random selection of breeder mice for lines WC and AC in generation 2, the remaining mice served as the base population for a selection study on feed consumption. Lines were developed for maximum intake (IH) and minimum intake (IL), and a control intake line (IC) was maintained. Thirty single paired matings were used to perpetuate the lines each generation. From the standardized litters of four males and four females, three pups of each sex were randomly chosen and housed together. Intake was measured from three to seven weeks of age for these groups of full sibs and selection was made on the basis of total feed consumption per mouse over the test period. Thus, within-sex, full-sib family selection was used to choose the 10 cages of males and 10 cages of females as the selected parents of the

next generation. The control line IC was maintained exactly as IH and IL were, and 10 cages of males and of females were randomly chosen to supply breeders for each generation.

Intake was measured according to the method of Jara-Almonte and White (1973). Feed (in the form of pellets) was placed in jars with mouths down on each cage top so that the mice were able to chew feed off the pellets but were not actually able to take chunks of feed into the cage. The weight of feed and jar were obtained before putting it on a cage and at the end of each test period. The first two test periods were six days long and all subsequent test periods were four days long (since the mice did not consume as much feed immediately postweaning as they did as more mature animals). The difference between beginning feed-plus-jar weight and ending feed-plus-jar weight yielded the amount of feed consumed during each test period. The sum of all individual test period scores served as the family mean which was used as the criterion of selection for the intake lines.

Correlated Responses

Selection was practiced in the various lines described above and control lines were maintained with them until generation 7, resulting in five generations of selection for the SC, activity and weight lines and in four generations of selection for the intake lines. After the usual selection, mating, littering and weaning of generation 7, the same single paired matings of parents were repeated in order to replicate generation 7 for study of correlated responses. Fifteen litters

from each of the 12 lines were randomly selected from this replicate of generation 7 and the litters of eight pups were divided at weaning and tested in the following manner.

Two randomly chosen males were housed together and two randomly chosen females were housed together. A total feed intake value was obtained for these full brothers and full sisters from three to seven weeks of age. These four mice were then tested for SC between 57 and 62 days of age. The remaining four mice of each litter were tested for voluntary physical activity at 28 and 49 days of age.

After all testing was complete in the group of mice replicated to measure correlated responses, one male and one female from 10 litters in every line were maintained until approximately 70 days of age for body moisture analysis. At this time they were fasted for 16 hours, weighed and overdosed with CO_2. The carcasses were immediately wrapped in individual plastic bags and frozen ($4^{o}C$) for at least 24 hours. The frozen carcasses were then chopped into one to two cm wide slices and lyophilized in a Virtis freeze dryer. Using the fasted, live weight as a basis, the moisture content of each individual was calculated.

Thus, in all eight selected lines and four control lines, SC, activity, 56-day body weight and feed intake were measured to provide information on whether selection for one of the traits may have altered the expression of another trait. Other physiological characteristics, such as litter weight at 12 days, body weights at 21 and 42 days and percentage of body moisture were also obtained and analyzed for alterations due to artificial selection.

Aging Study

After the routine random selection of 30 breeding pairs of mice from the control serum cholesterol line in generation 2, the remaining 130 males and females were housed four to a cage and maintained until they were approximately 1.5 years old. Each mouse was weighed every three weeks during this period and blood samples were obtained every 18 weeks for SC determination. Although several animals died during this time and a few were euthanized due to serious wounds inflicated by cagemates, there was no indication that these older animals had begun to die as a result of old age. After the fifth SC determination (at 567 days of age) the longevity study was terminated and the collected data analyzed for trends in body weight and SC over time.

Statistical Analysis

Traits for which direct selection were practiced (SC, activity, 56-day body weight and feed intake), as well as other traits which may have been influenced by the selection program, were studied. In analyzing the data, selection differentials, response to selection, realized heritability and correlated responses among traits were calculated.

Selection differential. The selection differential (S) is the mean value of a quantitative character in the group of individuals selected as parents of the next generation deviated from the mean value of that quantitative trait in the group of all possible parents. It can be expressed as the mean difference of the selected parents from the

general mean of the population.

In the actual selection experiment the selection differential which is planned is not always achieved. That is, due to differences in fertility of the parental group, differences in viability of the offspring and accidental deaths, those individuals selected as parents of the next generation do not always contribute equally to the offspring generation. Therefore, a distinction is made between the expected and the effective S, and the effective S is weighted according to the actual number of offspring measured in the next generation which each parent contributes. By comparing the expected and effective S, it can be ascertained whether natural and artificial selection were working in concert or in opposition.

In order to standardize S, that is, to allow the comparison of the selection differentials of different traits in different populations, S is divided by a measure of the variability of the trait, the phenotypic standard deviation (σ_p). The resulting value is called the intensity of selection and is designated by i.

$$i = \frac{S}{\sigma_p} \qquad (1)$$

Response to selection. The progress that occurs by selecting for or against a certain character is called the response to selection (R). This response is the difference in mean phenotypic value of the parental generation before selection and the mean phenotypic value of the offspring of the selected parents. The progeny of selected parents, rather than having an average phenotypic value for a selected trait

identical with that of their parents, have one intermediate between the selected parental mean and the mean of the parental population before selection. This regression of offspring on midparent value ($b_{O\bar{P}}$) is equivalent to heritability in the narrow sense (h^2), provided there are no non-genetic causes of resemblance between offspring and parent. Thus, the relationship between R and S is:

$$R = b_{O\bar{P}} S = h^2 S . \qquad (2)$$

That is, the response to selection is the difference between the mean phenotypic value of a trait in the selected parents and that of the whole population regressed by the amount of that difference which is reflected in the offspring.

Realized heritability. In this selection experiment, R and S were measured and their ratio (R/S) was called the realized heritability (h^2_R). This value is estimated by plotting generation means (deviated from the control line means) against the cumulative effective selection differential (obtained by accruing selection differentials over generations) and fitting a regression line to the points. Then h^2_R, the regression of an individual's breeding value on its phenotypic value, is the slope of the fitted regression line.

Correlated responses. Artificial selection for one trait is often accompanied by changes in the means of associated traits. The magnitude of the phenotypic correlations are obtained by simple product-moment

correlations calculated over generations.

Due to limitations in time and facilities, it was impossible to measure all traits in all 12 of the developed lines throughout the study. Specifically, three criteria of selection (SC, activity and feed intake) were measured only in the lines where they were employed for selection. Therefore, a replicate of generation 7 was created and randomly chosen representatives from every line were tested for body weights at 12, 21, 42 and 56 days of age, SC, activity, feed intake and body moisture content. Then, by using Duncan's new multiple range test, the 12 lines were ranked according to their progress for each trait.

Inbreeding. The amount of inbreeding in a population is purely a relative term; that is, inbreeding is measured relative to some specific time. In this selection experiment, two unselected, random-bred lines of mice were reciprocally crossed, after 28 generations of within-line mating. The inbreeding coefficient (F) at this time was assumed to be zero and was then calculated according to the following formula (Falconer, 1960) which gives F per generation:

$$F = \frac{1}{8N_m} + \frac{1}{8N_f} \qquad (3)$$

where,

N_m = number of males used as breeders per generation, and

N_f = number of females used as breeders per generation.

The expected F was 1% per generation or 6% inbreeding over the course of the study for a random-breeding population. This estimate was slightly

inflated since the restriction of avoidance of sibbing was used in the breeding program. The small amount of inbreeding was assumed to have little or no effect on the short-term selection experiment being described.

Transformations. Since correlations occurred between means and variances for the four criteria of selection (SC, activity, 56-day body weight and feed intake), transformations to common logarithms were performed on all data to eliminate the correlations before statistical tests of significance were performed. In the interest of clarity from a biological standpoint, data are presented in the text and tables in terms of the original scales of measurement. However, all the data are presented in transformed form in the Appendices for reference.

RESULTS AND DISCUSSION

Cholesterol Lines

Means, standard deviations and coefficients of variation for the three cholesterol lines are shown in Table 1. Since a correlation between means and variances occurred in the cholesterol lines, all tests of significance were performed on common logarithmic transformations of the data, although raw data values were used in this and subsequent tables in the interest of clarity from a biological standpoint. Beginning values (at generation 2) were quite similar for males in all three lines and for females across lines. The similarity occurred by chance since division of the mice from one large population into separate lines was purely random. Upward progress in SC means of the CH line was unsteady for both males and females. Similar fluctuations occurred in the control line, however, with a gradual decrease in SC between generations 2 and 7. The low line, CL, was perhaps the least variable of the three, experiencing only one increase in mean SC at generation 3.

By deviating the two selected lines from the control, environmental influences were theoretically eliminated since the control line was developed at exactly the same time and under the same environmental circumstances as the selected lines, the only difference being that no selection was practiced. Table 1 lists the divergence of CH from the control as the response. A steady upward trend in SC response was ap-

Table 1. Means, standard deviations, coefficients of variation and responses to selection for serum cholesterol values in selected and control SC lines.

Generation	Line CH					Line CC				Line CL				
	N[a]	Mean	S.D.	C.V.	R[b]	N	Mean	S.D.	C.V.	N	Mean	S.D.	C.V.	R
Males														
2	95	157.4[c]	31.3	19.9	0.9	101	156.5	35.2	22.5	90	150.9	36.0	23.9	-5.6
3	87	144.3	38.2	26.5	15.9	80	128.5	31.7	24.7	74	111.5	24.7	22.2	-16.9
4	104	185.1	37.4	20.2	31.2	100	153.8	38.9	25.3	84	118.1	26.4	22.3	-35.8
5	102	171.8	57.2	33.3	46.8	101	125.0	33.6	26.9	95	90.0	18.7	20.7	-35.0
6	93	161.8	45.3	28.0	64.6	95	97.1	26.9	27.7	105	64.0	16.1	25.2	-33.1
7	74	191.9	44.4	23.1	86.4	87	105.5	34.9	33.1	93	60.6	15.8	26.1	-44.9
Females														
2	94	128.5	23.8	18.6	0.3	88	128.2	32.8	25.6	84	128.9	28.9	22.4	0.7
3	96	116.4	29.2	25.1	5.3	79	111.1	27.6	24.8	74	86.3	18.8	21.8	-24.8
4	95	159.8	38.7	24.2	31.1	99	128.6	33.1	25.8	99	97.2	21.3	21.9	-31.4
5	94	143.5	47.1	32.8	46.2	98	97.3	23.3	23.9	100	72.4	15.6	21.6	-24.8
6	107	126.4	33.7	26.7	49.9	103	76.5	22.6	29.6	91	51.4	12.1	23.5	-25.1
7	93	163.0	39.8	24.4	79.3	85	83.7	21.7	25.9	104	50.0	16.8	33.7	-33.7

[a]Number of observations per mean.
[b]Response (selected line generation mean deviated from control line generation mean).
[c]mg / 100 ml.

parent for both males and females. Also, Table 1 shows the steady decrease in the response of SC due to downward selection (line CL) after correction had been made for environmental influences.

Two basic methods of observing selection progress are given in Table 2. Phenotypic progress was defined as the regression of the generation means of SC on generation number ($b_{R:GEN}$). Genetic progress was obtained by regressing the deviation of selected line generation means from control line generation means on generation number ($b_{DR:GEN}$).

It is apparent by inspecting the phenotypic progress in Table 2 that some environmental factor caused a downward trend in SC values since the unselected control line experienced a significant ($P<.05$) reduction in SC over the course of the selection study (10.79 and 10.22 mg / 100 ml drop per generation for males and females, respectively). Also, line CH made very little upward phenotypic progress (6.06 and 5.32 mg / 100 ml per generation for males and females) while CL males and females experienced a very sharp decline in SC values (17.77 and 14.97 mg / 100 ml per generation). Thus, the environment appeared to facilitate downward selection for SC and to hinder upward SC selection.

By deviating the selected line generation means from the control means, however, the genetic progress from selecting for maximum and minimum SC was obtained (Table 2 and Figure 1). Almost threefold greater genetic progress for SC selection was achieved in line CH than in line CL (16.83 versus -6.99 mg / 100 ml for males and 15.55 versus -4.75 mg / 100 ml for females).

The selection differentials (S) and selection intensities (i) for

Table 2. Phenotypic and genetic responses to selection for high and low serum cholesterol.

Line	$b_{R:GEN}$ ± S.E.[a]		$b_{DR:GEN}$ ± S.E.[b]	
	Males	Females	Males	Females
CH	6.06 ± 3.67[c]	5.32 ± 4.33	16.83 ± 0.61*	15.55 ± 1.62*
CC	-10.79 ± 3.59*	-10.22 ± 2.99*	-0-	-0-
CL	-17.77 ± 2.58**	-14.97 ± 2.86**	-6.99 ± 1.65*	-4.75 ± 2.27

[a]Regression of generation means on generation number.
[b]Regression of generation means deviated from control on generation number.
[c]mg / 100 ml.
*(P<.05). **(P<.01). Statistical tests of significance were performed on data transformed to common logarithms.

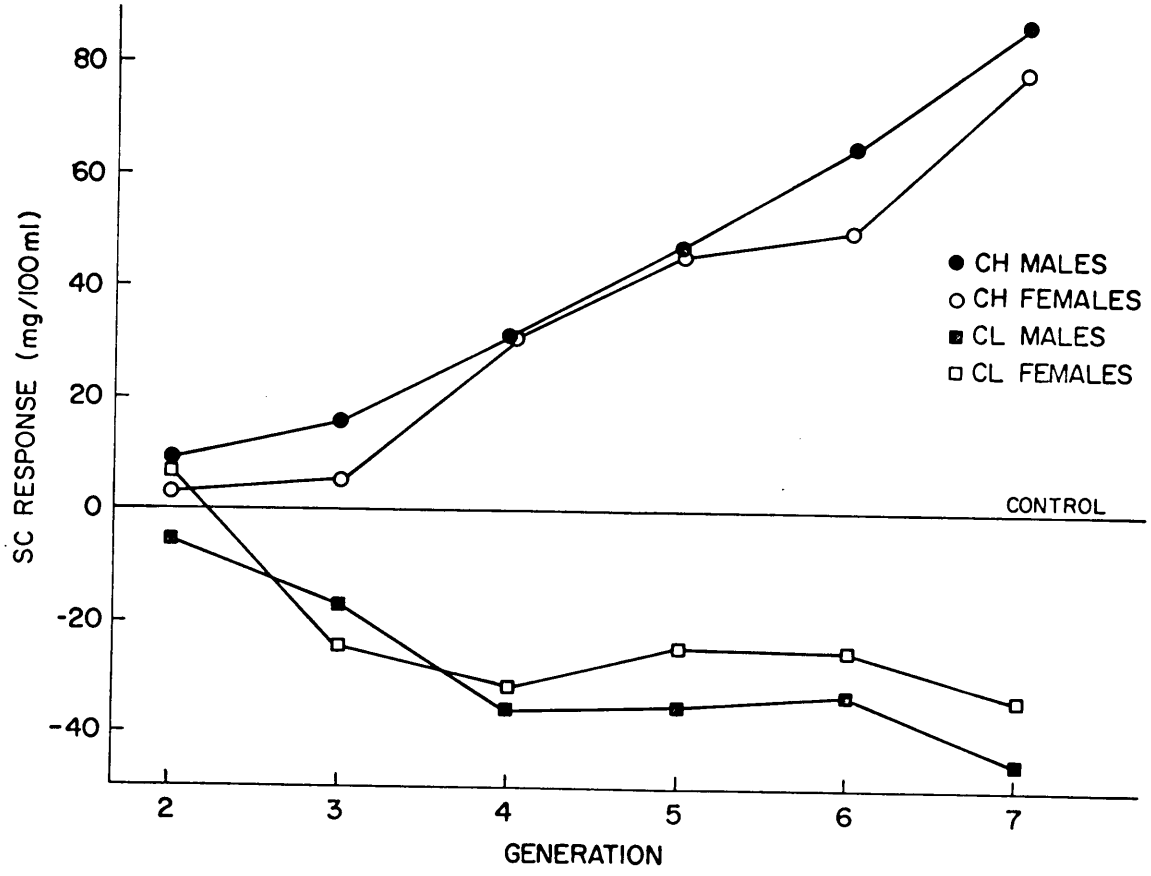

Figure 1. Response to selection for serum cholesterol by generation number.

lines CH and CL are given in Tables 3 and 4, respectively. The expected S indicates the difference each generation between the mean of all possible parents and the mean of the selected parents, assuming each selected parent contributed an equal number of offspring to the next generation. Due to variable fertility of parents, differing viability of offspring and accidental deaths, the expected S was not an accurate figure after the offspring generation had been raised. Therefore, an effective S, based on the actual number of offspring of each parent which lived to be tested in the next generation, was calculated.

By comparing the expected and effective selection differentials as a ratio (effective S / expected S), an idea of the relationship between natural and artificial selection was obtained. In the case of line CH this ratio was always less than unity, that is, the effective S was always less than the expected S. This situation was interpreted to mean that natural selection worked in opposition to or hindered artificial selection, since animals of lower selected value were either more fertile, contributed more offspring or contributed more viable offspring than animals of greater selected value. However, if a situation occurred in which the S ratios were consistently greater than unity, it would indicate that animals of greater selection value were more prolific or had produced more viable offspring than animals of lesser selection value. In this particular study the power of such a comparison is somewhat reduced since all litters were standardized to eight pups at five days of age. Thus, very prolific parents were not given full credit for their exceptional ability to reproduce. However, for

Table 3. Expected and effective selection differentials and intensities for high cholesterol line.

Generation	Expected Selection Differential		Effective Selection Differential		Cumulative Effective Selection Differential		S Ratio (EffS/ExpS)
Males	S[a]	i[b]	S	i	S	i	
2	39.7	1.3	35.0	1.1	35.0	1.1	.88
3	56.6	1.5	42.9	1.1	77.9	2.2	.92
4	51.4	1.4	45.7	1.2	123.6	3.4	.89
5	82.7	1.4	78.0	1.4	201.6	4.8	.94
6	58.2	1.4	50.4	1.1	252.0	5.9	.87
7	50.8	1.1	40.2	0.9	292.2	6.8	.79
Females							
2	30.6	1.3	27.4	1.2	27.4	1.2	.89
3	39.2	1.3	33.3	1.1	60.7	2.3	.85
4	50.6	1.3	42.6	1.1	103.3	3.4	.84
5	62.2	1.3	59.3	1.3	162.6	4.7	.95
6	48.2	1.4	43.5	1.3	206.1	6.0	.90
7	49.8	1.3	48.1	1.2	254.2	7.2	.97

[a] S = selection differentials in mg / 100 ml.
[b] i = S/σ_p = selection differentials in standard deviation units.

Table 4. Expected and effective selection differentials and intensities for low cholesterol line.

Generation	Expected Selection Differential		Effective Selection Differential		Cumulative Effective Selection Differential		S Ratio (EffS/ExpS)
Males	S[a]	i[b]	S	i	S	i	
2	-38.1	-1.1	-33.9	-0.9	-33.9	-0.9	.89
3	-24.5	-1.0	-22.9	-0.9	-56.8	-1.8	.94
4	-30.0	-1.1	-27.6	-1.0	-84.4	-2.8	.92
5	-21.4	-1.1	-18.9	-1.0	-103.3	-3.8	.88
6	-18.8	-1.2	-18.4	-1.1	-121.7	-4.9	.98
7	-18.8	-1.2	-17.3	-1.1	-139.0	-6.0	.92
Females							
2	-32.6	-1.1	-33.0	-1.1	-33.0	-1.1	1.01
3	-18.9	-1.0	-17.1	-0.9	-50.1	-2.0	.90
4	-21.4	-1.0	-20.1	-0.9	-70.2	-2.9	.94
5	-14.3	-0.9	-13.6	-0.9	-83.8	-3.8	.95
6	-12.5	-1.0	-11.5	-1.0	-95.3	-4.8	.92
7	-14.6	-0.9	-14.4	-0.9	-109.7	-5.7	.98

[a] S = selection differentials in mg / 100 ml.
[b] $i = S/\sigma_p$ = selection differentials in standard deviation units.

lines CH and CL, the S ratio indicated slight opposition between natural and artificial selection.

By accumulating the effective selection intensities over generations, an estimate of the number of standard deviation units of progress resulting from selection was obtained. The cumulative effective selection intensity for line CH was 6.8 for males and 7.2 for females and for line CL was -6.0 for males and -5.7 for females.

Another extremely important concept that was obtained from the information in Tables 3 and 4 was the realized heritability (h^2_R). Realized heritability was defined here as the regression of response (selected means deviated from control means) on cumulative effective selection differential. These values are given in Table 5 for the cholesterol lines and are graphed in Figure 2. The h^2_R for CH males was 0.31 ± 0.02 and for CH females was 0.33 ± 0.03. For line CL the respective male and female h^2_R were 0.34 ± 0.07 and 0.33 ± 0.14. All regressions were found to differ significantly from zero ($P<.01$) when statistical tests of significance were performed on data transformed to common logarithms.

The magnitude of h^2_R for serum cholesterol agreed well with estimates obtained by Dunnington et al. (1977b) for mice and was slightly higher than estimates in swine (Rothschild and Chapman, 1976) and in chickens (Cherms et al., 1960; Wilcox et al., 1963). It is somewhat lower than the h^2_R reported for plasma cholesterol in mice by Weibust (1973) in a similar five-generation selection study.

Almost threefold greater genetic progress from selection was

Table 5. Realized heritabilities in selected serum cholesterol lines.

	$h_R^2 \pm S.E.$[a]	
Line	Males	Females
CH	0.31 ± 0.02**	0.33 ± 0.03**
CL	0.34 ± 0.07**	0.33 ± 0.14**

[a]Realized heritability is expressed as the regression of selected means deviated from control means on cumulative, effective selection differential.
**(P<.01). Statistical tests of significance were performed on data transformed to common logarithms.

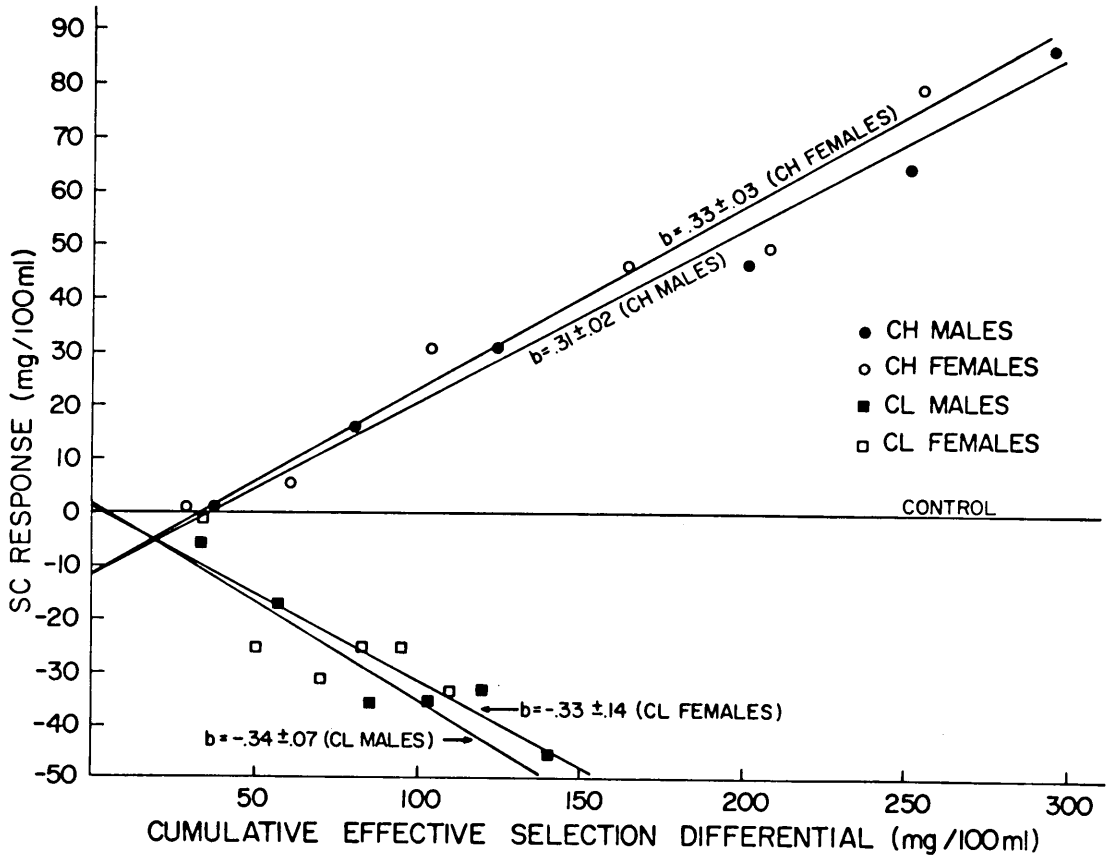

Figure 2. Response to selection for serum cholesterol by cumulative effective selection differential.

achieved in line CH than in line CL (Table 2 and Figure 1). This difference between lines CH and CL in genetic progress seemed to indicate that asymmetry of response had occurred. As Falconer (1954) pointed out in evaluating a similar situation, however, the genetic progress regressed on generation number afforded a "superficial" view of the asymmetry. His suggestion was to further examine the asymmetry by regressing response on the cumulative effective selection differential, that is, to compare h_R^2 in the two divergent selected lines. These h_R^2 were 0.31 ± 0.02, 0.33 ± 0.03, 0.34 ± 0.07 and 0.33 ± 0.14 for CH males, CH females, CL males and CL females, respectively. None of these regressions differed significantly from each other and, in this respect, no asymmetry of response was apparent. Figure 2, however, illustrated that considerably different selection differentials were obtained, with line CH mice achieving maximum cumulative effective selection differentials of 250 to 300 mg / 100 ml and line CL mice attaining selection differentials of only 100 to 150 mg / 100 ml. This sizable difference in selection differentials of the two divergent selected lines suggested the possibility of a physiological selection limit for minimum SC selection in the near future of these selected lines.

Falconer and King (1953) stated that reduction of the selection differential while h^2 remained constant indicated a physiological limit to selection but that progressive reduction of h^2 over generations implied some selection limit other than a physiological one (for example, loss of genetic variance due to inbreeding or opposing natural selection). Since only five generations of selection had been com-

pleted at the time of this writing, calculation of the trend in h^2 over time was not yet feasible. Other factors, however, suggest that a physiological limit might be near.

The means before selection in generation 2 were approximately 150 mg / 100 ml and 128 mg / 100 ml for males and females, respectively. By the conclusion of this short-term selection experiment, some CH mice had SC values well above 350 mg / 100 ml while the lowest CL mice had SC of about 30 mg / 100 ml. Thus in the upward direction, response had more than doubled and no physiological limit appeared near. (Strains of mice with mean SC values of 600 mg / 100 ml have been reported - Roberts and Thompson, 1976). Conversely, in the downward direction, the mice may soon reach a level of SC below which fitness will be impaired to the point where life will be impossible (since cholesterol is a precursor for sex hormones, constitutes a sizable portion of the dry matter in the brain and nervous system and is an intermediary in many biochemical pathways in the body). Therefore, as SC levels are gradually reduced through selective breeding, a threshold should be reached below which SC can not drop in a living, reproducing animal. Although there may be a threshold of SC value in the upward direction beyond which SC cannot increase in a living, reproducing animal, this study has indicated that the thresholds are not symmetrical about the mean. Mice which have added over 200 mg / 100 ml to the original mean have been raised and have reproduced, whereas no mice have survived with an SC value reduced 120 mg / 100 ml below the original mean. Thus, the approach of a physiological limit to selection for minimum SC appears

likely.

Activity Lines

Means, standard deviations and coefficients of variation of final activity score for maximum, control and minimum activity lines (AH, AC and AL, respectively) are given in Table 6. Due to the random assignment of mice to these lines at the beginning of the study and the highly variable nature of this trait, the mean values of total activity were highest in line AL, intermediate in the control and lowest in AH. With slight fluctuations line AH activity means progressed upward for both males and females from generation 2 through 7. The downward trend in activity score means of line AL was consistent. Although some fluctuations in the control activity line did occur, the values at generation 2 and at generation 7 were quite similar in both sexes, indicating no discernible time trend. It is of interest to note the high variability of this trait in all lines, as evidenced by the coefficients of variation ranging from 38% to 76%. The same magnitude of variation was reported in measuring activity with exercise wheels in earlier mouse studies (Dunnington et al., 1977a,b). The significant, positive correlation between means and variances of these data were nullified by a common logarithmic transformation of the data in order to perform tests of significance. Raw data values are presented in all tables however, so that the results are more easily interpretable in terms of the units of measurement.

The responses to selection, expressed as deviations from the con-

Table 6. Means, standard deviations, coefficients of variation and responses to selection for physical activity scores in selected and control physical activity lines.

Generation	Line AH					Line AC				Line AL				
	N[a]	Mean	S.D.	C.V.	R[b]	N	Mean	S.D.	C.V.	N	Mean	S.D.	C.V.	R
Males														
2	102	12071[c]	7324	60.7	-1075	91	13146	7727	58.8	90	13781	9456	68.6	636
3	96	16116	9006	55.9	728	97	15389	7119	46.3	94	12821	5843	45.6	-2568
4	104	15984	7507	47.0	1654	103	14331	7049	49.2	111	11122	6633	59.6	-3209
5	74	19894	9228	46.4	3422	80	16472	9530	57.9	95	10200	6937	68.0	-6272
6	88	20809	9957	47.9	7005	95	13804	7796	56.5	95	10122	6660	65.8	-3681
7	94	22063	9841	44.6	8290	92	13774	7459	54.2	94	8151	5602	68.7	-5623
Females														
2	88	12935	7565	58.5	-874	89	13808	9092	65.8	88	15510	7838	50.5	1701
3	84	17473	9179	52.5	-854	98	18328	8534	46.6	95	13908	7501	53.9	-4420
4	96	19351	9064	46.8	3515	103	15837	7139	45.1	89	13534	8153	60.2	-2303
5	62	20697	8631	41.7	5794	83	14903	8220	55.2	89	10999	5199	56.4	-3904
6	84	20191	8311	41.2	4105	87	16086	8025	49.9	91	10952	7020	64.1	-5135
7	96	21136	8117	38.4	6971	89	14165	6894	48.8	86	7802	5887	75.5	-6364

[a]Number of observations per mean.
[b]Response (selected line generation mean deviated from control line generation mean).
[c]revolutions.

trol line, are also given in Table 6 for lines AH and AL. In both lines and both sexes generation 2 yielded activity means in the opposite direction to which selection was to be applied. This occurrance was due to the sampling error in the random assignment of mice to the original lines and to the high variability of the trait. With one generation of selection for AH males and AL males and females and with two generations of selection for AH females, the activity scores showed definite (although somewhat fluctuating) response to selection in the appropriate directions.

Phenotypic and genetic progress for maximum and minimum physical activity are presented in Table 7. As the rather steady means for activity scores in line AC suggested (Table 6), there was no significant phenotypic trend in AC activity scores over generation in either sex. Phenotypic progress in AH was highly significant ($P<.01$) for males and significant ($P<.05$) in females. The phenotypic progress made was 1941.4 and 1443.1 revolutions per generation for males and females. Selection for reduced activity yielded highly significant ($P<.01$) phenotypic progress of -1061.9 and -1427.0 revolutions per generation for males and females, respectively.

However, when the means of the two selected lines were deviated from the control line means and then regressed on generation number (Table 7 and Figure 3), genetic progress differed considerably from the phenotypic progress. The regressions of response (with environmental influences removed) on generation number were significantly different from zero for AH males ($P<.01$), and for AH females and AL males ($P<.05$),

Table 7. Phenotypic and genetic responses to selection for high and low physical activity.

	$b_{R:GEN} \pm S.E.$[a]		$b_{DR:GEN} \pm S.E.$[b]	
Line	Males	Females	Males	Females
AH	1941.4 ± 256.5**[c]	1443.1 ± 393.5*	1926.3 ± 175.5**	1610.8 ± 367.3*
AC	15.1 ± 328.3	-167.8 ± 430.3	-0-	-0-
AL	-1061.9 ± 110.2**	-1427.0 ± 182.1**	-1077.1 ± 377.3*	-1259.2 ± 423.7

[a]Regression of generation means on generation number.
[b]Regression of generation means deviated from control on generation number.
[c]revolutions.
*(P<.05). **(P<.01). Statistical tests of significance were performed on data transformed to common logarithms.

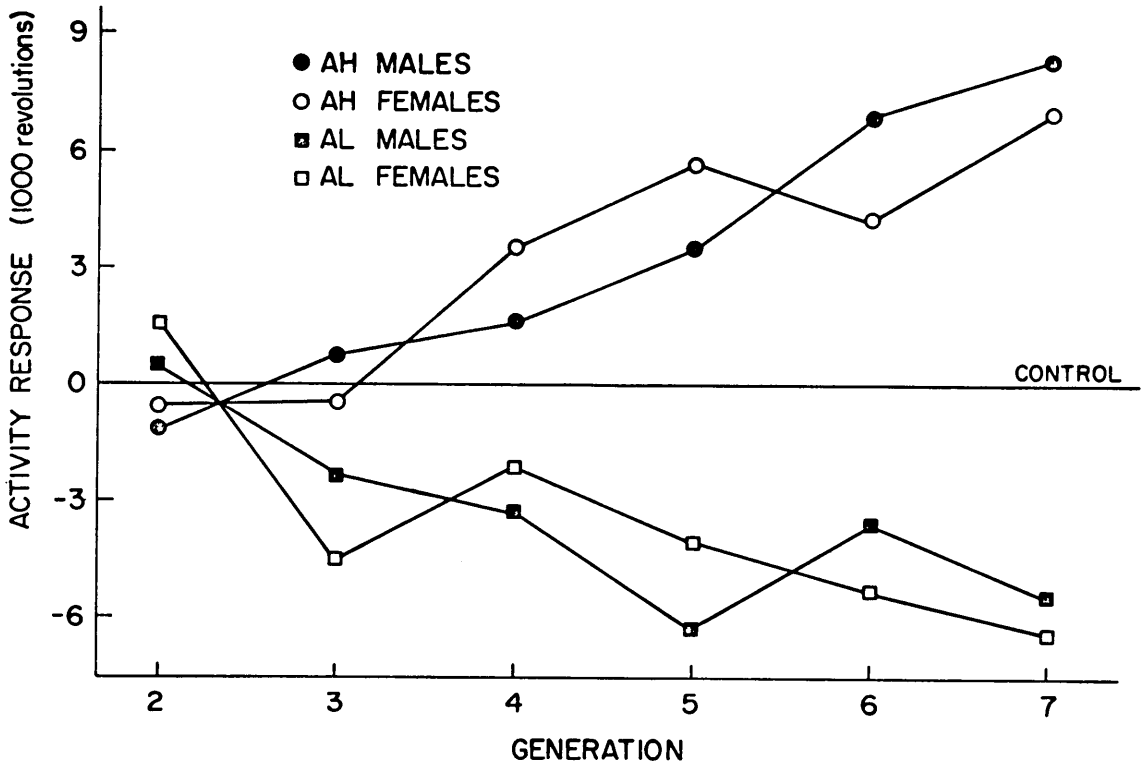

Figure 3. Response to selection for physical activity by generation number.

whereas the AL females did not differ from zero in genetic progress.

Expected and effective selection differentials and selection intensities are given in Tables 8 and 9 for the selected activity lines. Over the course of the study the cumulative effective selection intensities indicated maximum reach in standard deviation units of 6.7 and 6.1 for AH males and females and of -5.6 and -5.9 for AL males and females, respectively.

A comparison of effective S to expected S yielded ratios less than unity for both sexes in AH and AL. These S ratios indicated that natural selection opposed the effects of artificial selection in both lines. That is, mice selected for maximum and for minimum activity scores were not the most naturally fit animals in reproductive and general health aspects.

The h_R^2 obtained for voluntary physical activity are presented in Table 10 and are graphed in Figure 4. Upward selection yielded h_R^2 of 0.20 ± 0.02 and 0.19 ± 0.04 for males and females while downward selection resulted in h_R^2 of 0.19 ± 0.06 and 0.18 ± 0.06 for males and females respectively. In testing the common logarithmic transformed data for differences of the regressions from zero, it was found that h_R^2 in the AH males did differ from zero ($P<.01$) and in the AL line both male and female h_R^2 differed from zero ($P<.05$). The response in terms of selection units was symmetrical in the upward and downward directions.

Estimates of the heritability of activity obtained by a sire-son regression were reported by Dunnington et al. (1977a) to be 0.31 ± 0.12, 0.50 ± 0.11 and 0.27 ± 0.14 at 28, 49 and 70 days of age, respectively.

Table 8. Expected and effective selection differentials and intensities for high physical activity line.

Generation	Expected Selection Differential		Effective Selection Differential		Cumulative Effective Selection Differential		S Ratio (EffS/ExpS)
Males	S[a]	i[b]	S	i	S	i	
2	9933	1.4	9344	1.3	9344	1.3	.94
3	10836	1.2	9767	1.1	19111	2.4	.90
4	10477	1.4	8829	1.2	27940	3.6	.84
5	10019	1.1	8418	0.9	36358	4.5	.84
6	12275	1.2	10996	1.1	47354	5.6	.90
7	11531	1.2	11192	1.1	58546	6.7	.97
Females							
2	9107	1.2	8084	1.1	8084	1.1	.89
3	10418	1.1	9407	1.0	17491	2.1	.90
4	11777	1.3	9681	1.1	27172	3.2	.82
5	8309	1.0	7641	0.9	34813	4.1	.92
6	9501	1.1	8249	1.0	43062	5.1	.87
7	9609	1.2	8507	1.0	51569	6.1	.89

[a] S = selection differentials in revolutions.
[b] $i = S/\sigma_p$ = selection differentials in standard deviation units.

Table 9. Expected and effective selection differentials and intensities for low physical activity line.

Generation	Expected Selection Differential		Effective Selection Differential		Cumulative Effective Selection Differential		S Ratio (EffS/ExpS)
Males	S[a]	i[b]	S	i	S	i	
2	-8650	-0.9	-7611	-0.8	-7611	-0.8	.88
3	-6868	-1.2	-6027	-1.0	-13638	-1.8	.88
4	-7639	-1.2	-6812	-1.0	-20450	-2.8	.89
5	-7039	-1.0	-6670	-1.0	-27120	-3.8	.95
6	-6462	-1.0	-5921	-0.9	-33041	-4.7	.92
7	-5708	-1.0	-5205	-0.9	-38246	-5.6	.91
Females							
2	-8699	-1.1	-7974	-1.0	-7974	-1.0	.91
3	-8627	-1.2	-8051	-1.1	-16025	-2.1	.93
4	-8440	-1.0	-7557	-0.9	-23582	-3.0	.90
5	-7069	-1.1	-6692	-1.1	-30274	-4.1	.95
6	-7130	-1.0	-6391	-0.9	-36665	-5.0	.90
7	-5830	-1.0	-5231	-0.9	-41896	-5.9	.90

[a] S = selection differentials in revolutions.
[b] $i = S/\sigma_p$ = selection differentials in standard deviation units.

Table 10. Realized heritabilities in selected physical activity lines.

	$h_R^2 \pm$ S.E.[a]	
Line	Males	Females
AH	0.20 ± 0.02**	0.19 ± 0.04
AL	0.19 ± 0.06*	0.18 ± 0.06*

[a]Realized heritability is expressed as the regression of selected means deviated from control means on cumulative, effective selection differential. *(P<.05). **(P<.01). Statistical tests of significance were performed on data transformed to common logarithms.

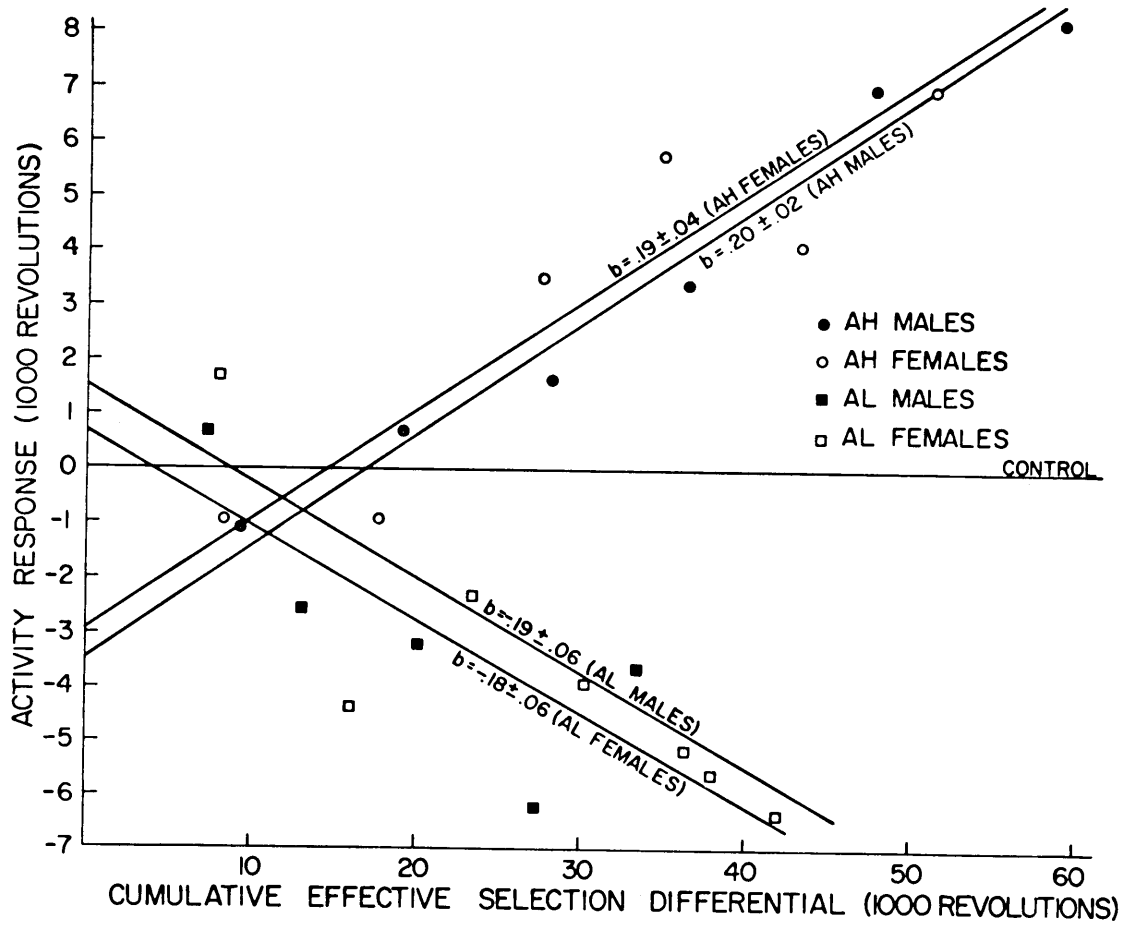

Figure 4. Response to selection for physical activity by cumulative effective selection differential.

Heritability of the combined (total) activity scores in that study was 0.54 ± 0.12. The results of the present study were considerably less than the h^2 estimate of total activity score referenced. Since h^2 applies to the particular population and time for which it is calculated and is influenced by the method of estimation, such a difference in magnitude was not surprising.

Fifty-six-day Body Weight Lines

The means and responses from the bidirectional selection experiment and control for 56-day body weight are given in Table 11. Selection for maximum 56-day body weight in line WH resulted in a steady increase in weight from generation 2 through 6, but a slight decrease in generation 7 in both sexes occurred. A similar trend occurred in the control line but generation 2 and 7 means were closer together in WC than in WH. Line WL, selected for minimum 56-day body weight, increased slightly in mean values and then a gradual reduction in means occurred.

Correcting the selected line means for environmental influences by deviating them from control line means yielded steady responses in the appropriate directions for the five generations of selection (Table 11).

Table 12 presents both phenotypic and genetic progress from selection for maximum and minimum 56-day body weight. Inspection of the regression of generation means on generation number in the control WC showed non-significant but slightly negative regressions for both sexes. Phenotypic progress in the WH line was positive but non-significant for both sexes, while in the WL line regressions were significantly below

Table 11. Means, standard deviations, coefficients of variation and responses to selection for 56-day body weight in selected and control 56-day body weight lines.

Generation	Line WH					Line WC				Line WL				
	N[a]	Mean	S.D.	C.V.	R[b]	N	Mean	S.D.	C.V.	N	Mean	S.D.	C.V.	R
Males														
2	88	33.7[c]	3.3	9.9	1.2	83	32.6	3.5	10.8	96	32.7	2.6	8.0	0.2
3	82	35.0	2.7	7.7	1.1	72	33.9	2.5	7.3	90	32.9	2.5	7.5	-1.0
4	97	37.7	2.5	6.6	2.2	97	35.5	2.8	7.9	109	33.1	2.6	7.8	-2.4
5	95	37.8	2.6	6.9	2.2	115	35.7	3.1	8.6	100	30.6	3.0	9.8	-5.1
6	91	38.6	2.8	7.2	4.2	100	34.4	3.0	8.8	93	29.0	2.8	9.8	-5.4
7	74	36.4	3.1	8.5	4.5	89	31.9	2.7	8.3	95	26.3	2.8	10.7	-5.6
Females														
2	94	26.0	2.3	8.8	-0.5	85	26.5	2.1	7.9	87	26.8	2.2	8.2	0.2
3	89	27.0	1.7	6.4	0.6	83	26.4	2.2	8.5	90	25.6	2.0	7.9	-0.8
4	97	29.5	2.3	7.7	1.5	100	28.0	1.8	6.4	112	26.3	1.9	7.1	-1.7
5	97	30.1	2.3	7.5	2.5	109	27.6	2.3	8.4	91	24.9	2.2	8.9	-2.7
6	95	30.4	2.2	7.3	3.3	100	27.1	2.1	7.6	95	23.4	1.6	6.9	-3.7
7	69	28.6	2.3	8.1	3.1	98	25.5	2.2	8.6	95	21.7	1.8	8.2	-3.9

[a]Number of observations per mean.
[b]Response (selected line generation mean deviated from control line generation mean).
[c]grams.

Table 12. Phenotypic and genetic responses to selection for high and low 56-day body weight.

	$b_{R:GEN}$ ± S.E.[a]		$b_{DR:GEN}$ ± S.E.[b]	
Line	Males	Females	Males	Females
WH	0.70 ± 0.36	0.68 ± 0.33	0.73 ± 0.13**	0.77 ± 0.11**
WC	-0.05 ± 0.41	-0.09 ± 0.24	-0-	-0-
WL	-1.32 ± 0.30*	-0.96 ± 0.19**	-1.29 ± 0.18*	-0.86 ± 0.06**

[a]Regression of generation means on generation number.
[b]Regression of generation means deviated from control on generation number.
[c]grams.
*(P<.05). **(P<.01). Statistical tests of significance were performed on data transformed to common logarithms.

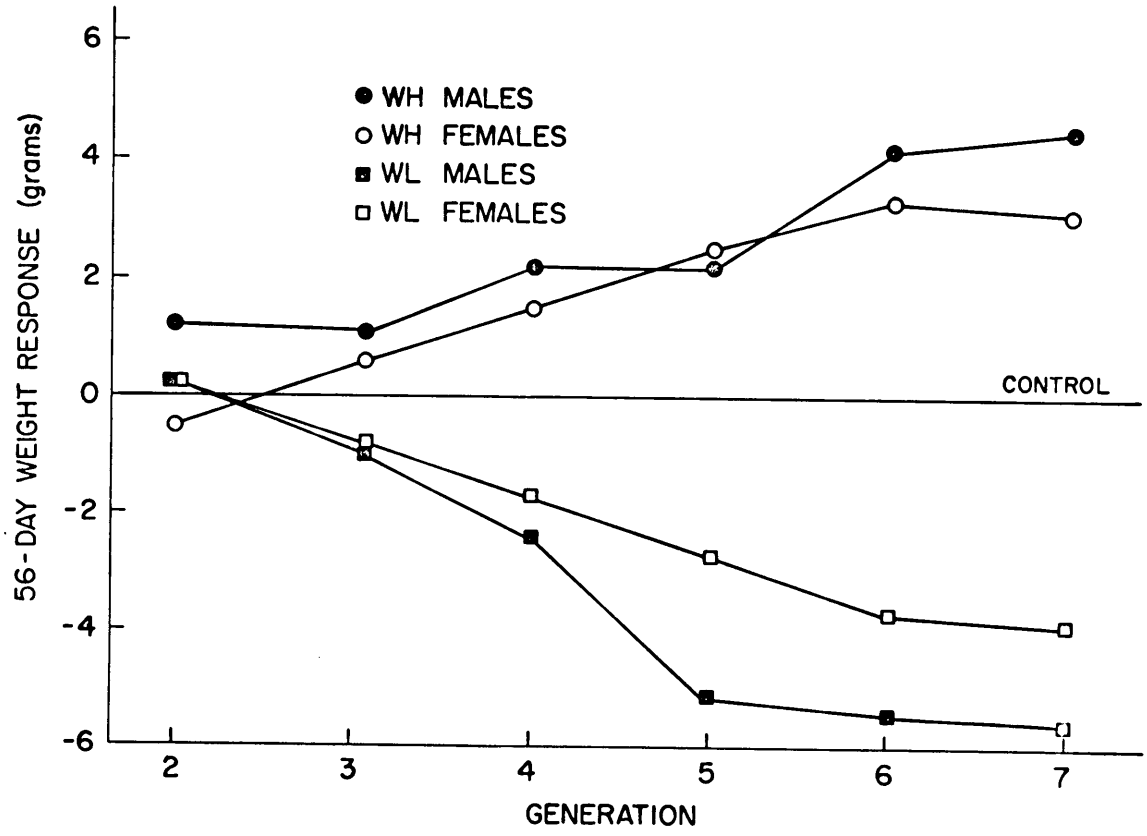

Figure 5. Response to selection for 56-day body weight by generation number.

zero (males - $P<.05$, females - $P<.01$). By deviating selected means from control means and regressing the response on generation number (Table 12 and Figure 5), highly significant ($P<.01$) positive genetic progress was found to occur in line WH males and females and significant negative genetic progress was apparent in line WL (males - $P<.05$, females - $P<.01$).

Cumulative effective selection intensities (Tables 13 and 14) indicated progress in terms of standard deviation units to be 6.2 for line WH (both sexes) and -7.0 for line WL (both sexes). Except for one sizable discrepancy in generation 4 of WL females, all comparisons of effective and expected S were less than unity, implying that mice which had either extremely high or extremely low 56-day body weight were not the most reproductively fit and viable of the breeding population. Since all S ratios for WL females except the one in generation 4 were similar and below unity, it was assumed that generation 4 WL females may have experienced peculiar circumstances and were not representative of the population as a whole.

Regressing deviated response to 56-day body weight selection on cumulative effective selection differential yielded the h^2_R given in Table 15 and graphed in Figure 6. Although point estimates of h^2_R for males and females in line WH were not in good agreement (0.26 ± 0.05 and 0.34 ± 0.05, respectively), the difference between them was not statistically significant. Both regressions did, however, differ significantly ($P<.01$) from zero. Selection for minimum 56-day body weight resulted in h^2_R of 0.40 ± 0.06 (males) and 0.39 ± 0.03 (females).

Table 13. Expected and effective selection differentials and intensities for high 56-day body weight line.

Generation	Expected Selection Differential		Effective Selection Differential		Cumulative Effective Selection Differential		S Ratio (EffS/ExpS)
Males	S[a]	i[b]	S	i	S	i	
2	4.1	1.2	3.7	1.1	3.7	1.1	.88
3	2.9	1.1	2.7	1.0	6.4	2.1	.95
4	3.1	1.2	2.8	1.1	9.2	3.2	.89
5	3.1	1.2	2.9	1.1	12.1	4.3	.93
6	3.3	1.2	2.8	1.0	14.9	5.3	.84
7	3.1	1.0	2.9	0.9	17.8	6.2	.92
Females							
2	2.6	1.1	2.4	1.0	2.4	1.0	.90
3	2.1	1.2	1.7	1.0	4.1	2.0	.84
4	2.6	1.1	2.2	1.0	6.3	3.0	.84
5	2.9	1.3	2.7	1.2	9.0	4.2	.91
6	2.7	1.2	2.5	1.1	11.5	5.3	.93
7	2.4	1.0	2.0	0.9	13.5	6.2	.83

[a]S = selection differentials in grams.
[b]$i = S/\sigma_p$ = selection differentials in standard deviation units.

Table 14. Expected and effective selection differentials and intensities for low 56-day body weight line.

Generation	Expected Selection Differential		Effective Selection Differential		Cumulative Effective Selection Differential		S Ratio (EffS/ExpS)
Males	S[a]	i[b]	S	i	S	i	
2	-3.5	-1.4	-3.2	-1.2	-3.2	-1.2	.92
3	-3.0	-1.2	-2.9	-1.2	-6.1	-2.4	.94
4	-3.7	-1.4	-2.8	-1.1	-8.9	-3.5	.76
5	-3.7	-1.2	-3.3	-1.1	-12.2	-4.6	.90
6	-3.6	-1.3	-3.5	-1.3	-15.7	-5.9	.97
7	-3.3	-1.2	-3.2	-1.1	-18.9	-7.0	.97
Females							
2	-2.6	-1.2	-2.4	-1.1	-2.4	-1.1	.91
3	-2.3	-1.2	-2.1	-1.1	-4.5	-2.2	.91
4	-1.4	-0.7	-2.2	-1.2	-6.7	-3.4	1.64
5	-2.6	-1.2	-2.5	-1.1	-9.2	-4.5	.94
6	-2.1	-1.3	-2.0	-1.3	-11.2	-5.8	.95
7	-2.2	-1.2	-2.1	-1.2	-13.3	-7.0	.95

[a]S = selection differentials in grams.
[b]i = S/σ_p = selection differentials in standard deviation units.

Table 15. Realized heritabilities in selected 56-day body weight lines.

	$h_R^2 \pm$ S.E.[a]	
Line	Males	Females
WH	0.26 ± 0.05**	0.34 ± 0.05**
WL	0.40 ± 0.06**	0.39 ± 0.03**

[a]Realized heritability is expressed as the regression of selected means deviated from control means on cumulative, effective selection differential.
**(P<.01). Statistical tests of significance were performed on data transformed to common logarithms.

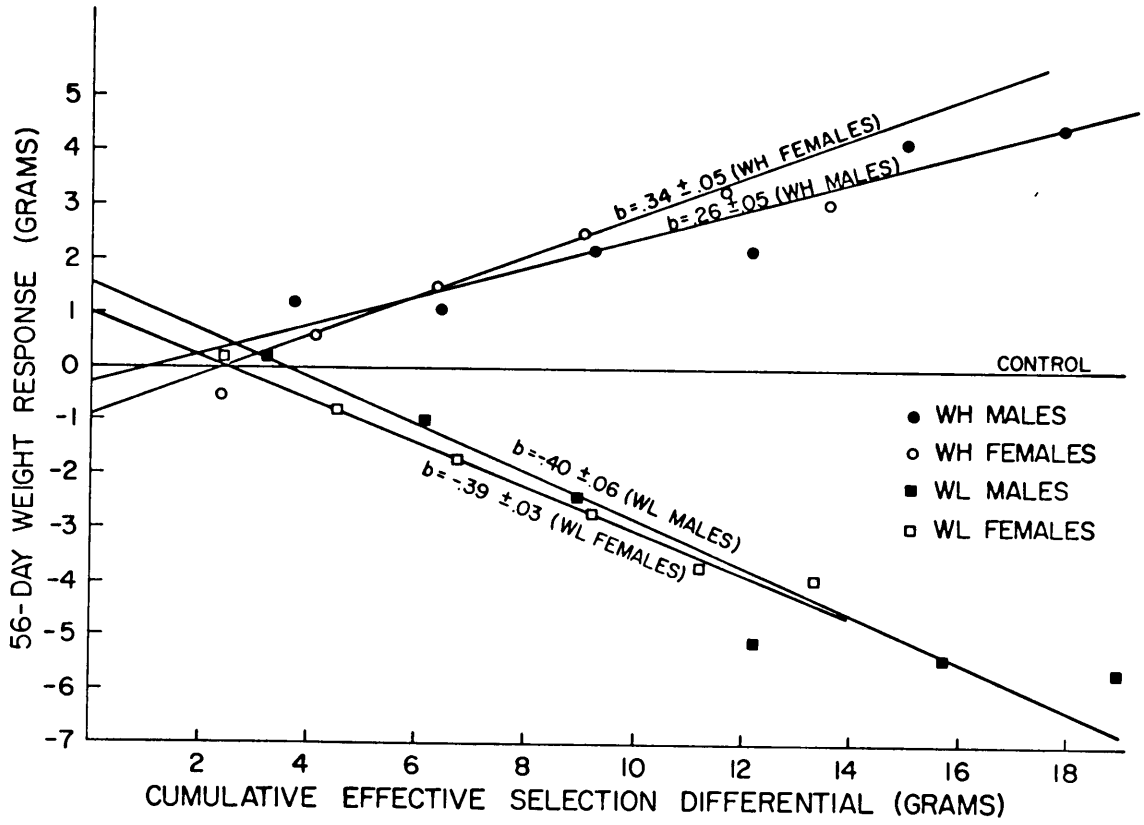

Figure 6. Response to selection for 56-day body weight by cumulative effective selection differential.

Tests of common logarithmic transformed data indicated that both regressions differed significantly from zero ($P<.01$).

Estimates of 56-day body weight in mice in the literature were in fair agreement with the results of this study, partially because the h^2_R presented here (0.26 ± 0.05 to 0.40 ± 0.06) covered most of the wide range of territory commonly labeled "moderate heritability". Jara-Almonte and White (1973) reported heritabilities of 56-day body weight to be 0.29 ± 0.13 and 0.27 ± 0.09 for lactating females and for pooled male and female data, respectively. Vinson et al. (1969) estimated 56-day body weight to be 0.49 ± 0.19 in mice.

Falconer (1953) found significant asymmetry in estimating h^2_R from selection for maximum and minimum 42-day body weight. Realized heritability in the upward direction was 0.18 ± 0.02 while in the downward direction h^2_R was 0.52 ± 0.02. Realized heritability in the present study indicated symmetrical response to selection for maximum and minimum 56-day body weight.

Feed Intake Lines

The remaining three lines to be discussed are those selected for feed intake. The criterion of selection in these lines was the total amount of feed consumed from three to seven weeks of age. Due to limitations in laboratory facilities, the individual consumption of each mouse could not be measured as this would have required individual housing. Instead, littermates of the same sex were housed three or less per cage and individual feed consumption was calculated by aver-

aging the intake of the full-brothers or full-sisters occupying each cage. Thus, rather than individual or mass selection, the intake lines were developed by within-sex, full-sib family selection.

Table 16 presents means, standard deviations and coefficients of variation for the intake lines. Random division of the original base population into three lines resulted in fairly uniform mean intake values for the males (ranging from 121 to 126 grams) and for the females (106 to 114 grams). The control lines remained relatively unchanged over the course of the study showing no appreciable trend in total intake for either males or females.

Line IH, selected for maximum feed intake, experienced steadily increasing generation means except for generation 6 where a sizable drop occurred. However, the alteration of the grams of feed consumed did not reach a very great magnitude, suggesting that rather slow progress in this trait might be realized.

The low line males were more erratic than IL females in reduction of grams of feed consumed and both sexes made a small magnitude of change during the five generations of selection.

Response to selection was obtained by diverging the selected line generation means from the control line means and is given in Table 16. Correction for environmental influences resulted in steady upward response for IH males although the females in IH experienced a setback in progress in the response mean of generation 7. Response in the low line was highly irregular. The male response figures fluctuated sharply with the generation 7 response being relatively close to the

Table 16. Means, standard deviations, coefficients of variation and responses to selection for feed intake values in selected and control feed intake lines.

Generation	Line IH					Line IC				Line IL				
	N[a]	Mean	S.D.	C.V.	R[b]	N	Mean	S.D.	C.V.	N	Mean	S.D.	C.V.	R
Males														
2	76	125.7[c]	8.2	6.5	-0.2	82	125.9	12.7	10.1	77	121.6	10.0	8.2	-4.3
3	76	130.6	8.2	6.3	7.7	77	122.8	13.1	10.7	77	124.8	8.7	6.9	1.9
4	73	133.8	8.3	6.2	9.2	74	124.6	10.6	8.5	80	121.4	14.2	11.7	-3.2
5	68	137.7	11.0	8.0	13.8	65	123.8	7.0	5.7	74	118.7	10.5	8.9	-5.2
6	73	124.3	11.9	9.6	14.8	42	109.5	15.2	13.9	67	106.8	16.4	15.4	-2.8
7	71	138.8	8.0	5.8	18.6	75	120.2	7.5	6.3	63	114.3	7.6	6.7	-5.8
Females														
2	75	108.3	8.8	8.1	1.5	85	106.9	9.6	9.0	73	113.7	8.4	7.4	6.9
3	77	111.9	5.4	4.8	5.3	73	106.6	8.1	7.6	76	112.3	14.4	12.8	5.7
4	73	119.0	7.7	6.5	11.6	74	107.4	9.1	8.5	70	109.7	8.0	7.3	2.3
5	65	122.6	7.3	5.9	12.5	67	110.1	7.4	6.7	79	106.0	6.8	6.4	-4.1
6	74	113.1	11.9	10.5	17.5	47	95.6	14.2	14.8	70	95.6	11.7	12.2	0.1
7	72	121.3	7.8	6.4	16.8	74	104.6	9.9	9.5	62	100.1	4.5	4.5	-4.5

[a]Number of observations per mean.
[b]Response (selected line generation means deviated from control line generation mean).
[c]grams.

response realized in generation 2. The female IL divergences were slightly more steady but the generation mean at generation 2 was so far above the control mean (6.9 grams) that reduction of IL means below the control did not occur until generation 5 (when the divergence was -4.1 grams).

Phenotypic and genetic progress for selection are presented in Table 17. Phenotypic regressions for the control line IC indicated an environmental trend which aided selection in the downward direction, that is, for reduced feed intake. Subtraction of these environmental influences yielded genetic progress (Table 17 and Figure 7) of 0.34 ± 0.04 and 0.33 ± 0.05 grams per generation increase in consumption for IH males and females, respectively, during the course of the study. When these data were transformed to common logarithms to perform statistical tests, only the female regression was significantly different from zero ($P<.05$). Although neither genetic response in line IL differed statistically from zero, the differing magnitudes (0.07 ± 0.07 and 0.23 ± 0.06 grams reduction per generation for males and females, respectively) again showed the considerably reduced amount of progress realized by the males.

Selection differentials, both in grams and in standard deviation units, are shown in Tables 18 and 19 for lines IH and IL, respectively. The cumulative reaches in standard deviation units were 5.3, 5.7, 5.2 and 4.7 for IH males, IH females, IL males and IL females, respectively. These figures were slightly lower but compared reasonably with reach calculated in the preceding selected lines.

Table 17. Phenotypic and genetic responses to selection for high and low feed intake.

	$b_{R:GEN} \pm S.E.$[a]		$b_{DR:GEN} \pm S.E.$[b]	
Line	Males	Females	Males	Females
IH	0.14 ± 0.14[c]	0.21 ± 0.11	0.34 ± 0.04	0.33 ± 0.05*
IC	-0.20 ± 0.13	-0.12 ± 0.12	-0-	-0-
IL	-0.27 ± 0.11	-0.35 ± 0.09*	-0.07 ± 0.07	-0.23 ± 0.06

[a]Regression of generation means on generation number.
[b]Regression of generation means deviated from control on generation number.
[c]grams.
*($P<.05$). Statistical tests of significance were performed on data transformed to common logarithms.

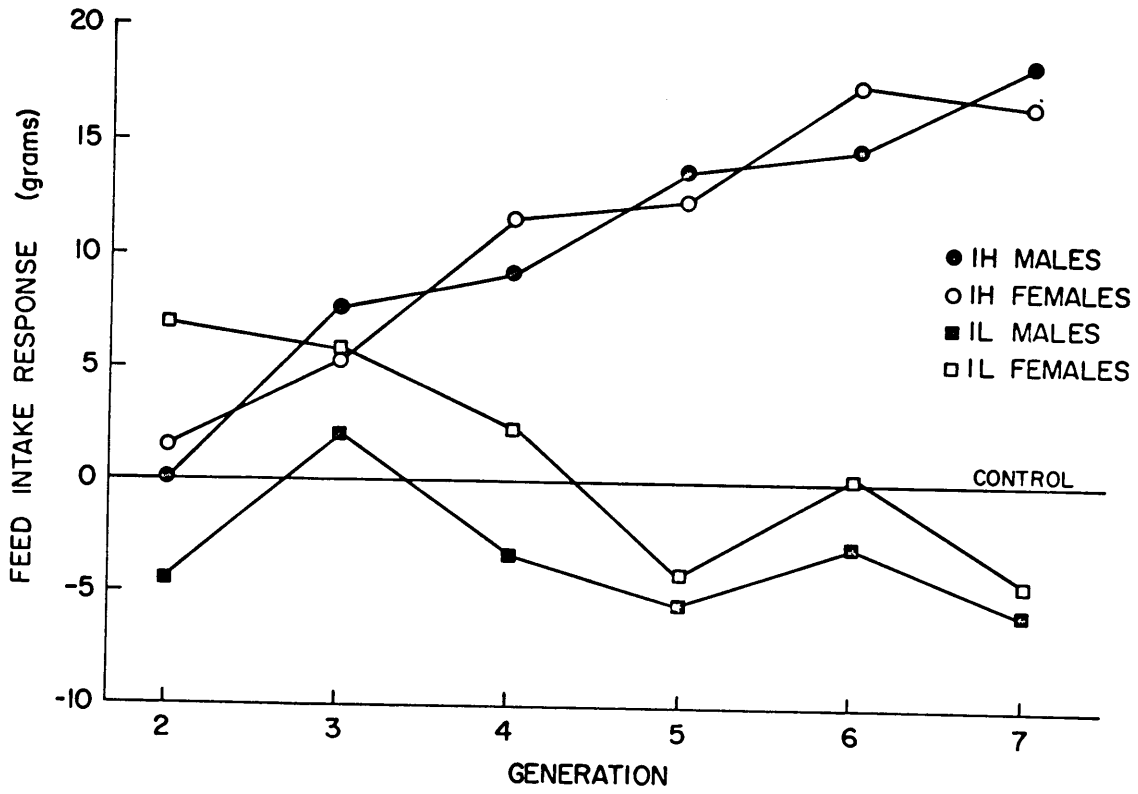

Figure 7. Response to selection for feed intake by generation number.

Table 18. Expected and effective selection differentials and intensities for high feed intake line.

Generation	Expected Selection Differential		Effective Selection Differential		Cumulative Effective Selection Differential		S Ratio (EffS/ExpS)
Males	S[a]	i[b]	S	i	S	i	
2	8.1	1.0	8.4	1.0	8.4	1.0	1.04
3	7.0	0.8	6.2	0.7	14.6	1.7	.88
4	7.3	0.9	7.3	0.9	21.8	2.6	.99
5	9.0	0.8	8.8	0.8	30.7	3.4	.98
6	11.6	1.0	11.7	1.0	42.3	4.4	1.00
7	7.4	0.9	7.4	0.9	49.8	5.3	1.00[c]
Females							
2	6.9	0.8	7.0	0.8	7.0	0.8	1.02
3	5.3	1.0	5.5	1.0	12.5	1.8	1.03
4	6.6	0.9	7.6	1.0	20.1	2.8	1.15
5	5.9	0.8	6.3	0.9	26.4	3.7	1.06
6	11.6	1.0	12.8	1.1	39.2	4.8	1.10
7	6.9	0.9	6.9	0.9	46.0	5.7	1.00[c]

[a]S = selection differentials in grams.
[b]$i = S/\sigma_p$ = selection differentials in standard deviation units.
[c]Expected selection differentials for generation 7 were also used as the effective selection differentials.

Table 19. Expected and effective selection differentials and intensities for low feed intake line.

Generation	Expected Selection Differential		Effective Selection Differential		Cumulative Effective Selection Differential		S Ratio (EffS/ExpS)
Males	S[a]	i[b]	S	i	S	i	
2	-8.2	-0.8	-7.5	-0.7	-7.5	-0.7	.91
3	-8.9	-1.0	-8.8	-1.0	-16.2	-1.7	.99
4	-15.2	-1.1	-15.1	-1.1	-31.3	-2.8	.99
5	-10.0	-1.0	-9.2	-0.9	-40.6	-3.7	.92
6	-14.0	-0.9	-12.5	-0.8	-53.1	-4.5	.90
7	-5.7	-0.7	-5.7	-0.7	-58.8	-5.2	1.00[c]
Females							
2	-6.4	-0.8	-6.1	-0.7	-6.1	-0.7	.97
3	-11.1	-0.8	-11.0	-0.8	-17.1	-1.5	.98
4	-6.0	-0.8	-5.9	-0.7	-23.0	-2.2	.98
5	-5.3	-0.8	-4.9	-0.9	-27.9	-3.1	.92
6	-9.9	-0.8	-9.2	-0.8	-37.1	-3.9	.93
7	-3.7	-0.8	-3.7	-0.8	-40.8	-4.7	1.00[c]

[a] S = selection differentials in grams.
[b] $i = S/\sigma_p$ = selection differentials in standard deviation units.
[c] Expected selection differentials for generation 7 were also used as the effective selection differentials.

In observing the S ratio (effective S / expected S), it should be noted that for generation 7, the effective and expected S were equivalent in each line-sex subgroup. This occurred because, at the time of this analysis, generation 7 had just been tested and selection of parents for the next generation had been made. However, these parents had not yet been bred so generation 8 did not exist and it was impossible to know exactly how many offspring each parent would contribute to generation 8. Therefore, the expected S was used as the best estimate of the effective S.

The S ratio in the low line indicated that natural and artificial selection had generally worked in opposition. In line IH, however, a few S ratios for the males and all female S ratios indicated that mice selected for maximum intake were generally more fit than the less intensively selected mice. That is, mice with greater intake scores either produced more offspring or produced more viable offspring.

Realized heritabilities based on within-sex, full-sib family means are given in Table 20 and graphed in Figure 8 for the feed intake lines. Line IH males and females yielded similar heritabilities (0.39 ± 0.07 and 0.40 ± 0.07, respectively) although only the female regression was significantly different from zero when tests of the data transformed to common logarithms were made. Adjustment of these h_R^2 of family means to individual h_R^2 (Falconer, 1960) resulted in estimates of 0.25 ± 0.05 and 0.26 ± 0.05 for males and females, respectively. The individual h_R^2 were somewhat smaller than the feed intake heritabilities estimated by Jara-Almonte and White (1973) but slightly greater than that reported

Table 20. Realized heritabilities in selected feed intake lines.

	$h_R^2 \pm$ S.E.[a]	
Line	Males	Females
IH	0.39 ± 0.07**	0.40 ± 0.07**
IL	0.06 ± 0.06	0.32 ± 0.10*

[a]Realized heritability is expressed as the regression of selected means deviated from control means on cumulative, effective selection differential. *(P<.05). **(P<.01). Statistical tests of significance were performed on data transformed to common logarithms.

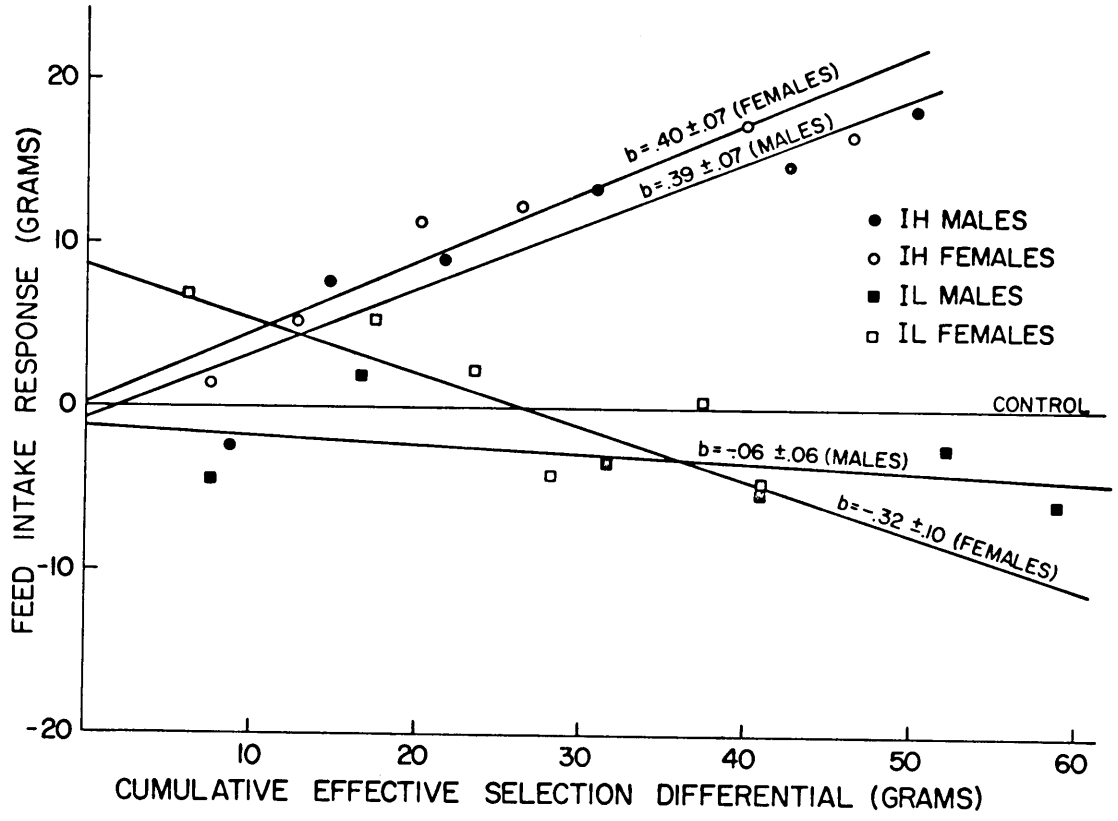

Figure 8. Response to selection for feed intake by cumulative effective selection differential.

by Sutherland et al. (1970).

The estimates of realized heritabilities obtained in the low feed intake line (based on within-sex, full-sib family selection) differed greatly between the sexes, though neither regression differed significantly from zero. The magnitude of heritability for IL females was similar to that found in line IH mice (0.32 ± 0.10), whereas the estimate in males (0.06 ± 0.06) was considerably lower. Heritabilities based on individual selection (corrected for family means - Falconer, 1960) did not reflect as large a difference in male and female h^2_R values (0.03 ± 0.03 for males and 0.20 ± 0.06 for females). Although inspection of the erratic responses shown in Table 16 for IL males revealed why low values were obtained when regressing response on cumulative, effective S, the biological interpretation was not obvious. Due to sampling error, the females in line IL had a population mean 6.9 grams above the control line in generation 2. Selection for reduced feed intake resulted in cumulative response of -4.5 grams (4.5 grams below the control line) in generation 7. The males of line IL, again due to sampling error, began the selection experiment with a population mean 4.3 grams below the control mean. After five generations of selection the cumulative response had only dropped to -5.8 grams. This very small amount of progress was the reason for the extremely low h^2_R obtained for IL males. Since reasonable selection differentials were realized (slightly less than one standard deviation unit per generation), it appeared that the trait was very lowly heritable.

Variances According to Hill

The estimates of realized heritabilities and their standard errors were calculated for this paper according to standard regression techniques. The h_R^2 was defined as the regression of cumulative response (selected means deviated from control means) on cumulative effective selection differential in each selected line (Falconer, 1960). The standard error of each h_R^2 was calculated as:

$$S.E. = \sqrt{\frac{\Sigma y^2 - (\Sigma xy)^2 / \Sigma x^2}{(n - 2)}} \Big/ \Sigma x^2$$

(Steel and Torrie, 1960). The correlations between means and variances were nullified by transformations to common logarithms. An assumption made for the validity of the calculation of the standard errors was that the observations of progressive generations were uncorrelated.

Hill (1971) pointed out that, in a selection project of this sort, the assumption of uncorrelated observations is not accurate. With genetic sampling or drift, the variances of the mean of the population increase with each generation and the means become correlated. Therefore, variances calculated by standard regression techniques are biased downward. In later papers (Hill, 1972a,b) the specific type of selection experiment used in the present study was treated. That is, Hill gave methods for calculating unbiased estimates of the variance of h_R^2 for directional selection in which a random-bred, non-inbred control line was maintained. These methods have been employed in this section to calculate variances of h_R^2.

In applying Hill's theoretical calculations, several assumptions were made about the data. Genetic and phenotypic variances were assumed to remain unchanged over the course of the study. This assumption implied that many genes (each having a small effect) influenced the character for which selection was practiced, that inbreeding did not become high and that there were no confounding linkage effects. The present experiment was short-term and involved traits influenced by numerous systems in the body, so the assumptions mentioned were not unreasonable. Since a control line was maintained, common environmental effects were eliminated as long as it was assumed that any genotype by environment interactions were of little import.

The values of h_R^2, the standard error of the regression calculated by standard regression techniques (S.E.), the standard error calculated by Hill's technique [$\sqrt{V(b_c)}$], as well as the phenotypic variance ($\hat{\sigma}^2$), the drift variance ($\hat{\sigma}_d^2$), and the error variance ($\hat{\sigma}_e^2$) are given in Table 21 for each selected line.

Very little difference in the standard errors calculated by different methods [S.E. and $\sqrt{V(b_c)}$] actually resulted. In testing for differences of the regressions from zero, 12 of the 16 line-sex groups remained the same in levels of significance for both methods. However, in comparing Hill's variances with Hill's estimates of the expected values of $(S.E.)^2$ [$U(b_c)$], $V(b_c)$ was consistently two to four times larger than $U(b_c)$. Thus, the expected value of $(S.E.)^2$ did not agree with the S.E. actually obtained in analyzing the data, perhaps because each of the regressions fitted only six points, resulting in large

Table 21. Realized heritabilities, standard errors and drift and error variances for selected lines of mice.

Line	h^2_R	S.E.	$\sqrt{V(b_c)}$	$U(b_c)$	$V(b_c)$	df	$\hat{\sigma}^2$	$\hat{\sigma}^2_d$	$\hat{\sigma}^2_e$	$\hat{\sigma}^2_d/\hat{\sigma}^2_e$
Males										
CH	.41	.03**	.05**	.000497	.002237	549	.01283	.00017	.00011	1.52
CL	.37	.02**	.05**	.000493	.002135	535	.01058	.00013	.00009	1.39
AH	.27	.03**	.08*	.001516	.005708	552	.20220	.00194	.00193	1.01
AL	.13	.04*	.04*	.000572	.001497	573	.24492	.00117	.00248	0.47
WH	.28	.05**	.05**	.000549	.002049	521	.00119	.00001	.00001	1.04
WL	.40	.05**	.05**	.000494	.002200	577	.00161	.00002	.00001	1.48
IH	.41	.06**	.06**	.000865	.003448	431	.00100	.00001	.00001	1.14
IL	.08	.06	.06	.001074	.001949	432	.00203	.00001	.00003	0.21
Females										
CH	.44	.03**	.05**	.000462	.002148	573	.01203	.00017	.00010	1.65
CL	.37	.07**	.06**	.000780	.003358	556	.01653	.00020	.00015	1.37
AH	.24	.09	.08*	.001738	.006246	504	.21466	.00190	.00208	0.91
AL	.19	.06*	.04**	.000612	.001945	530	.29643	.00204	.00290	0.70
WH	.37	.04**	.05**	.000582	.002510	535	.00114	.00001	.00001	1.37
WL	.39	.02**	.04**	.000427	.001877	564	.00120	.00001	.00001	1.43
IH	.44	.08**	.06**	.000831	.003423	430	.00098	.00001	.00001	1.23
IL	.29	.09*	.06**	.001187	.004036	424	.00144	.00001	.00002	0.81

effects due to sampling error.

Phenotypic variances were estimated by pooling within-line, within-sex, within-generation values. Then, estimates of drift and error variances were obtained from the phenotypic variances and realized heritabilities calculated from regressions of data transformed to common logarithms. Estimates of the drift and error variances comprised from one to two percent of the total phenotypic variance.

The ratio of drift variance to error variance ($\hat{\sigma}^2_d$ / $\hat{\sigma}^2_e$) was variable among the different line-sex groups. Lines CH, CL, WH, WL and IH resulted in drift variance approximately one to two times larger than the error variances indicating that genetic sampling contributed a larger proportion of the variance than did pure error. Three of the four activity line-sex groups, however, had error variances larger than the corresponding drift variances. It is conceivable that the large proportion of variance due to error was a result of the rather large variances associated with measurement of activity in this study (coefficients of variation for generation means of activity ranged from 38% to 76%). Also, the error variances of both male and female mice from line IL were greater than drift variances, particularly in the case of males ($\hat{\sigma}^2_d$ / $\hat{\sigma}^2_e$ = 0.21).

Inbreeding

The actual inbreeding coefficients (F) were calculated (Falconer, 1960) for each line and accrued over the course of the study. These results, shown in Table 22, indicated that no more than 6.6% inbreeding

Table 22. Inbreeding coefficients for selected and control lines.

Generation	CH	CC	CL	AH	AC	AL	WH	WC	WL	IH	IC	IL
2	.0096	.0114	.0119	.0104	.0093	.0100	.0109	.0114	.0100	.0192	.0167	.0132
3	.0096	.0100	.0100	.0100	.0096	.0096	.0100	.0100	.0093	.0208	.0167	.0179
4	.0100	.0100	.0100	.0125	.0109	.0109	.0100	.0086	.0096	.0208	.0156	.0179
5	.0096	.0100	.0100	.0109	.0104	.0100	.0104	.0100	.0104	.0208	.0208	.0192
6	.0104	.0104	.0096	.0104	.0100	.0109	.0147	.0096	.0100	.0208	.0208	.0192
7	.0089	.0096	.0093	.0100	.0100	.0100	.0100	.0093	.0096	.0167	.0147	.0132
Accumulated F	.0581	.0614	.0608	.0642	.0602	.0614	.0660	.0589	.0589	.1190	.1053	.1006

built up in the cholesterol, activity and weight lines where individual selection was practiced and less than 12% inbreeding accrued in the intake lines which were subject to within-sex, full-sib family selection. It may be assumed that the degree of inbreeding had little or no effect on the traits measured.

Control Lines

Although the expected S and expected i for each control line in this study was zero (since no selection was practiced), the mean of the selection criterion differed somewhat between all possible parents and the actual parents simply due to chance. An unusually large sampling error or a trend of sampling errors, all in the same direction, could drastically reduce the validity of a control line, particularly in a short-term experiment. In order to check for such an occurrance, the effective selection intensities were calculated and accrued over generations for each control line. These results are presented in Table 23. The range of accumulated selection intensity was only -0.97 to 1.06 standard deviation units. Thus, the sampling errors encountered in random selection of control line breeders were not at all unusual and indicated no large sampling errors.

Correlated Responses I

Artificial selection for a trait or traits is often accompanied by changes in the means of associated traits. Two methods of observing for changes in unselected traits were employed in this selection study.

Table 23. Effective selection intensities resulting in the four control lines.

Generation	CC	AC	WC	IC
Males				
2	-0.18[a]	0.20	0.34	-0.67
3	0.08	0.09	0.20	-0.49
4	-0.10	-0.01	0.29	-0.03
5	0.08	-0.06	0.12	0.43
6	0.14	-0.04	0.18	0.19
7	-0.20	-0.27	-0.18	-0.03
Accumulated i	-0.18	-0.09	0.95	-0.60
Females				
2	0.18	0.10	-0.05	-1.02
3	0.13	0.25	-0.03	-0.17
4	0.21	0.09	-0.02	0.09
5	0.13	0.14	-0.12	-0.16
6	0.22	-0.02	-0.09	0.22
7	0.19	-0.11	-0.04	0.07
Accumulated i	1.06	0.45	-0.35	-0.97

[a]Standardized effective selection differential.

This section deals with the discussion of phenotypic correlations and genetic regressions. Information on any unselected traits which were measured in the selected lines each generation was used to calculate phenotypic (product-moment) correlations over generations. Realized genetic regressions were calculated by regressing the response of unselected traits (selected line means deviated from control line means) on generation number.

Some traits, although of interest, were not measured in the selected lines every generation. The following section (Correlated Responses II) deals with the evaluation of how selection affected these traits. In order to ascertain any alterations in these unselected traits, a replicate of generation 7 was produced by a repeated mating of the same pairs of selected breeders and various traits were measured in representatives from each selected line. Then the lines were ranked according to their performance for the various traits.

Phenotypic correlations. Within-line phenotypic correlations calculated over generations are presented in Tables 24, 25, 26 and 27 for the SC, activity, 56-day body weight and feed intake lines, respectively. Several very distinct trends occurred in these phenotypic correlations. Body weights at all ages were highly, positively correlated among themselves in all lines (Tables 24, 25, 26 and 27) and feed intake was positively correlated with all body weights (Table 27). SC and body weights were also positively correlated, with comparatively low correlations at 12 days and much higher correlations for 21-, 42- and 56-day

Table 24. Within-line phenotypic correlations in serum cholesterol lines.

	Line	Percent Females Littering	Offspring Alive At Five Days	WT 12	WT 21	WT 42	WT 56	SC
Average	CH	-.270**	-.053	.016	-.102	.040	.106	-.243*
Littering	CC	.116	-.007	-.099	-.092	-.045	-.024	-.156
Interval	CL	-.039	.030	.024	-.015	.033	.045	-.308**
Percent	CH		.182	.269**	.387**	.233*	.234*	.166
Females	CC		-.134	-.419**	-.467**	-.514**	-.227*	-.464**
Littering	CL		-.124	.018	-.252*	-.041	-.068	-.373**
Offspring	CH			.140	.192	.178	.235*	.050
Alive At	CC			.240*	.291**	.274**	.240*	-.011
Five Days	CL			.016	.130	.019	.188	-.065
Littermates	CH			.081*	.138**	.104**	.089*	-.005
Alive At	CC			-.172**	-.128**	-.006	-.025	.042
Five Days	CL			-.113**	-.144**	-.026	-.027	.012
	CH				.590**	.259**	.180**	.021
WT 12	CC				.706**	.278**	.193**	.250**
	CL				.652**	.312**	.209**	.087*
	CH					.561**	.499**	.134**
WT 21	CC					.517**	.442**	.347**
	CL					.513**	.384**	.298**
	CH						.918**	.241**
WT 42	CC						.909**	.387**
	CL						.931**	.341**
	CH							.245**
WT 56	CC							.336**
	CL							.286**

*(P<.05). **(P<.01).

Table 25. Within-line phenotypic correlations in physical activity lines.

	Line	Percent Females Littering	Offspring Alive At Five Days	WT 12	WT 21	WT 42	WT 56	Physical Activity
Average Littering Interval	AH	.169	-.174	-.013	-.019	-.079	-.144	-.171
	AC	.184	-.034	.056	.203*	.061	-.062	-.074
	AL	-.124	.087	-.165	-.173	-.216*	-.107	-.178
Percent Females Littering	AH		-.024	-.026	.041	-.164	-.194	.044
	AC		.087	-.059	-.129	-.235*	-.348**	-.134
	AL		-.007	.303**	.229*	.483**	.375**	.244*
Offspring Alive At Five Days	AH			.101	.232*	.331**	.404**	-.035
	AC			.145	.194	.180	.156	.034
	AL			.075	.259*	.341**	.373**	.107
Littermates Alive At Five Days	AH			-.174**	-.119**	.014	-.031	.015
	AC			-.003	.012	.055	.052	.142**
	AL			-.219**	-.137**	-.042	-.014	.010
WT 12	AH				.744**	.334**	.299**	-.019
	AC				.409**	.233**	.195**	.175**
	AL				.684**	.352**	.292**	.079*
WT 21	AH					.550**	.480**	.025
	AC					.506**	.415**	.195**
	AL					.589**	.524**	.156**
WT 42	AH						.881**	-.056
	AC						.892**	.032
	AL						.915**	.080*
WT 56	AH							-.117**
	AC							.031
	AL							.023

*(P<.05). **(P<.01).

Table 26. Within-line phenotypic correlations in 56-day body weight lines.

	Line	Percent Females Littering	Offspring Alive At Five Days	WT 12	WT 21	WT 42	WT 56
Average Littering Interval	WH	-.021	-.069	.127	.076	-.084	-.170
	WC	-.064	-.173	.215*	-.033	.072	-.042
	WL	.165	.078	-.185	-.219*	-.422**	-.279**
Percent Females Littering	WH		-.058	-.044	.314**	.124	.142
	WC		-.026	-.125	-.327**	-.318**	-.303**
	WL		-.036	-.437**	-.453**	-.566**	-.642**
Offspring Alive At Five Days	WH			.162	.101	.100	.008
	WC			.299**	.185	.264**	.200*
	WL			.150	.308**	.285**	.237*
Littermates Alive At Five Days	WH			-.296**	-.260**	-.148**	-.105**
	WC			.039	-.140**	-.084*	-.075*
	WL			.077*	-.037	.057	.066
WT 12	WH				.607**	.283**	.171**
	WC				.642**	.345**	.269**
	WL				.759**	.416**	.330**
WT 21	WH					.542**	.389**
	WC					.554**	.456**
	WL					.595**	.502**
WT 42	WH						.893**
	WC						.934**
	WL						.895**

*(P<.05). **(P<.01).

Table 27. Within-line phenotypic correlations in feed intake lines.

	Line	Percent Females Littering	Offspring Alive At Five Days	WT 12	WT 21	WT 42	WT 56	Feed Intake
Average	IH	-.091	-.033	-.201*	-.191	-.003	.019	-.006
Littering	IC	-.191*	-.135	-.085	-.038	-.044	-.045	-.008
Interval	IL	-.315**	-.050	-.136	-.109	-.199*	-.310**	-.156
Percent	IH		-.016	.267**	-.034	.264**	.242*	.034
Females	IC		.010	-.056	-.004	-.072	-.029	-.255*
Littering	IL		.012	-.053	.009	.478**	.404**	.668**
Offspring	IH			.057	.196	.132	.241*	.071
Alive At	IC			.129	.135	-.032	.263*	-.048
Five Days	IL			.114	.249*	.391**	.395**	.200*
Littermates	IH			-.083*	-.068	-.077*	-.077*	-.080*
Alive At	IC			-.034	.025	.002	.014	.013
Five Days	IL			.046	.041	.107*	.134**	.101**
	IH				.583**	.221**	.173**	.245**
WT 12	IC				.581**	.258**	.203**	.236**
	IL				.736**	.385**	.331**	.403**
	IH					.441**	.367**	.371**
WT 21	IC					.521**	.408**	.422**
	IL					.593**	.507**	.498**
	IH						.917**	.799**
WT 42	IC						.915**	.790**
	IL						.900**	.786**
	IH							.733**
WT 56	IC							.726**
	IL							.721**

*(P<.05). **(P<.01).

weights (Table 24). Activity and 12- and 21-day weight were significantly, positively correlated in lines AC and AL while line AH showed a negative trend in correlation between activity and body weight, significant only at 56 days of age (Table 25). The positive correlation between weaning weight and activity has been observed before (Dunnington et al., 1977b) and is explained in more detail in the discussion concerning the replicate.

Before discussing the phenotypic correlations which involve reproductive traits, exact definitions of these traits need to be given. The first possible littering date for each line in each generation was taken to be the nineteenth day after females in the line were first exposed to males. Then, each day past the first possible littering date was weighted by the number of litters born on that day and a weighted average littering interval (ALI) was calculated for each line every generation. Mice that did not litter were not given any weight in calculating ALI. Percentage of females littering (PFL) was the percentage of those females in each line exposed to males for 14 consecutive days which littered within the 14 days after the first possible littering date. It is important to note that the reproductive traits involved only selected mice each generation while the selection criteria and body weights included the entire population each generation.

Since ALI and PFL were traits actually concerned with the reproducing females, the phenotypic correlations presented represent comparisons of each dam and her subsequent reproductive record. A third

reproductive trait, pups alive at five days of age, was of interest in two respects. It was of interest to compare a female's own record, that is, her body weights, etc., with the number of viable offspring she produced. Also, however, it was desired to compare how the number of littermates alive at five days might influence the body weights of those litter members as they matured. Therefore, the trait "offspring alive at five days" (OA5D) compared the number of pups alive in a litter at five days with the dam's record, while "littermates alive at five days" (LA5D) compared the number of pups per litter at five days with the subsequent records of each pup.

Significant negative correlations occurred between ALI and PFL in lines CH, IC and IL. Judging from the performance of those three lines, it appeared that line CH had reduced conception rate and a rather long littering interval while lines IC and IL conceived readily and littered rapidly.

No significant correlations occurred in any of the lines between OA5D and either ALI or PFL.

Although no significant correlations occurred between ALI and individual body weights of the littering females in the SC lines (Table 24) and no trend was apparent in the activity lines (Table 25), the weight and intake lines showed a definite pattern. Females in lines WL and IL (selected respectively for low 56-day body weight and low feed intake) showed significant negative correlations between ALI and post-weaning body weight, indicating that in groups of relative low-weight mice, the heavier females conceived and reproduced more quickly

than the very light individuals. Although ALI was not significantly correlated with either activity or feed intake, significant negative correlations occurred between ALI and SC in lines CH and CL, suggesting that low SC was associated with longer littering intervals.

The relationship between PFL and individual body weights of the dams was rather difficult to interpret. Lines CH, AL, WH, IH and IL had significant positive correlations between PFL and most or all of the body weights. All of these lines except AL and IL were generally high in body weight (see the results of the Correlated Responses II section), perhaps indicating that in relatively high-weight groups of mice, heavier mice had higher conception rates while lighter mice had lower conception rates. Conversely, significant negative correlations occurred between PFL and body weights in lines CC, CL, AC, WC and WL. Results of the Correlated Responses II section showed that CC, AC, WC and WL all ranked medium to low in body weights when compared to the rest of the developed lines. Thus, in groups of mice with moderate to low weights, the heavier mice appeared to have lower conception rates. Employing all the data on these traits then, they could be interpreted to mean that females of average body weights (lighter mice in the heavy lines and heavier mice in the light lines) conceive in smaller percentage than either very heavy or very light individuals. These results are not consistent with the S ratios found in the 56-day body weight lines which indicated that mice selected for very high or very low body weights were not as reproductively fit as animals of less extreme weights.

Negative correlations between SC and PFL were found in lines CC and CL, indicating that low SC levels were associated with high conception percentages. A low significant positive correlation between PFL and activity in AL suggested that reduced activity was associated with reduced PFL. A rather large positive correlation between PFL and feed intake in line IL indicated that relatively high levels of feed intake in the mice which were selected to consume very little were accompanied by high levels of littering in the females.

Product-moment correlations between the number of offspring alive at five days of age (OA5D) and the body weights of the dams of those litters showed remarkable consistency across all lines. The correlations were positive in every case except for one very low negative value and were generally higher correlations at the more mature body weights. Thus, females which were relatively heavy produced larger litters with offspring viable at least to five days than lighter females. Although no significant correlations between OA5D and activity or SC occurred, one significant positive correlation between OA5D and feed intake occurred in line IL. Extrapolating from the previous OA5D correlations, this could be interpreted to indicate that higher intake in line IL females was associated with greater ability to produce large litters of pups.

The relationship between littermates alive at five days of age (LA5D) and subsequent body weights of those littermembers was, in most cases, a negative one. It was not surprising that a large number of pups in a litter generally caused the pups to be of small size (es-

pecially up until weaning), since competition for their food supply was increased. Even though the litters in this study were standardized to eight pups at five days of age, some of the influence of that early competition was still apparent in the significant negative correlations between LA5D and subsequent body weights, particularly at 12 and 21 days of age. This phenomenon occurred in lines CC, CL, AH, AL, WH, WC and IH. In three lines (CH, WL and IL), though, a positive correlation between litter number and body weight occurred. In lines CH and IL these correlations were with 42- and 56-day body weight and probably indicated compensatory growth after weaning. However, the correlation in line WL was with 12-day body weight and was not readily explainable.

Correlations between LA5D and SC were not significant. One significant positive correlation between LA5D and activity occurred in line AC and LA5D and feed intake were correlated negatively in line IH and positively in line IL. All of these values were rather low (less than .200) and no biological explanation was apparent.

Realized genetic regressions. Realized genetic regressions were calculated for unselected traits which were measured every generation in each line. Environmental influences were removed by deviating each selected line mean from its respective control line mean. The resulting genetic responses were then regressed on generation number to obtain any trends in the unselected traits over the course of the selection study. Genetic regressions were calculated for reproductive traits (PFL, pups alive at five days and ALI) and for body weights (at

12, 21, 42 and 56 days of age).

Table 28 shows that none of the reproductive traits experienced a significant trend in any of the selected lines during the five-generation selection study.

Significant trends did occur in the weight traits for several of the lines and are given in Table 29. Females in the line selected for maximum SC experienced significant gain in 42- and 56-day body weight and those females selected for minimum SC decreased signficantly in 56-day body weight, although the body weights of CH and CL males did not change. The female weights agreed with the results of the phenotypic correlations where a significant, positive phenotypic correlation between mature body weight and SC occurred. Neither males nor females in the selected activity lines experienced altered body weights during the selection study. The regressions of body weight over time in the high activity line were, however, consistently negative. Significant increases in 42- and 56-day body weights occurred in line WH males and females while both sexes in line WL decreased significantly in body weight during selection. Since the criterion of selection in these lines was 56-day body weight, these results simply indicated that the selection program was successful. Mice of both sexes in line IH increased significantly in 42- and 56-day body weight. Thus, selection for increased feed consumption caused definite increases in body weight. Although selection for decreased feed intake resulted in negative body weight regressions for both males and females at all four ages, these regressions were not significantly different from zero, perhaps because

Table 28. Genetic regressions of reproductive traits on generation number in selected and control lines.

Line	Percent Females Littering	Pups Alive At Five Days	Average Littering Interval
CH	-0.02 ± 0.02[a]	-0.23 ± 0.20	0.18 ± 0.10
CL	0.00 ± 0.02	-0.09 ± 0.22	0.01 ± 0.19
AH	0.01 ± 0.02	0.08 ± 0.19	-0.11 ± 0.18
AL	-0.01 ± 0.02	-0.14 ± 0.11	-0.28 ± 0.18
WH	-0.03 ± 0.03	-0.32 ± 0.34	0.09 ± 0.22
WL	0.01 ± 0.01	-0.58 ± 0.22	-0.08 ± 0.04
IH	0.00 ± 0.04	0.12 ± 0.16	0.02 ± 0.34
IL	-0.02 ± 0.04	-0.49 ± 0.16	-0.07 ± 0.46

[a]Regression of response (selected mean deviated from control mean) on generation number.
*(P<.05).

Table 29. Genetic regressions of body weight on generation number in selected and control lines.

Line	WT 12	WT 21	WT 42	WT 56
Males				
CH	0.15 ± 0.06[a]	0.31 ± 0.09	0.21 ± 0.25	0.16 ± 0.20
CL	0.00 ± 0.07	-0.03 ± 0.09	-0.03 ± 0.20	0.05 ± 0.15
AH	-0.03 ± 0.05	-0.12 ± 0.10	-0.03 ± 0.20	-0.45 ± 0.15
AL	0.02 ± 0.06	-0.05 ± 0.12	-0.12 ± 0.10	0.03 ± 0.14
WH	0.05 ± 0.06	0.26 ± 0.14	0.56 ± 0.11*	0.75 ± 0.13**
WL	-0.21 ± 0.04	-0.19 ± 0.12	-0.78 ± 0.20*	-1.27 ± 0.19*
IH	0.15 ± 0.07	1.22 ± 1.88	0.70 ± 0.17*	0.95 ± 0.24*
IL	-0.05 ± 0.04	-1.64 ± 1.01	-0.34 ± 0.13	-0.31 ± 0.17
Females	±			
CH	0.13 ± 0.05*	0.21 ± 0.08	0.36 ± 0.09*	0.26 ± 0.08*
CL	-0.03 ± 0.08	-0.09 ± 0.07	0.04 ± 0.15	-0.09 ± 0.15**
AH	-0.01 ± 0.07	-0.07 ± 0.13	-0.07 ± 0.20	-0.12 ± 0.15
AL	0.01 ± 0.08	-0.04 ± 0.09	0.00 ± 0.04	-0.09 ± 0.08
WH	0.03 ± 0.06	0.24 ± 0.08	0.70 ± 0.11*	0.77 ± 0.10**
WL	-0.19 ± 0.05	-0.13 ± 0.12	-0.66 ± 0.12**	-0.86 ± 0.07**
IH	0.15 ± 0.07	1.74 ± 1.56	0.82 ± 0.10*	0.89 ± 0.03**
IL	-0.05 ± 0.04	-2.67 ± 1.11	-0.29 ± 0.11	-0.36 ± 0.12

[a]Regression of response (selected mean deviated from control mean) on generation number.

*(P<.05). **(P<.01). Statistical tests of significance were performed on data transformed to common logarithms.

selection for lower feed consumption did not result in significant progress.

Correlated Responses II

Due to limitations in time and facilities, it was impossible to measure all traits of interest in all 12 lines throughout the study. SC, activity and feed intake were only measured in the lines where they were the criteria of selection and in the associated control line. In order to observe how these traits interacted, a replicate of generation 7 was produced. (It is important to note that the replicate was created after five generations of selection in cholesterol, activity and weight lines but after four generations of selection in the intake lines since the intake lines were originated one generation later). Traits measured in all 12 lines of the replicate were SC, activity, feed intake, body weights and body moisture percentage (PBM).

For each trait mentioned above except PBM the data were transformed to common logarithms to remove the existing correlations between the means and variances. Analyses of variance were calculated for each trait in each set of three lines (that is, the high, control and low cholesterol lines, the high, control and low activity lines, etc.) using line and sex as main effects and a line by sex interaction. The resulting analysis of variance tables (although too numerous to present here in full) indicated significant line by sex interactions ($P<.05$) in only three instances - feed consumption in the intake lines, feed consumption in the SC lines and 42-day body weight in the SC

lines. The only instances where significant differences between the sexes ($P<.05$) did not occur were in 12-day body weight for all lines and final activity score in the activity and 56-day body weight lines.

After obtaining this information, the sexes were analyzed separately. Duncan's new multiple range test was used to rank the 12 lines for each of the measured traits and to test for significant differences among the means. The multiple range test results are presented along with the means, standard deviations and coefficients of variation in following tables.

Body weights as correlated responses. In order to present a comprehensive view of the maturing mouse, the correlated responses of body weights at 12, 21, 42 and 56 days of age will be discussed together in terms of the four sets of selected lines. Means and rankings are given in Tables 30, 31, 32 and 33, and graphs are presented in Figures 9, 10, 11 and 12 for body weights at 12, 21, 42 and 56 days of age, respectively.

For clearer understanding in discussing this section, the rank of a particular line will be used to indicate how that line's mean for a trait compared with the other 11 lines' means for the same trait. Thus, if a line ranked third for a trait, two lines had means higher and nine lines had means lower. If two ranks are mentioned for one trait, they refer to the male and female positions, respectively.

The three cholesterol lines were interesting in their relative ranking of body weight. Line CH, selected for maximum SC, ranked

Table 30. Means, standard deviations and coefficients of variation of 12-day body weight in replicate of selected lines.

Line	N[a]	Mean	DNMRT[b,c]	S.D.	C.V.
Males					
CH	69	8.0[d]	9	0.8	9.7
CC	62	8.3	3	0.5	5.6
CL	63	8.6	1	0.6	7.1
AH	59	8.2	4	0.5	6.7
AC	63	8.0	7	0.6	7.1
AL	53	8.0	8	0.6	6.9
WH	59	8.3	2	0.4	4.5
WC	59	8.2	4	0.9	10.7
WL	60	7.8	11	0.5	6.9
IH	65	8.2	5	0.8	9.5
IC	54	7.8	10	0.7	9.6
IL	63	8.1	6	0.6	7.4
Females					
CH	60	8.1	6	0.8	9.5
CC	61	8.2	4	0.5	5.7
CL	63	8.6	1	0.6	7.1
AH	68	8.1	5	0.6	7.4
AC	62	8.0	8	0.5	6.8
AL	62	8.1	7	0.7	8.4
WH	57	8.4	2	0.4	4.5
WC	62	8.1	5	0.9	11.0
WL	64	7.7	10	0.5	6.5
IH	60	8.3	3	0.7	8.5
IC	58	7.8	9	0.7	8.8
IL	59	8.1	5	0.6	7.3

[a] Number of observations per mean.
[b] DNMRT = Duncan's new multiple range test. Tests of significance were performed on data transformed to common logarithms.
[c] For each group of twelve lines, means are ranked numerically in descending order. Means with the same DNMRT number are not significantly different ($P<.05$).
[d] grams.

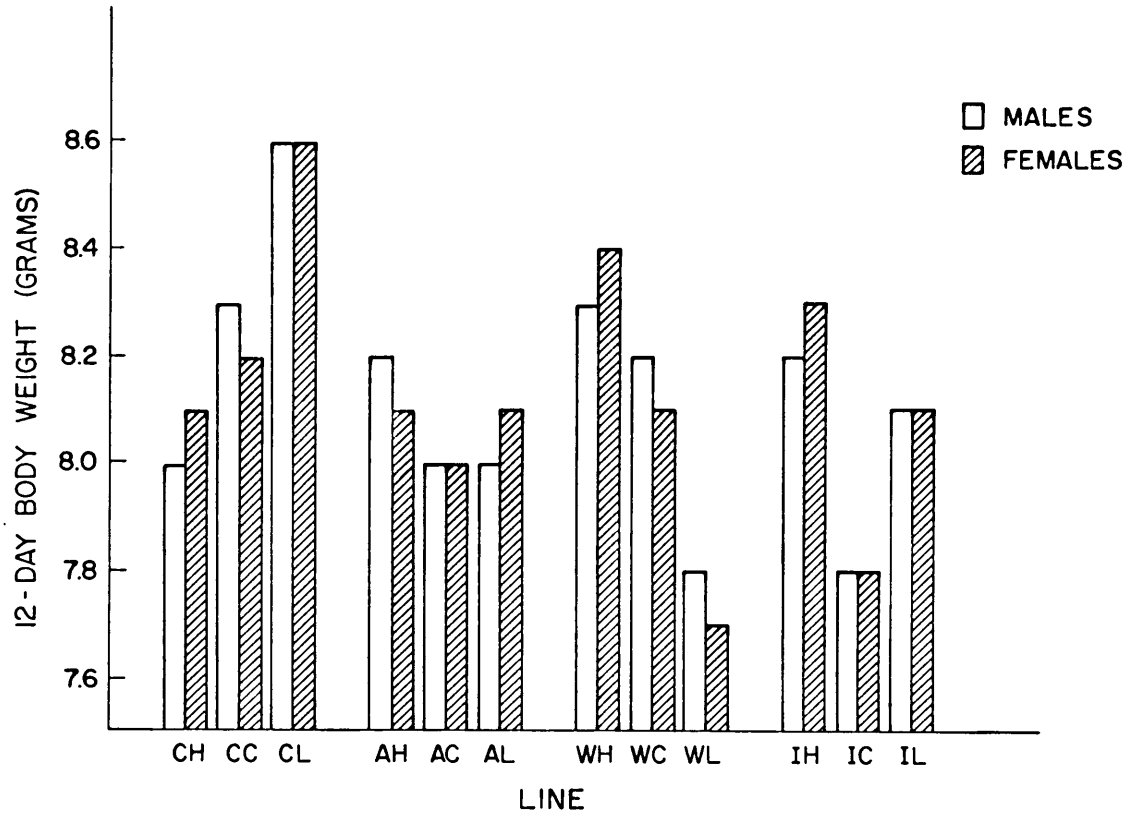

Figure 9. Relative performance of twelve selected and control lines for 12-day body weight in replicate.

Table 31. Means, standard deviations and coefficients of variation of 21-day body weight in replicate of selected lines.

Line	N[a]	Mean	DNMRT[b,c]	S.D.	C.V.
Males					
CH	69	13.6[d]	4	2.1	15.7
CC	62	13.6	5	1.8	13.0
CL	63	14.5	1	1.3	9.2
AH	59	13.3	8	1.3	10.1
AC	63	13.1	10	1.7	13.1
AL	53	12.2	12	1.7	14.1
WH	59	14.4	2	1.7	11.8
WC	59	13.5	6	1.7	12.5
WL	60	12.4	11	1.3	10.6
IH	65	14.3	3	2.1	14.7
IC	54	13.4	7	1.6	12.3
IL	63	13.3	9	1.8	13.4
Females					
CH	60	13.4	3	1.6	11.6
CC	61	13.0	5	1.6	12.0
CL	63	13.7	2	1.2	8.9
AH	68	12.8	7	1.5	11.7
AC	62	12.5	9	1.2	9.8
AL	62	12.3	11	1.8	14.3
WH	57	13.4	4	1.9	14.5
WC	62	12.8	6	1.6	12.3
WL	64	11.8	12	1.2	9.7
IH	60	14.1	1	1.4	10.3
IC	58	12.5	10	1.5	11.7
IL	59	12.7	8	1.7	13.4

[a]Number of observations per mean.
[b]DNMRT = Duncan's new multiple range test. Tests of significance were performed on data transformed to common logarithms.
[c]For each group of twelve lines, means are ranked numerically in descending order. Means with the same DNMRT number are not significantly different (P<.05).
[d]grams.

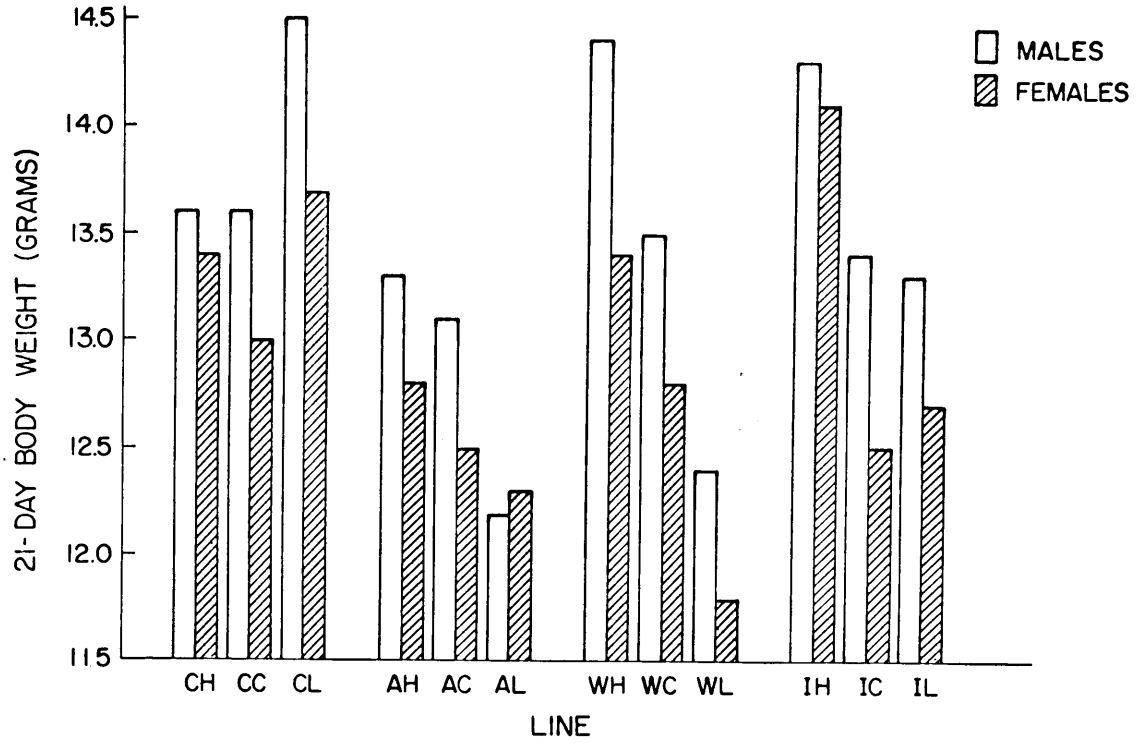

Figure 10. Relative performance of twelve selected and control lines for 21-day body weight in replicate.

Table 32. Means, standard deviations and coefficients of variation of 42-day body weight in replicate of selected lines.

Line	N[a]	Mean	DNMRT[b,c]	S.D.	C.V.
Males					
CH	69	30.9[d]	3	2.7	8.6
CC	62	29.2	7	2.9	9.9
CL	63	30.8	4	2.5	8.3
AH	59	30.5	5	2.4	7.9
AC	63	29.0	8	3.7	12.7
AL	53	28.4	10	4.2	10.7
WH	59	34.5	1	3.2	9.2
WC	59	30.4	6	3.7	12.3
WL	60	26.6	12	2.9	10.8
IH	65	32.2	2	2.9	8.9
IC	54	29.0	9	2.3	8.0
IL	63	28.1	11	2.6	9.3
Females					
CH	60	26.0	3	2.0	7.8
CC	61	25.2	4	1.8	7.3
CL	63	25.1	5	1.7	6.7
AH	68	25.0	6	2.0	8.2
AC	62	24.4	8	2.2	9.0
AL	62	24.3	9	2.4	10.0
WH	57	28.2	1	3.0	10.7
WC	62	24.9	7	2.8	11.3
WL	64	21.9	12	1.8	8.2
IH	60	27.0	2	1.9	7.1
IC	58	23.9	10	1.8	7.5
IL	59	23.7	11	1.9	8.1

[a] Number of observations per mean.
[b] DNMRT = Duncan's new multiple range test. Tests of significance were performed on
[c] data transformed to common logarithms. For each group of twelve lines, means are ranked numerically in descending order. Means with the same DNMRT number are not
[d] significantly different (P<.05). grams.

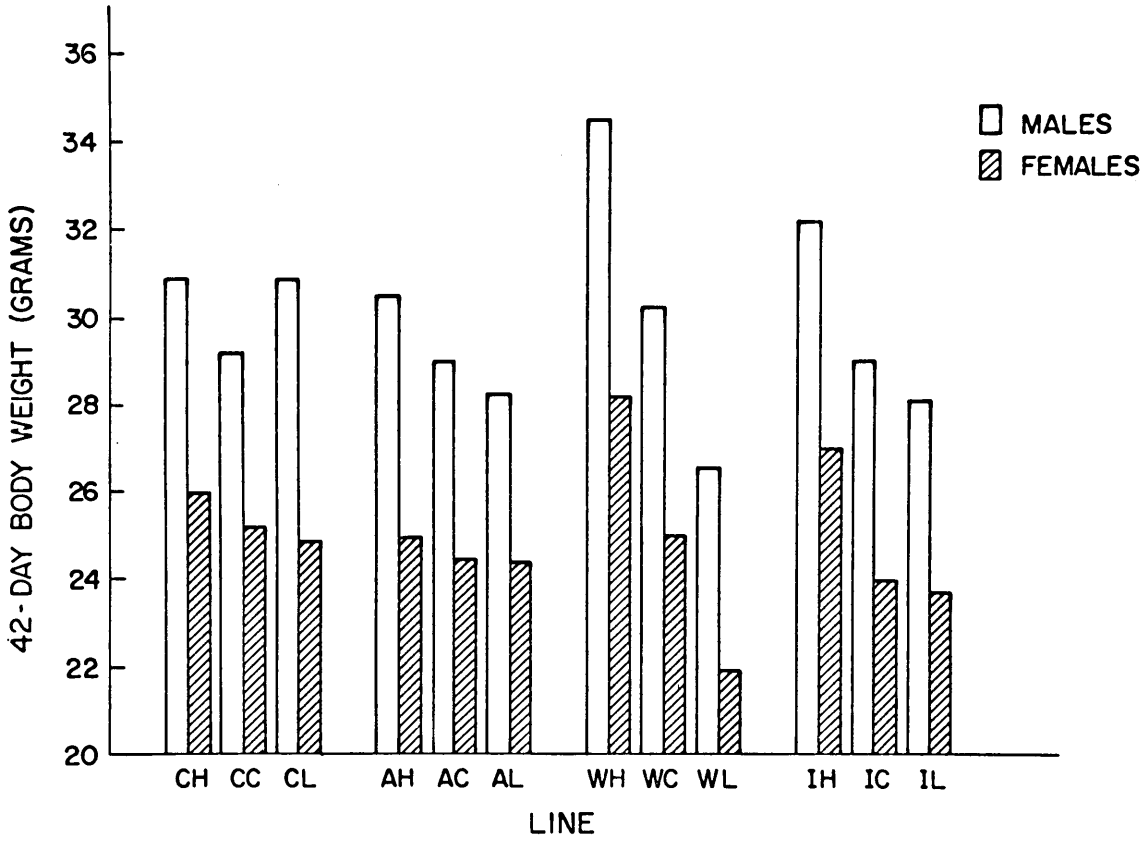

Figure 11. Relative performance of twelve selected and control lines for 42-day body weight in replicate.

Table 33. Means, standard deviations and coefficients of variation of 56-day body weight in replicate of selected lines.

Line	N[a]	Mean	DNMRT[b,c]	S.D.	C.V.
Males					
CH	69	33.0[d]	3	2.7	8.2
CC	62	31.6	6	2.5	7.8
CL	63	32.2	5	2.8	8.7
AH	59	31.3	7	2.6	8.3
AC	63	30.7	10	3.2	10.3
AL	53	30.8	9	3.3	10.7
WH	59	36.8	1	3.7	10.0
WC	59	32.4	4	3.1	9.6
WL	60	27.8	12	3.3	11.9
IH	65	34.5	2	2.5	7.2
IC	54	31.0	8	2.6	8.4
IL	63	30.0	11	2.7	8.9
Females					
CH	60	26.6	3	2.4	9.2
CC	61	25.9	5	1.9	7.4
CL	63	26.1	4	1.9	7.3
AH	68	24.8	9	2.4	9.7
AC	62	25.1	8	1.9	7.5
AL	62	25.3	7	2.2	8.5
WH	57	29.0	1	3.1	10.5
WC	62	25.7	6	2.2	8.7
WL	64	21.9	12	1.8	8.4
IH	60	27.7	2	1.8	6.5
IC	58	24.2	11	1.9	7.9
IL	59	24.5	10	2.2	9.2

[a]Number of observations per mean.
[b]DNMRT = Duncan's new multiple range test. Tests of significance were performed on data transformed to common logarithms.
[c]For each group of twelve lines, means are ranked numerically in descending order. Means with the same DNMRT number are not significantly different ($P<.05$).
[d]grams.

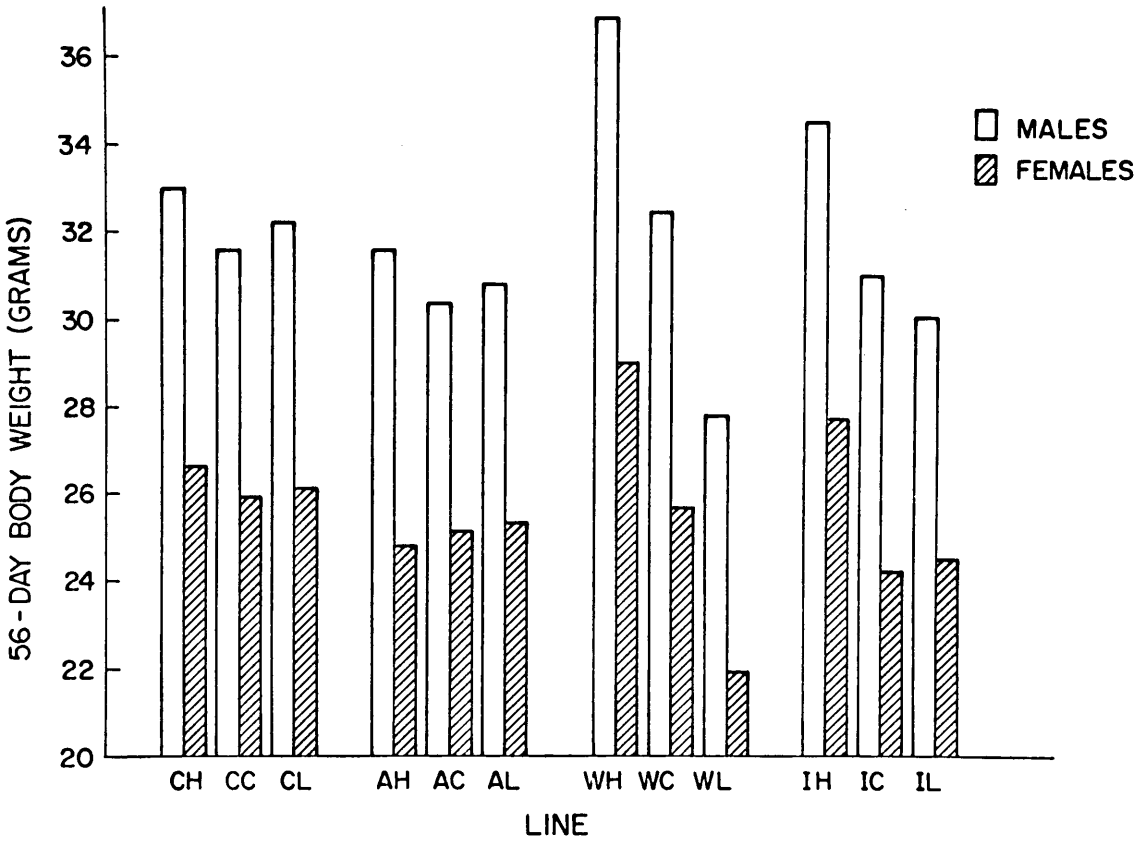

Figure 12. Relative performance of twelve selected and control lines for 56-day body weight in replicate.

rather low (ninth and sixth) in 12-day body weight. By weaning age, however, both male and female means ranked about third position from the top and remained there through 56 days with only the WH and IH lines being heavier. Conversely, line CL with reduced SC values had the heaviest mean weight of all the lines for both sexes at 12 days and was surpassed only by IH females in 21-day body weight. Thereafter, CL means dropped to fourth and fifth rankings. The control cholesterol line, CC, remained fairly constant in ranking with body weights ranging from third to seventh and with no discernible trend.

In other mouse studies Dunnington et al. (1977a) observed that mice gained weight rapidly either from birth to 21 days or just after weaning (21 to about 42 days). The clear division of CH and CL mice as to period of weight gain suggested that gaining weight early in life (before weaning) is associated with lower adult SC value, perhaps because in early weight gain a larger proportion of protein is produced. In contrast, gaining a relatively large part of adult weight post-weaning was, here, associated with higher adult SC values, perhaps since weight gained after weaning is made up of proportionately more fat (Lang and Legates, 1969; White, 1974).

Mice selected for maximum activity gradually dropped from fourth and fifth positions in 12-day body weight to seventh and ninth positions by 56 days of age. The control line, AC, remained quite constant in weight, ranking between eighth and 10th position consistently. AL mice were ranked eighth and seventh at 12 days, dropped to 12th and 11th places at weaning and then gradually increased to about eighth position

by 56 days.

Another interesting phenomenon observed by Thye (1973) and by Dunnington et al. (1977a) is evident here. It was found in earlier studies that mice which were relatively heavy at weaning accumulated higher activity scores than relatively light mice since the heavier animals had more stamina and/or weight necessary to turn the exercise wheels. However, as the mice matured, lighter animals were more likely to exercise than those mice which had become heavy. Exactly the same phenomenon occurred in this selection study. Mice selected for high physical activity ranked high in early (pre-weaning) weights but gradually dropped to relatively low adult weights. Those mice selected for low activity scores, however, had much lower pre-weaning weights and gradually increased in weight as they approached maturity.

The weight rankings of the three 56-day body weight lines indicated that selection for maximum and minimum 56-day body weight was successful. Line WH ranked from second to fourth in 12- and 21-day weight and had the largest weight means for 42- and 56-day weights. The control line, WC, ranged from fourth to seventh place with no noticable trend occurring during maturation. The low weight line, WL, ranked 11th and 10th at 12 days, then had the lowest weight means in all subsequent age-sex groups except 21-day-old males which ranked 11th.

The close relationship between feed consumption and body weights was evidenced in the rankings of the three feed intake lines. Mice selected for maximum feed intake were relatively high in body weight at 12 and 21 days of age and were second only to the WH line in 42- and

56-day body weight. The control (IC) and low (IL) intake lines were not quite as distinct in their positions. Line IC showed considerable variability, ranging from seventh to 11th positions with no noticable trend. Line IL began at a middle ranking for 12-day weight and gradually dropped to 11th place for weight at 42 days (the only lighter line was WL). At 56 days the males were still ranked 11th and IL females were 10th.

SC as a correlated response. Progress in the selection for maximum and minimum levels of SC was evidenced by the rankings of the three cholesterol lines in the replicate (Table 34 and Figure 13). Line CH males and females had the largest SC mean, CL males and females had the lowest SC means of all 12 lines and the control line, CC, held fifth and sixth positions in the ranking. As a correlated trait some interesting rankings occurred. Mice in the low activity line were ranked second in SC while high activity and high weight lines were third and fourth. Since the control activity line occupied positions nine and seven, it appeared that divergent selection for activity altered both the high and low activity lines by increasing SC to almost the same degree in both cases. Conversely, selection for high and low 56-day body weight was accompanied by an increase in SC of line WH (to positions four and three) and a decrease in SC of line WL (to 10th and 11th ranks), while the control weight line, WC, took median positions six and seven. The intake lines were rather surprising in their response to SC testing. Instead of behaving somewhat like the lines selected for 56-day body weight, as might be suspected, the maximum feed intake

Table 34. Means, standard deviations and coefficients of variation of serum cholesterol in replicate of selected lines.

Line	N[a]	Mean	DNMRT[b,c]	S.D.	C.V.
Males					
CH	36	186.2[d]	1	47.8	25.7
CC	31	103.4	5	25.4	24.6
CL	32	73.1	11	18.5	25.4
AH	29	112.7	3	36.2	32.1
AC	33	97.6	7	26.7	27.3
AL	28	113.8	2	33.7	29.6
WH	30	105.2	4	42.9	40.7
WC	29	98.7	6	38.1	38.7
WL	32	92.0	9	31.9	34.7
IH	32	91.3	10	26.4	28.9
IC	28	97.1	8	34.7	35.7
IL	33	97.6	7	26.2	26.9
Females					
CH	29	142.7	1	42.4	29.7
CC	28	80.1	6	23.9	29.9
CL	32	59.2	12	16.4	27.8
AH	35	81.6	4	19.9	24.4
AC	31	72.9	9	21.5	29.5
AL	33	91.7	2	24.8	27.1
WH	30	84.8	3	31.5	37.2
WC	31	77.1	7	23.9	31.0
WL	34	70.1	11	19.9	28.4
IH	30	71.3	10	22.1	31.0
IC	28	80.5	5	22.5	27.9
IL	28	73.6	8	20.3	27.5

[a]Number of observations per mean.
[b]DNMRT = Duncan's new multiple range test. Tests of significance were performed on data transformed to common logarithms.
[c]For each group of twelve lines, means are ranked numerically in descending order. Means with the same DNMRT number are not significantly different ($P<.05$).
[d]mg / 100 ml.

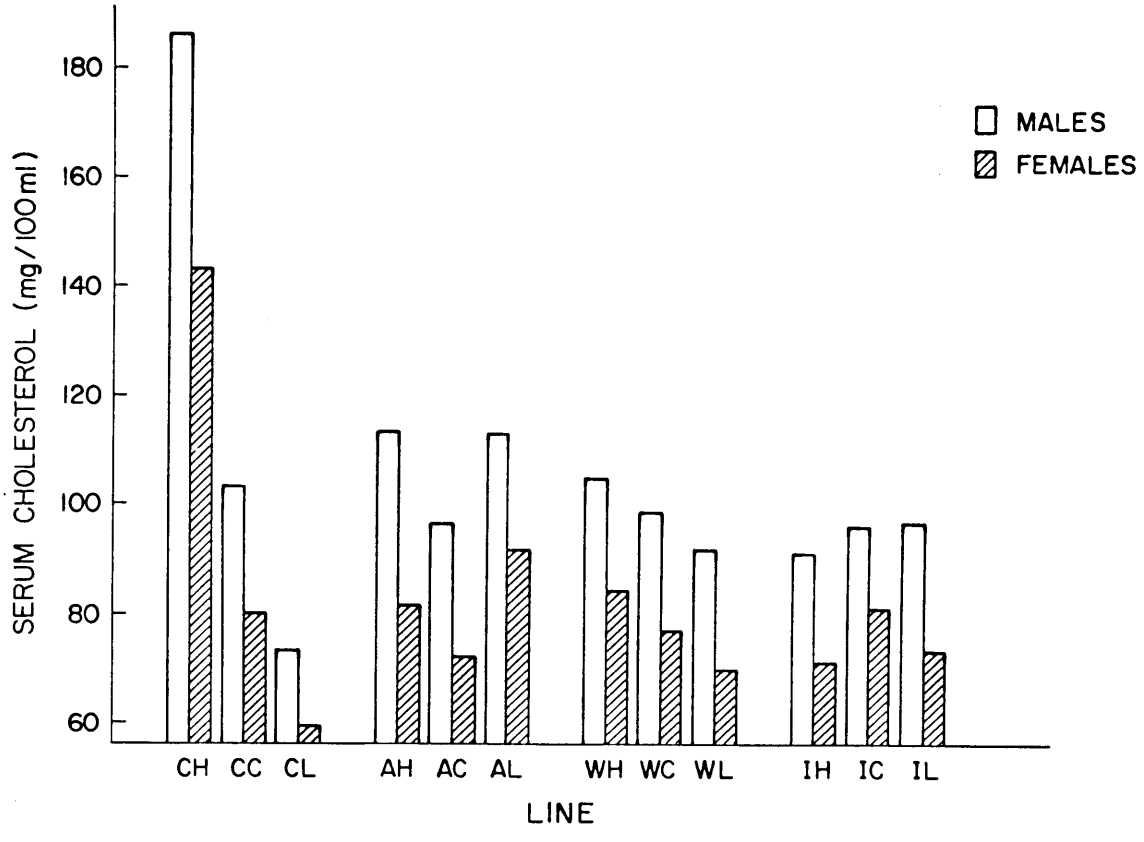

Figure 13. Relative performance of twelve selected and control lines for serum cholesterol in replicate.

line ranked very low (10th place), the minimum intake line was rather higher in seventh and eighth places, and the control line was the most variable with males ranked eighth and females fifth.

Activity as a correlated response. A clear-cut separation of the three activity lines indicated that progress was made in this portion of the selection study (Table 35 and Figure 14). Activity scores in the replicate were highest for line AH, lowest for line AL and intermediate (seventh and sixth places) for the control. The feed intake lines were very consistent between sexes with IH fourth, IL fifth and IC ninth. Again, it appeared that divergent selection (for feed intake in this instance) caused the correlated response, activity, to increase in both selected lines as compared to their control. All the cholesterol line-sex groups were intermediate in positions six to 10 except CH females which ranked second in activity score. No reason was apparent for the rather large difference between CH male and female activity. Another unusual occurrance concerned the weight lines. While WL males and females ranked quite high in activity (second and third) and the control line was 11th, WH males ranked third and WH females ranked 10th. A possible explanation for the greater activity scores of WH males is that males are generally later in depositing fat in the body than females (Lang and Legates, 1969; White, 1974), and so, were more active at 28 and 49 days of age, when activity scores were recorded.

Table 35. Means, standard deviations and coefficients of variation of total activity scores in replicate of selected lines.

Line	N[a]	Mean	DNMRT[b,c]	S.D.	C.V.
Males					
CH	33	13076[d]	6	6705	51.3
CC	31	10808	10	5407	50.0
CL	31	11590	8	4941	42.6
AH	30	29449	1	11213	38.1
AC	30	12949	7	6934	53.5
AL	25	6404	12	3989	62.3
WH	29	16029	3	8922	55.7
WC	30	8174	11	5114	62.6
WL	28	19652	2	7976	40.6
IH	33	13262	4	8091	61.0
IC	26	11318	9	8559	75.6
IL	30	13208	5	9417	71.3
Females					
CH	31	17769	2	9691	54.5
CC	33	13773	8	7043	51.1
CL	31	14119	7	6490	46.0
AH	33	22568	1	10274	45.5
AC	31	15186	6	7263	47.8
AL	29	9034	12	7735	85.6
WH	27	12121	10	7790	64.3
WC	31	11322	11	8159	72.1
WL	30	16480	3	7614	46.2
IH	30	16438	4	8858	53.9
IC	30	13103	9	8865	67.7
IL	31	15609	5	10019	64.2

[a]Number of observations per mean.
[b]DNMRT = Duncan's new multiple range test. Tests of significance were performed on data transformed to common logarithms.
[c]For each group of twelve lines, means are ranked numerically in descending order. Means with the same DNMRT number are not significantly different ($P<.05$).
[d]revolutions.

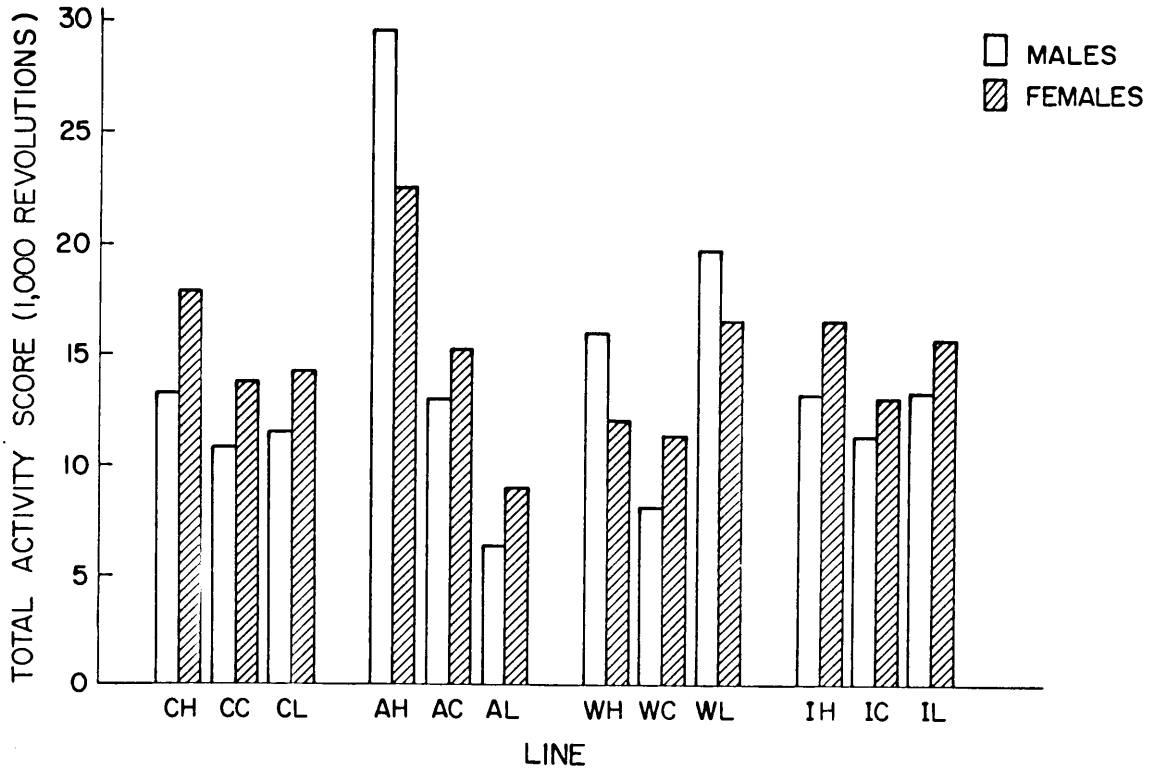

Figure 14. Relative performance of twelve selected and control lines for physical activity in replicate.

Feed intake as a correlated response. The results of ranking all 12 lines according to quantity of feed consumed from three to seven weeks of age provided interesting information about the progress made in selection for feed intake (Table 36 and Figure 15). Line WH males and females consumed a greater amount of feed than did the IH mice which were selected specifically for high feed intake. While IL males consumed the least of all tested lines, IL females ranked eighth in feed intake, consuming more feed than two control lines (IC and CC) and than line WL. This immediately suggested that it was more efficient to select for high and low 56-day body weight in order to produce mice which consume, respectively, more and less. However, this conclusion must be tempered by the knowledge that the intake lines differed from the other nine lines in several respects. The three intake lines had only undergone four generations of selection when the replicate was created, compared to five generation of selection in the other nine lines. Family selection was practiced in the intake lines and individual selection in the remaining nine lines. Also, the phenotypic standard deviations for intake differed from those of the other selected traits, particularly that of physical activity. The two selected cholesterol lines both ranked very high in feed intake while the control SC line took positions eight and 10. A similar ranking occurred when these cholesterol lines were tested for 56-day body weight. Line AH occupied positions four and five in the feed consumption ranking and the low activity line ranked ninth and eighth, indicating that the high activity line consumed considerably more than the

Table 36. Means, standard deviations and coefficients of variation of total feed intake in replicate of selected lines.

Line	N[a]	Mean	DNMRT[b,c]	S.D.	C.V.
Males					
CH	36	139.2[d]	5	9.7	7.0
CC	31	134.4	8	9.2	6.8
CL	32	143.9	3	10.1	7.0
AH	29	141.0	4	8.9	6.2
AC	33	136.7	7	12.5	9.2
AL	28	130.9	9	19.6	14.9
WH	30	152.8	1	16.2	10.6
WC	29	138.7	6	15.5	11.2
WL	32	126.1	10	11.9	9.4
IH	32	146.3	2	13.1	9.0
IC	28	136.7	7	13.7	10.0
IL	33	123.8	11	7.0	5.6
Females					
CH	29	129.5	3	7.4	5.7
CC	28	117.3	10	8.0	6.8
CL	32	127.0	4	7.2	5.6
AH	35	126.6	5	9.0	7.1
AC	31	120.9	7	12.3	10.2
AL	33	118.9	8	12.7	10.6
WH	30	138.6	1	17.9	12.9
WC	31	125.8	6	13.3	10.6
WL	34	113.5	12	7.5	6.6
IH	30	135.6	2	7.1	5.2
IC	28	114.8	11	6.6	5.8
IL	28	118.6	9	10.8	9.1

[a] Number of observations per mean.
[b] DNMRT = Duncan's new multiple range test. Tests of significance were performed on data transformed to common logarithms.
[c] For each group of twelve lines, means are ranked numerically in descending order. Means with the same DNMRT number are not significantly different ($P<.05$).
[d] grams.

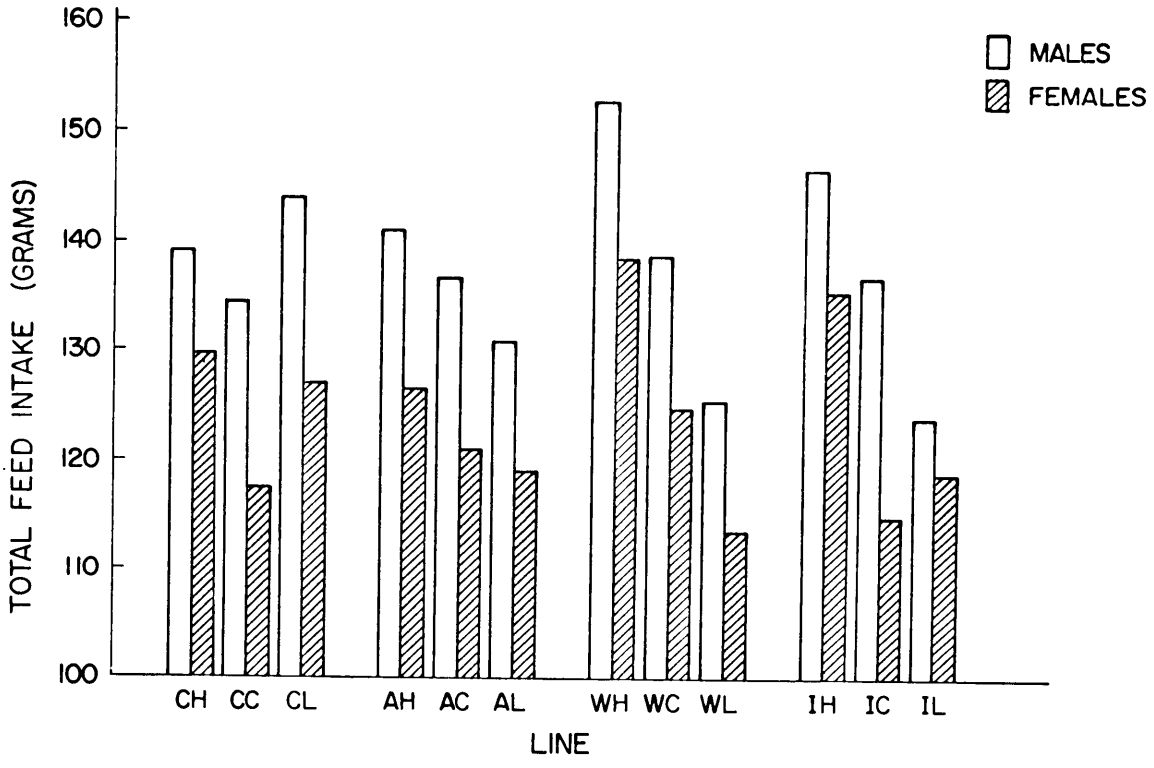

Figure 15. Relative performance of twelve selected and control lines for feed intake in replicate.

low line but did not weigh very much more at 56 days of age, presumably because of their higher level of physical activity.

Body moisture content as a correlated response. After the measurement of all mice in the replicate (after approximately 60 days of age), a sample of one male and one female from each of 10 litters in every line was randomly chosen for a body moisture analysis. The percentage of body moisture (PBM) was calculated using lyophilized whole carcasses and based on the live weight of the mice after 16 hours of fasting.

Analyses of variance were performed on each set of three lines (that is, the three cholesterol lines, the three activity lines, etc.) with line and sex as the main effects and a line by sex interaction. These analyses resulted in significant differences only among lines in the three feed intake lines and in a significant line by sex interaction in the cholesterol lines. An analysis including all 12 lines resulted in significant differences among lines. There was no significant difference in PBM due to sex in any of the analyses which agreed with the findings of Lang and Legates (1969) that the percentage of body fat (found to have a high negative correlation with PBM) was essentially the same for both male and female mice at eight weeks of age.

Table 37 gives means, standard deviations and coefficients of variation of PBM data for males and females of the 12 lines with the means presented graphically in Figure 16. As the analyses of variance

Table 37. Ranking, means, standard deviations and coefficients of variation of percent body moisture in replicate of selected lines.

Line	N[a]	Mean	DNMRT[b,c]	S.D.	C.V.
Males					
WC	10	66.81[d]		7.74	11.58
AC	10	65.54		1.53	2.34
AL	10	64.73		2.95	4.56
CH	10	64.41		3.84	5.96
IL	10	63.78		1.50	2.35
CC	10	63.67		2.05	3.22
WH	10	63.66		3.27	5.14
AH	10	63.53		2.59	4.07
CL	10	62.90		3.63	5.77
WL	10	62.29		2.70	4.34
IC	10	61.10		2.39	3.92
IH	10	60.60		2.31	3.81
Females					
CL	10	65.61		3.24	4.94
AL	10	65.03		1.84	2.82
AC	10	64.30		3.14	4.88
IL	10	64.15		1.79	2.79
CC	10	63.46		3.43	5.41
AH	10	63.37		3.32	5.24
WH	10	62.56		2.31	3.70
WL	10	62.23		3.71	5.96
CH	10	61.85		3.23	5.23
WC	10	61.78		3.05	4.93
IH	10	61.21		3.31	5.41
IC	10	60.54		5.28	8.72

[a]Number of observations per mean.
[b]DNMRT = Duncan's new multiple range test.
[c]Means connected by a line are not significantly different ($P<.05$).
[d]percent.

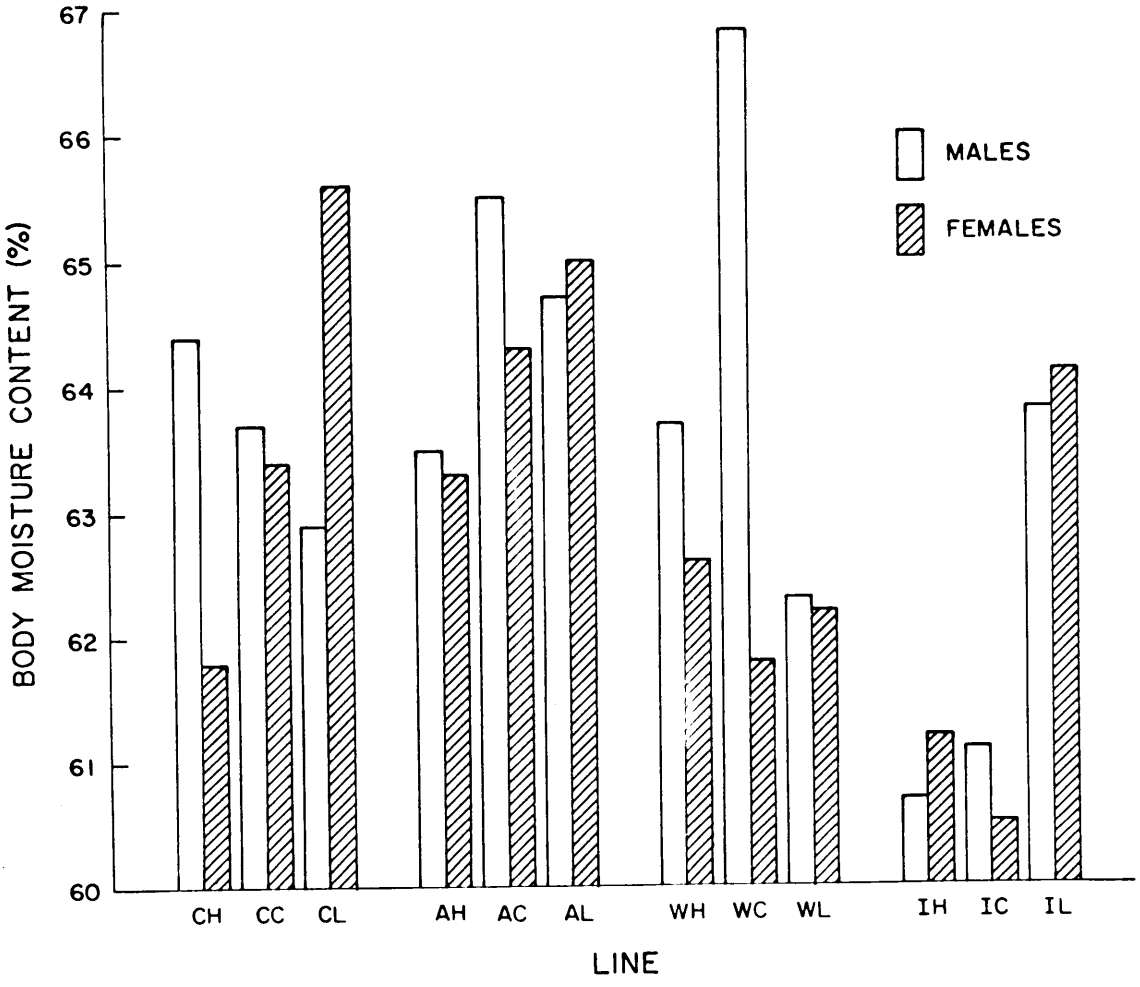

Figure 16. Relative performance of twelve selected and control lines for percentage of body moisture in replicate.

indicated, the cholesterol lines had a significant line by sex interaction. The reason for this interaction can be seen from the relative ranking of the lines. The rank of CH males was higher (although not significantly) than that of CL males, while CL females had significantly higher ranks than CH females. The reason for the reverse order of the lines in the two sexes was not apparent. Line AL and AC males and females were consistently high in PBM, suggesting relatively low percentages of body fat. Ranks of the AH and AL lines were not different. The WH and WC males ranked significantly higher in PBM than WL males; WH and WL females ranked significantly higher than WC. The consistent ranking of WH as relatively high in PBM was surprising since one might expect selection for increased mature body weight to increase the percentage of body fat which is inversely related to PBM (Lang and Legates, 1969; White, 1974).

Although many of the lines did not differ from each other according to Duncan's new multiple range test, both sexes in lines IC and IH were consistently lowest in PBM (and thus, relatively higher in body fat). Conversely, line IL ranked with the highest group of means for PBM in both sexes. It was also surprising that, in both sexes, line WH mice ranked significantly higher than IH mice. Apparently selection for increased feed consumption rather than selection for increased mature body weight caused a discernible increase in the percentage of body fat.

Effects of Maturation on SC and Body Weight

The selection study and evaluation of correlated responses in this project have dealt with SC, activity, body weight and feed intake in young, adult mice. A sample of 68 males and 58 females obtained from the control cholesterol line (CC) after the random selection of breeders for generation 2 was used to learn more about trends in SC and body weight in older animals. Originally, maintenance of these mice until natural death was intended, but the study was terminated when the mice reached 567 days of age (1.55 years) since a large proportion of them were in poor physical condition. Their problems stemmed largely from wounds inflicted by cagemates, particularly in the case of males. Also, it had become increasingly difficult to draw blood by sinus orbital bleeding, probably due to the formation of scar tissue in the ocular orbit.

During the one and one-half years that they were maintained, all mice were weighed at three-week intervals and blood samples were obtained every 18 weeks, beginning at 63 days of age for SC determination. A total of 110 mice (56 males and 54 females) lived until the termination of the project and analyses were based on those mice.

The means, standard deviations and coefficients of variation of SC and of body weights are shown in Tables 38 and 39 and in Figures 17 and 18, respectively. Males consistently had higher SC and greater body weights than females at the same age. Also, females generally showed greater variability in both traits (as evidenced by corresponding coefficients of variation), perhaps due to cycling in the females.

Table 38. Means, standard deviations and coefficients of variation of serum cholesterol in adult mice.

	Males[a]			Females[b]		
Age	Mean	S.D.	C.V.	Mean	S.D.	C.V.
63[c]	158.3[d]	33.8	21.3	123.1	32.2	26.2
189	144.2	35.6	24.7	101.9	32.1	31.5
315	126.3	35.1	27.8	85.8	26.0	30.3
441	118.9	33.0	27.7	94.9	46.8	49.3
567	105.6	34.2	32.4	85.7	43.7	51.0

[a] 56 observations per mean.
[b] 54 observations per mean.
[c] days.
[d] mg / 100 ml.

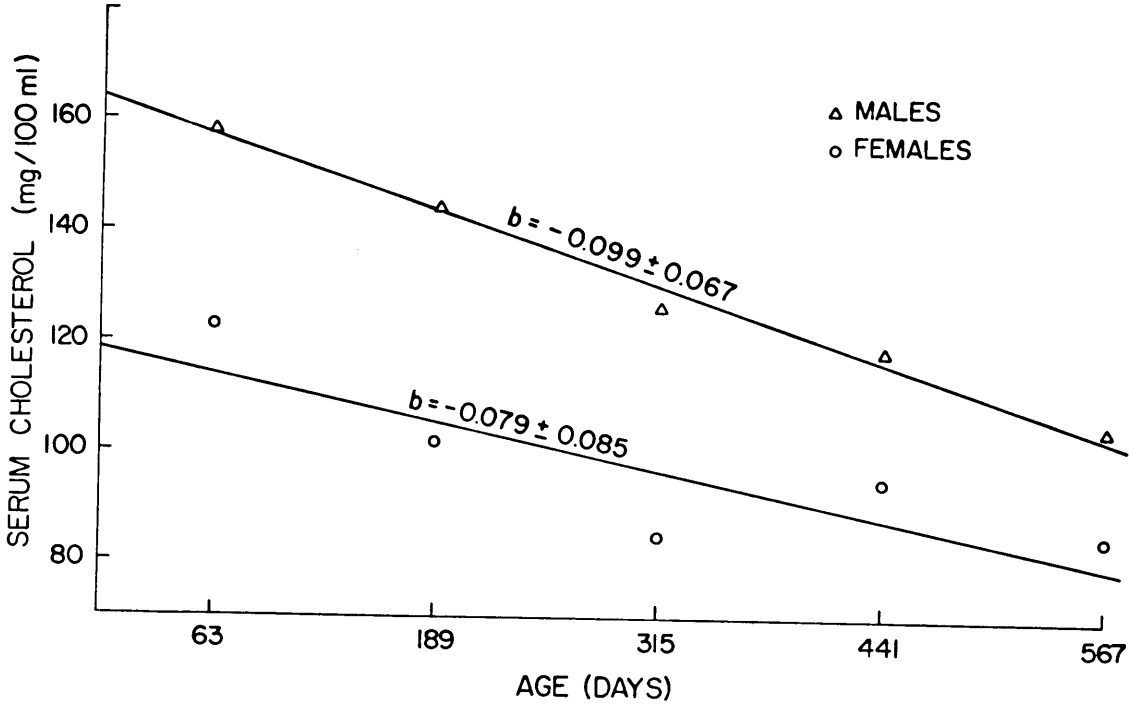

Figure 17. Mean values of serum cholesterol in adult mice at 18-week intervals.

Table 39. Means, standard deviations and coefficients of variation of body weight in adult mice.

	Males[a]			Females[b]		
Age	Mean	S.D.	C.V.	Mean	S.D.	C.V.
21[c]	12.9[d]	1.7	13.1	12.3	1.5	12.2
42	31.2	2.3	7.5	25.4	1.8	7.0
56	33.7	2.4	7.1	26.7	2.1	8.0
63	34.4	2.6	7.5	26.9	1.9	7.0
84	37.1	2.6	6.9	28.7	2.1	7.2
105	38.9	2.3	5.9	30.3	2.3	7.4
126	39.3	2.3	5.9	30.7	2.4	7.8
147	39.7	2.3	5.8	31.3	2.5	8.1
168	40.7	2.5	6.1	32.2	2.3	7.1
189	41.9	2.6	6.2	33.3	2.6	7.9
210	41.9	2.3	5.4	32.9	2.7	8.2
231	42.6	2.5	5.9	33.5	2.7	8.0
252	43.3	2.8	6.4	34.2	2.6	7.7
273	44.0	2.7	6.2	34.8	2.8	7.9
294	43.3	2.5	5.8	34.1	2.6	7.8
315	44.1	3.0	6.7	35.0	3.0	8.5
336	44.6	2.8	6.2	34.8	3.0	8.6
357	45.7	3.1	6.9	35.7	2.9	8.1
378	44.4	3.9	8.8	35.7	3.0	8.4
399	44.3	2.9	6.6	36.1	3.2	8.9
420	44.5	3.0	6.7	36.0	3.0	8.3
441	44.5	3.3	7.4	36.4	3.4	9.4
462	44.9	3.1	6.8	36.8	3.3	8.9
483	45.5	3.5	7.7	37.4	3.7	9.9
504	45.0	3.5	7.7	37.5	3.5	9.4
525	45.3	3.4	7.5	38.0	4.0	10.4
546	43.7	3.1	7.2	36.8	3.2	8.8
567	44.0	3.7	8.3	37.5	3.4	9.2

[a] 56 observations per mean.
[b] 54 observations per mean.
[c] days.
[d] grams.

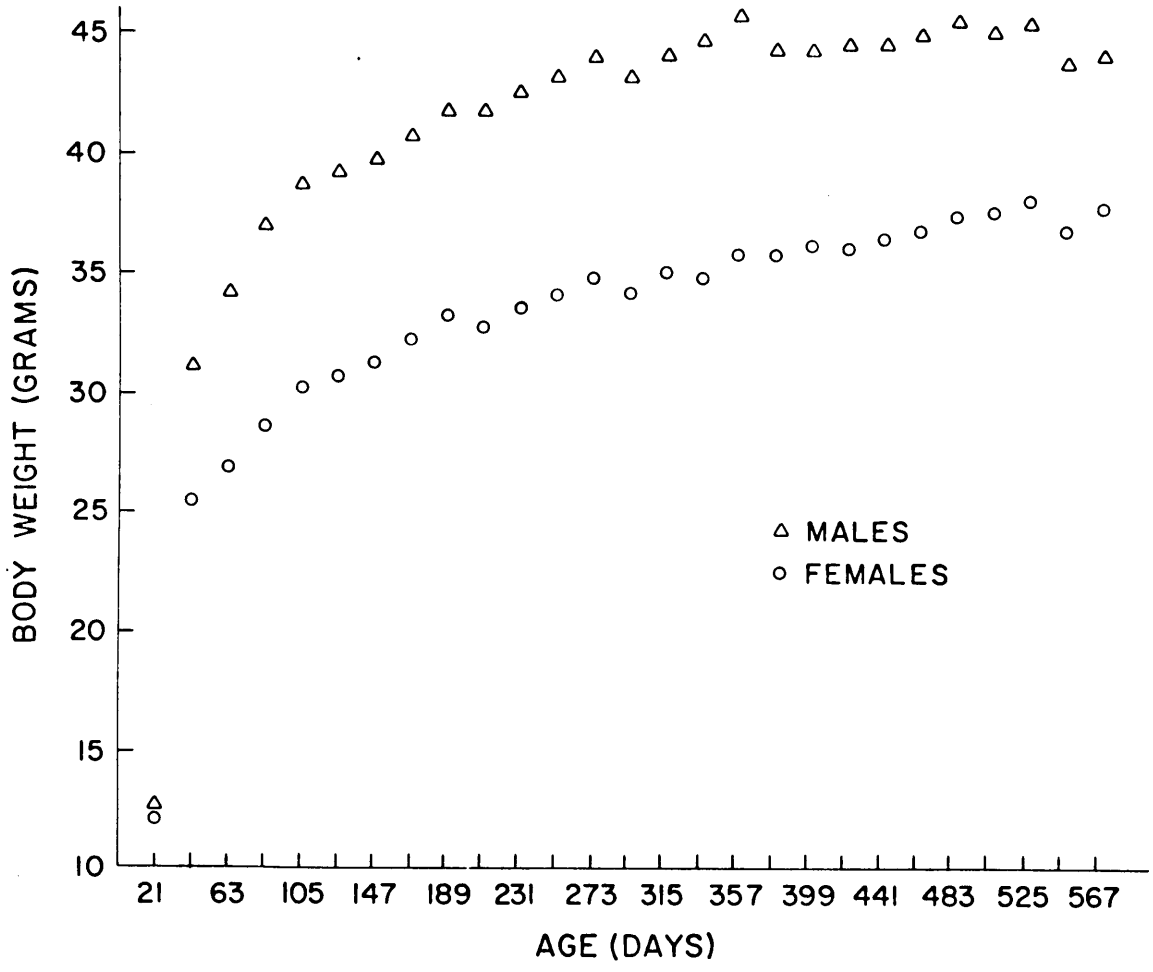

Figure 18. Mean values of body weight in adult mice from 21 to 567 days of age at 3-week intervals.

The data resulting from this study were found to have correlated means and variances. Also, Bartlett's test (Steel and Torrie, 1960) indicated that the variances were heterogeneous. Various transformations of the data did not result in either independence of means and variances or homogeneity of variances. Since these two assumptions are required for validity of the analysis of variance (Cochran, 1947), neither an analysis of variance nor a regression could be used in evaluating the data. Therefore, a weighted regression analysis using generalized least squares was performed to obtain regressions of SC and of body weight on age. Normally, such an analysis employs the reciprocal of the variance as the weighting factor (thus giving greater relative weight to groups with small variances and lesser relative weight to groups with large variances). In such a procedure, however, all covariances among groups are assumed to be zero. For this particular set of data, there were substantial coveriances among different age groups, so the entire variance-covariance matrix was used as the weighting factor.

The regression coefficients and their standard errors for male and female SC are shown in Table 40. Neither regression (-0.099 ± 0.067 and -0.079 ± 0.085) was significantly different from zero and they did not differ significantly from each other. The linear regressions fit quite well with r^2 values of .998 and .980 respectively for males and females and when a quadratic term was used in the model, it was non-significant. Therefore, the regression of SC on age from sexual maturity until one and one-half years of age was linear in both sexes and

Table 40. Regressions of SC on days of age in adult mice.

	Males	Females
Intercept	161.538	118.489
b ± S.E.	-0.099 ± 0.067	-0.079 ± 0.085
r^2	.998	.980

*(P<.05).

did not change statistically, although there was a decreasing trend throughout the study, particularly in the males. These results agreed with those by Bruell et al. (1962) who reported no significant change in SC values of mice from two to 12 months of age.

The regressions of body weight on age are presented in Table 41. When body weights after sexual maturity (from 42 to 567 days of age) were analyzed, slight but significant positive linear regressions were obtained (0.019 ± 0.005 and 0.018 ± 0.003) for males and females. The regression coefficients for males and for females did not differ from each other and the fit of these two regressions to linearity was quite good, with r^2 values of .961 and .975. When a quadratic term was used in the model, it was not statistically significant in either sex ($P<.05$).

However, if body weights from weaning (21 days) until the termination of the project were used, the linear regressions fit very poorly, with r^2 values of .396 and .696, for males and females, respectively. By including a quadratic term in the model, a much better fit (r^2 values of .702 and .845) resulted. The linear and quadratic terms (statistically significant at $P<.01$ in both sexes) are given in Table 41. The linear regressions (0.152 ± 0.010 and 0.099 ± 0.009) differed significantly from each other with males having the steeper slope, that is, gaining more weight from 21 to 567 days of age.

Product-moment correlations among SC, body weight and age were calculated separately for males and females and are presented in Table 42. Highly significant positive correlations between age and weight

Table 41. Regressions of body weight on days of age in adult mice.

	42 to 567 days of age	
	Males	Females
Intercept	34.2	25.4
b ± S.E.	0.019 ± 0.005**	0.018 ± 0.003**
r^2	.961	.975

	21 to 567 days of age	
	Males	Females
Intercept	13.8	13.4
b ± S.E.		
Linear	0.152 ± 0.010**	0.099 ± 0.009**
Quadratic	-0.00021 ± 0.00002**	0.00012 ± 0.00001**
r^2	.702	.845

**(P<.01).

Table 42. Phenotypic correlations among SC, body weight and age for adult mice.

	Males		Females	
	Weight	Age	Weight	Age
SC	-0.281**	-0.471**	-0.169*	-0.295**
Weight		0.639**		0.727**

*(P<.05). **(P<.01).

were obtained for both males and females, agreeing with the positive regression lines estimated for body weight on age. SC and age were negatively correlated for both sexes with the correlation being substantially higher for males than for females. The relationship between SC and body weight was negative in both sexes. This would be expected in view of their inverse relationship with age discussed above.

GENERAL DISCUSSION

Elevated circulating cholesterol levels have long been suspected of contributing to the development of atherosclerosis. This suspicion has recently been enforced as intensive research has attempted to stem the increasing incidence in humans of this lethal condition. Several factors such as degree of physical activity, type and quantity of food consumed and body weight have been shown to influence the amount of circulating cholesterol, so their specific effects on cholesterol levels (and thus their potential effects on atherosclerosis) must also be ascertained.

The present study has provided an evaluation of the extent to which heredity influences SC, activity, body weight and feed intake in mice. By completing a five-generation divergent selection study for those four traits, a reliable estimate of the degree to which these characteristics are heritable was obtained. All the criteria of selection except minimum feed intake were found to be moderately heritable with realized heritabilities ranging from 0.18 to 0.40. These results indicate that the genetic potential for certain levels of circulating cholesterol, activity and body weight are influenced by ancestors and, thus, are only partially subject to control by an individual. The existence of moderate heritability warns individuals with affected ancestors that the same problems may befall them and allows them the

benefit of preventative care and early treatment.

Relationships among SC, activity, body weight and feed consumption were of especial interest in this study. The degree to which SC may be reduced by controlling food consumption, body weight and physical activity is of great importance in combating the deleterious effects caused by elevated circulating cholesterol. Results of this project indicated that, phenotypically, mature body weight was positively correlated with SC and with feed intake but was negatively correlated with physical activity in mice.

In evaluating the performance of each selected and control line for eight traits (12-, 21-, 42- and 56-day body weight, SC, physical activity, feed intake and percentage of body moisture) more interesting relationships surfaced. Representatives of the lines selected for maximum and minimum physical activity ranked almost the same in SC values, indicating no reduction in SC values due to differing levels of voluntary physical activity (The distinction between voluntary and forced activity should be made here. In several previous studies - Papadoupoulos et al., 1969; Lewis et al., 1961; Jones et al., 1964 - enforced exercise regimes have successfully reduced SC.) Mice in the line selected for maximum mature body weight had significantly greater SC than mice selected for minimum mature body weight, reconfirming the positive, phenotypic correlation found between mature body weight and SC. Also, both male and female mice in the minimum mature body weight line were more inclined to exercise than mice of the maximum weight line, agreeing with the negative, phenotypic correlation between mature

body weight and activity.

It is interesting to note that, although the preceding paragraphs show considerable changes in SC of the selected weight and activity lines, the lines selected for maximum and minimum SC did not show any remarkable results when tested for activity or body weight. That is, increased or decreased activity and body weight caused changes in SC levels but widely diverged SC levels were not, reciprocally, associated with changes in activity or body weight. One can surmise that a cause and effect relationship has been outlined by these results, indicating that reduced activity and/or high mature body weight contributed to elevated SC.

Another aspect of the circulatory cholesterol problem was also treated in this study. The trends in SC and in body weight during maturation of male and female mice were recorded. It was found, in both sexes, that SC did not statistically change during the mature lifetime of the mice and that body weight increased gradually but essentially stabilized after approximately one year of age.

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Appendix A. Means and standard errors of SC for logarithmic transformed data in selected and control SC lines.

Generation	log (SC ± S.E.)		
	Line CH	Line CC	Line CL
Males			
2	2.1880 ± 0.0092[a]	2.1825 ± 0.0107	2.1666 ± 0.0108
3	2.1440 ± 0.0126	2.0966 ± 0.0115	2.0369 ± 0.0113
4	2.2582 ± 0.0089	2.1743 ± 0.0105	2.0612 ± 0.0108
5	2.2121 ± 0.0140	2.0818 ± 0.0115	1.9455 ± 0.0090
6	2.1917 ± 0.0129	1.9712 ± 0.0124	1.7932 ± 0.0105
7	2.2712 ± 0.0120	2.0035 ± 0.0138	1.7675 ± 0.0122
Females			
2	2.1014 ± 0.0084	2.0944 ± 0.0116	2.0994 ± 0.0108
3	2.0527 ± 0.0110	2.0329 ± 0.0119	1.9260 ± 0.0107
4	2.1913 ± 0.0106	2.0953 ± 0.0111	1.9782 ± 0.0092
5	2.1360 ± 0.0137	1.9771 ± 0.0097	1.8515 ± 0.0084
6	2.0866 ± 0.0112	1.8670 ± 0.0117	1.6843 ± 0.0239
7	2.1990 ± 0.0114	1.9092 ± 0.0118	1.6814 ± 0.0114

[a]log (mg / 100 ml).

Appendix B. Means and standard errors of activity scores for logarithmic transformed data in selected and control physical activity lines.

Generation	log (activity ± S.E.)		
	Line AH	Line AC	Line AL
Males			
2	3.8902 ± 0.0664[a]	3.9772 ± 0.0531	3.9866 ± 0.0580
3	4.0456 ± 0.0669	4.0987 ± 0.0426	4.0197 ± 0.0423
4	4.1414 ± 0.0259	4.0910 ± 0.0273	3.9026 ± 0.0521
5	4.2219 ± 0.0413	4.1348 ± 0.0320	3.8402 ± 0.0580
6	4.2608 ± 0.0257	4.0554 ± 0.0318	3.8995 ± 0.0404
7	4.2983 ± 0.0222	4.0723 ± 0.0268	3.7653 ± 0.0478
Females			
2	3.8791 ± 0.0856	3.9011 ± 0.0815	4.1342 ± 0.0270
3	4.1124 ± 0.0566	4.1753 ± 0.0462	3.9687 ± 0.0731
4	4.1962 ± 0.0448	4.1499 ± 0.0221	3.9558 ± 0.0672
5	4.2737 ± 0.0259	4.0239 ± 0.0675	3.9117 ± 0.0564
6	4.2608 ± 0.0232	4.1352 ± 0.0309	3.9123 ± 0.0474
7	4.2798 ± 0.0237	4.0784 ± 0.0322	3.6972 ± 0.0657

[a]log (revolutions).

Appendix C. Means and standard errors of 56-day body weight for logarithmic transformed data in selected and control 56-day body weight lines.

	log (WT 56 ± S.E.)		
Generation	Line WH	Line WC	Line WL
Males			
2	1.5257 ± 0.0046[a]	1.5100 ± 0.0053	1.5133 ± 0.0036
3	1.5430 ± 0.0038	1.5288 ± 0.0038	1.5158 ± 0.0035
4	1.5757 ± 0.0029	1.5490 ± 0.0036	1.5190 ± 0.0034
5	1.5770 ± 0.0031	1.5506 ± 0.0035	1.4832 ± 0.0043
6	1.5854 ± 0.0033	1.5344 ± 0.0041	1.4597 ± 0.0045
7	1.5591 ± 0.0044	1.5025 ± 0.0039	1.4168 ± 0.0050
Females			
2	1.4135 ± 0.0040	1.4223 ± 0.0037	1.4260 ± 0.0038
3	1.4299 ± 0.0030	1.4203 ± 0.0040	1.4066 ± 0.0036
4	1.4692 ± 0.0035	1.4466 ± 0.0028	1.4196 ± 0.0029
5	1.4774 ± 0.0033	1.4388 ± 0.0035	1.3944 ± 0.0042
6	1.4811 ± 0.0033	1.4317 ± 0.0033	1.3682 ± 0.0031
7	1.4553 ± 0.0044	1.4057 ± 0.0039	1.3341 ± 0.0037

[a]log (grams).

Appendix D. Means and standard errors of feed intake for logarithmic transformed data in selected and control feed intake lines.

Generation	log (intake ± S.E.)		
	Line IH	Line IC	Line IL
Males			
2	2.0983 ± 0.0033[a]	2.0978 ± 0.0048	2.0833 ± 0.0043
3	2.1149 ± 0.0032	2.0867 ± 0.0055	2.0950 ± 0.0034
4	2.1256 ± 0.0032	2.0940 ± 0.0043	2.0813 ± 0.0058
5	2.1374 ± 0.0043	2.0922 ± 0.0031	2.0726 ± 0.0046
6	2.0924 ± 0.0049	2.0354 ± 0.0092	2.0230 ± 0.0085
7	2.1417 ± 0.0030	2.0789 ± 0.0032	2.0572 ± 0.0037
Females			
2	2.0334 ± 0.0040	2.0270 ± 0.0043	2.0547 ± 0.0037
3	2.0485 ± 0.0024	2.0267 ± 0.0039	2.0475 ± 0.0058
4	2.0748 ± 0.0032	2.0294 ± 0.0045	2.0392 ± 0.0038
5	2.0876 ± 0.0033	2.0410 ± 0.0035	2.0246 ± 0.0031
6	2.0511 ± 0.0052	1.9758 ± 0.0092	1.9774 ± 0.0064
7	2.0830 ± 0.0033	2.0178 ± 0.0042	2.0000 ± 0.0025

[a]log (grams).

Appendix E. Phenotypic and genetic responses calculated from logarithmic transformed data.

	log ($b_{R:GEN}$ ± S.E.)		log ($b_{DR:GEN}$ ± S.E.)	
Line	Males	Females	Males	Females
CH	0.0157 ± 0.0095[a]	0.0165 ± 0.0135	0.3432 ± 0.0958*	0.4458 ± 0.1206*
CC	-0.0374 ± 0.0123*	-0.0438 ± 0.0126*	-0-	-0-
CL	-0.0806 ± 0.0109**	-0.0817 ± 0.0134**	0.1543 ± 0.0477*	0.2388 ± 0.1289
AH	0.0496 ± 0.0081**[b]	0.0367 ± 0.0112*	0.2201 ± 0.0371**	0.1935 ± 0.0478*
AC	0.0006 ± 0.0096	-0.0040 ± 0.0118	-0-	-0-
AL	-0.0425 ± 0.0049**	-0.0541 ± 0.0091**	0.1569 ± 0.0552*	0.0940 ± 0.0345
WH	0.0085 ± 0.0043[c]	0.0106 ± 0.0050	0.1321 ± 0.0198**	0.1836 ± 0.0332**
WC	-0.0007 ± 0.0052	-0.0016 ± 0.0038	-0-	-0-
WL	-0.0192 ± 0.0045*	-0.0171 ± 0.0035**	0.2937 ± 0.0703*	0.2342 ± 0.0429**
IH	0.0047 ± 0.0048[c]	0.0078 ± 0.0043	0.3046 ± 0.1200	0.1964 ± 0.0505*
IC	-0.0072 ± 0.0047	-0.0051 ± 0.0051	-0-	-0-
IL	-0.0099 ± 0.0043	-0.0143 ± 0.0034	0.0380 ± 0.0446	-0.1957 ± 0.1931

[a] log (mg / 100 ml).
[b] log (revolutions).
[c] log (grams).

Appendix F. Realized heritabilities calculated for logarithmic transformed data.

Line	Males	Females
CH	0.41 ± 0.03**	0.44 ± 0.03**
CL	0.37 ± 0.02**	0.37 ± 0.07**
AH	0.27 ± 0.03**	0.24 ± 0.09
AL	0.13 ± 0.04*	0.19 ± 0.06*
WH	0.28 ± 0.05**	0.37 ± 0.04**
WL	0.40 ± 0.05**	0.39 ± 0.02**
IH	0.41 ± 0.06**	0.44 ± 0.08**
IL	0.08 ± 0.06	0.29 ± 0.09*

*(P<.05). **(P<.01).

Appendix G. Genetic regressions of body weights on generation number in selected and control lines for data transformed to common logarithms.

Line	WT 12	WT 21	WT 42	WT 56
Males				
CH	-0.0323 ± 0.0671[a]	0.0559 ± 0.0788	0.0963 ± 0.0837	0.0983 ± 0.0869
CL	-0.0118 ± 0.0883	0.0735 ± 0.0461	0.0167 ± 0.0610	-0.0838 ± 0.1167
AH	-0.0144 ± 0.1099	-0.0698 ± 0.0606	-0.0517 ± 0.1144	-0.0759 ± 0.0578
AL	-0.0279 ± 0.0445	-0.0498 ± 0.1203	-0.0991 ± 0.0671	-0.0080 ± 0.0736
WH	0.0308 ± 0.0363	0.1495 ± 0.0927	0.1903 ± 0.0469*	0.1367 ± 0.0207**
WL	0.0790 ± 0.0958	0.0238 ± 0.0417	0.1969 ± 0.0658*	0.3219 ± 0.0861*
IH	0.1768 ± 0.0847	0.0041 ± 0.0061	0.1554 ± 0.0501*	0.1779 ± 0.0592*
IL	0.1009 ± 0.1133	-0.0060 ± 0.0037	0.1402 ± 0.0584	0.0702 ± 0.1554
Females				
CH	-0.1254 ± 0.0442*	0.0508 ± 0.0779	0.2253 ± 0.0757*	0.1256 ± 0.0296*
CL	-0.0286 ± 0.1045	-0.0219 ± 0.0960	-0.0690 ± 0.0579	-0.1330 ± 0.0233**
AH	0.0791 ± 0.0621	-0.0106 ± 0.0756	0.0663 ± 0.1203	-0.0759 ± 0.1169
AL	-0.0776 ± 0.0538	0.0848 ± 0.0885	-0.0221 ± 0.0530	-0.0678 ± 0.0944
WH	0.0410 ± 0.0699	0.0813 ± 0.0393	0.1371 ± 0.0302*	0.1830 ± 0.0307**
WL	-0.0442 ± 0.1119	0.0021 ± 0.0806	0.2288 ± 0.0377**	0.2203 ± 0.0370**
IH	0.2050 ± 0.0982	0.0060 ± 0.0054	0.2006 ± 0.0473*	0.1573 ± 0.0270**
IL	0.1158 ± 0.0774	-0.0103 ± 0.0043	0.0298 ± 0.0769	-0.0425 ± 0.0539

[a]Regression of response (selected mean deviated from control mean) on generation number.
*(P<.05). **(P<.01).

Appendix H. Means and standard errors of 12- and 21-day body weights in replicate for logarithmic transformed data.

	log (WT 12 ± S.E.)		log (WT 21 ± S.E.)	
Line	Males	Females	Males	Females
CH	0.9022 ± 0.0071[a]	0.9099 ± 0.0072	1.1419 ± 0.0089	1.1274 ± 0.0094
CC	0.9185 ± 0.0041	0.9137 ± 0.0048	1.1278 ± 0.0104	1.1002 ± 0.0107
CL	0.9338 ± 0.0534	0.9338 ± 0.0054	1.1551 ± 0.0075	1.1308 ± 0.0081
AH	0.9110 ± 0.0061	0.9092 ± 0.0055	1.1187 ± 0.0089	1.0950 ± 0.0090
AC	0.9034 ± 0.0053	0.8978 ± 0.0059	1.1129 ± 0.0105	1.0899 ± 0.0082
AL	0.8974 ± 0.0065	0.9045 ± 0.0065	1.0784 ± 0.0112	1.0768 ± 0.0125
WH	0.9201 ± 0.0035	0.9214 ± 0.0035	1.1535 ± 0.0112	1.1198 ± 0.0124
WC	0.9156 ± 0.0073	0.9105 ± 0.0077	1.1372 ± 0.0089	1.1137 ± 0.0080
WL	0.8904 ± 0.0051	0.8858 ± 0.0051	1.0978 ± 0.0073	1.0737 ± 0.0083
IH	0.9158 ± 0.0061	0.9208 ± 0.0053	1.1667 ± 0.0084	1.1533 ± 0.0069
IC	0.8884 ± 0.0089	0.8992 ± 0.0059	1.1147 ± 0.0135	1.0937 ± 0.0112
IL	0.9047 ± 0.0060	0.9137 ± 0.0057	1.1139 ± 0.0110	1.1044 ± 0.0137

[a]log (grams).

Appendix I. Means and standard errors of 42- and 56-day body weights in replicate for logarithmic transformed data.

	log (WT 42 ± S.E.)		log (WT 56 ± S.E.)	
Line	Males	Females	Males	Females
CH	1.4875 ± 0.0058[a]	1.4150 ± 0.0057	1.5239 ± 0.0057	1.4377 ± 0.0065
CC	1.4641 ± 0.0078	1.4006 ± 0.0048	1.5044 ± 0.0058	1.4159 ± 0.0053
CL	1.4765 ± 0.0050	1.3959 ± 0.0056	1.5080 ± 0.0043	1.4203 ± 0.0057
AH	1.4748 ± 0.0066	1.3919 ± 0.0060	1.4960 ± 0.0062	1.4027 ± 0.0062
AC	1.4531 ± 0.0135	1.3782 ± 0.0084	1.4871 ± 0.0100	1.3988 ± 0.0068
AL	1.4444 ± 0.0138	1.3774 ± 0.0077	1.4915 ± 0.0103	1.3955 ± 0.0066
WH	1.5295 ± 0.0099	1.4538 ± 0.0091	1.5512 ± 0.0101	1.4588 ± 0.0095
WC	1.4744 ± 0.0123	1.3910 ± 0.0108	1.5043 ± 0.0093	1.4083 ± 0.0067
WL	1.4204 ± 0.0079	1.3416 ± 0.0065	1.4487 ± 0.0083	1.3477 ± 0.0062
IH	1.5031 ± 0.0058	1.4322 ± 0.0042	1.5392 ± 0.0050	1.4424 ± 0.0050
IC	1.4577 ± 0.0071	1.3735 ± 0.0058	1.4885 ± 0.0060	1.3811 ± 0.0065
IL	1.4391 ± 0.0066	1.3681 ± 0.0075	1.4688 ± 0.0059	1.3830 ± 0.0087

[a] log (grams).

Appendix J. Means and standard errors of SC and activity scores in replicate for logarithmic transformed data.

Line	log (SC ± S.E.)		log (activity ± S.E.)	
	Males	Females	Males	Females
CH	2.2558 ± 0.0190[a]	2.1368 ± 0.0235	4.0534 ± 0.0434[b]	4.1828 ± 0.0461
CC	2.0007 ± 0.0207	1.8840 ± 0.0253	3.9423 ± 0.0654	4.0832 ± 0.0398
CL	1.8499 ± 0.0199	1.7569 ± 0.0204	4.0201 ± 0.0374	4.1017 ± 0.0386
AH	2.0327 ± 0.0239	1.9004 ± 0.0164	4.3398 ± 0.1207	4.3043 ± 0.0382
AC	1.9751 ± 0.0194	1.8459 ± 0.0216	4.0358 ± 0.0517	4.0476 ± 0.1109
AL	2.0382 ± 0.0239	1.9476 ± 0.0202	3.6247 ± 0.1245	3.6856 ± 0.1391
WH	1.9904 ± 0.0304	1.9001 ± 0.0291	4.0315 ± 0.1202	3.9169 ± 0.0977
WC	1.9690 ± 0.0269	1.8692 ± 0.0223	3.7031 ± 0.1178	3.6882 ± 0.1810
WL	1.9419 ± 0.0240	1.8284 ± 0.0213	4.2558 ± 0.0359	4.1112 ± 0.0838
IH	1.9412 ± 0.0241	1.8306 ± 0.0268	3.9773 ± 0.1029	4.1455 ± 0.0483
IC	1.9617 ± 0.0287	1.8901 ± 0.0226	3.8029 ± 0.1534	3.9503 ± 0.1078
IL	1.9740 ± 0.0208	1.8515 ± 0.0222	3.7938 ± 0.1737	4.0550 ± 0.0792

[a]log (mg / 100 ml).
[b]log (revolutions).

Appendix K. Means and standard errors of feed intake in replicate for logarithmic transformed data.

	log (intake ± S.E.)	
Line	Males	Females
CH	2.1425 ± 0.0053[a]	2.1117 ± 0.0046
CC	2.1274 ± 0.0054	2.0684 ± 0.0054
CL	2.1572 ± 0.0051	2.1030 ± 0.0043
AH	2.1486 ± 0.0049	2.1014 ± 0.0052
AC	2.1337 ± 0.0077	2.0800 ± 0.0088
AL	2.1119 ± 0.0129	2.0727 ± 0.0081
WH	2.1814 ± 0.0092	2.1379 ± 0.0109
WC	2.1386 ± 0.0110	2.0971 ± 0.0087
WL	2.0988 ± 0.0071	2.0542 ± 0.0050
IH	2.1635 ± 0.0072	2.1317 ± 0.0041
IC	2.1335 ± 0.0084	2.0594 ± 0.0046
IL	2.0920 ± 0.0042	2.0725 ± 0.0073

[a]log (grams).

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SELECTION FOR SERUM CHOLESTEROL, VOLUNTARY PHYSICAL ACTIVITY, 56-DAY BODY WEIGHT AND FEED INTAKE IN ALBINO MICE

by

Elizabeth Ann Dunnington

(ABSTRACT)

A short-term selection experiment was conducted with ICR albino mice produced by the reciprocal crossing of two lines of unselected animals which had been random-bred for 28 generations. Lines were developed by selecting for maximum and minimum serum cholesterol (SC) (lines CH and CL), voluntary physical activity (lines AH and AL), 56-day body weight (lines WH and WL) and feed intake (lines IH and IL). An unselected, random-bred control line was maintained with each pair of divergent selected lines (CC, AC, WC and IC, respectively). In the lines selected for SC, physical activity and 56-day body weight, selection was based on individual performance. Twenty-five paired matings plus five extra paired matings were used to perpetuate the lines each generation for five generations. The feed intake lines were perpetuated by within-sex, full-sib family selection with 30 paired matings per generation for five generations.

Inbreeding coefficients calculated for each line resulted in maxi-

mum inbreeding of 12% over the course of the study.

Realized heritabilities (defined as selected means deviated from control means and regressed on cumulative, effective selection differential) plus their standard errors ($h^2_R \pm$ S.E.) were: 0.31 ± 0.02, 0.33 ± 0.03, 0.34 ± 0.07 and 0.33 ± 0.14 for CH males, CH females, CL males and CL females; 0.20 ± 0.02, 0.19 ± 0.04, 0.19 ± 0.06 and 0.18 ± 0.06 for AH males, AH females, AL males and AL females; 0.26 ± 0.05, 0.34 ± 0.05, 0.40 ± 0.06 and 0.39 ± 0.03 for WH males, WH females, WL males and WL females; 0.39 ± 0.07, 0.40 ± 0.07, 0.06 ± 0.06 and 0.32 ± 0.10 for IH males, IH females, IL males and IL females, respectively.

Genetic responses (selected line generation means deviated from control line generation means and regressed on generation number) were significantly different from zero ($P<.05$) in CH males and females, CL males, AH males and females, AL males, WH males and females, WL males and females and IH females.

Within-line phenotypic correlations indicated positive relationships among body weights at various ages, between body weights and feed intake, between mature body weight and SC, and between body weights of dams and number of offspring born to those dams (excluding reproductive failures).

A replicate of the last generation of this short-term selection experiment allowed ranking of representatives from all 12 lines for 12-, 21-, 42- and 56-day body weights, SC, activity, feed intake and percentage of body moisture (PBM). Mice selected for maximum SC had lower 12- and 21-day body weights but higher 42- and 56-day body weights than

than mice selected for minimum SC. High activity mice were generally heavier than low activity mice at 12, 21 and 42 days of age but had a lower mature body weight (56 days). There was a positive correlation between mature body weight and SC. Activity was elevated in the selected lines when compared to their respective controls, for SC, 56-day body weight and feed intake lines. Selection for 56-day body weight was more successful in altering feed consumption than was direct selection for high and low levels of feed intake. PBM was greater in line AL than AH and was consistently lowest of all 12 lines in lines IC and IH.

A random sample of mice (56 males and 54 females) was maintained for 1.55 years, weighed at three-week intervals and bled for SC determination at 18-week intervals. Results showed non-significant, negative, linear regressions in SC (-0.099 ± 0.067 for males and -0.079 ± 0.085 for females) from 63 to 567 days of age. Significant, positive regressions in mature body weights (0.019 ± 0.005 for males and 0.018 ± 0.003 for females) were found over time.