SINGLE-TRAIT AND ANTAGONISTIC INDEX SELECTION FOR LITTER SIZE AND BODY WEIGHT IN MICE[1]

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ABSTRACT

Individual selection based on female performance only was conducted in four lines of mice: L+ for increased litter size, W+ for increased 6-week body weight, L$^-$W+ for a selection index aimed at decreasing litter size and increasing 6-week body weight and L+W$^-$ for a selection index aimed at increasing litter size and decreasing 6-week body weight. A fifth line (K) served as an unselected control. All litters were standardized to eight mice at one day of age. Expected heritability was based on twice the regression of offspring on dam (h^2_d), which contains additive genetic variance due to direct ($\sigma^2_{A_o}$) and maternal ($\sigma^2_{A_m}$) effects and their covariance ($\sigma_{A_oA_m}$). Responses and correlated responses were measured either deviated (method 1) or not deviated (method 2) from the control line. Realized heritabilities (h^2_R) for litter size were 0.19 ± 0.04 (1) and 0.16 ± 0.03 (2), which were similar to h^2_d of 0.17 ± 0.04. The h^2_R for 6-week body weight of 0.55 ± 0.07 (1) and 0.44 ± 0.07 (2) agreed with h^2_d of 0.42 ± 0.02. Realized genetic correlations ($r^*_{G_R}$) between litter size and 6-week body weight calculated from the double-selection experiment were 0.52 ± 0.10 (1) and 0.52 ± 0.13 (2), which were not significantly different from the base population estimate of $r^*_{G_d} = 0.63 \pm 0.14$. Divergence (L$^-$W+ minus L+W$^-$) in the antagonistic index selection lines was 0.21 ± 0.01 index units ($I = 0.305\, P_W - 0.436\, P_L$, where P_W and P_L are the phenotypic values for 6-week body weight and litter size, respectively.). The h^2_R of index units of 0.14 ± 0.02 calculated from divergence agreed with h^2_d of 0.14 ± 0.04. Divergences in litter size (—0.19 ± 0.07) and 6-week body weight (0.46 ± 0.10) were in the expected direction. Antagonistic index selection yielded about one-half the expected divergence in litter size, while divergence in 6-week body weight was only slightly less than expected. Realized genetic correlations indicated that litter size, 6-week body weight and index units each showed positive pleiotropy with 3-week body weight, postweaning gain and weight at vaginal introitus and negative pleiotropy with age at vaginal introitus. Sex ratio and several components of fitness (days from joining to parturition, percent fertile matings and percent perinatal survival) did not change significantly in the selected lines.

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LITTER size at birth and postweaning body weight or weight gain are quantitative characters that have been intensely studied in laboratory mice. Fundamental research has focused on describing the genetic architecture and the dynamics of single-trait selection (ROBERTS 1965a, 1965b; EISEN 1974, 1976a). Litter size and body weight are of immense economic importance in livestock, so that quantitative genetic studies of these traits in mice serve an important role as animal models for evaluating animal breeding selection systems. In this connection, information is needed on the extent to which litter size and body weight can be manipulated by single- and multi-trait selection.

Single-trait selection studies on litter size and body weight have been reviewed by ROBERTS (1965a, 1965b) and EISEN (1974). Selection for body weight or weight gain has generally led to positive correlated responses in litter size (MACARTHUR 1944; FALCONER 1953; FOWLER and EDWARDS 1960; RAHNEFELD *et al.* 1966; LEGATES 1969; DOOLITTLE, WILSON and HULBERT 1972; EISEN, HANRAHAN and LEGATES 1973; WILSON 1973; BAKKER 1974). An exception to these results was reported by BRADFORD (1971), who found no change in litter size following selection for increased postweaning gain. Single-trait selection for litter size has been successful (FALCONER 1955, 1963; BATEMAN 1966; BRADFORD 1968; EKLUND and BRADFORD 1977). FALCONER (1963) mentioned that lines selected for high or low litter size showed positive correlated responses in 6-week body weight. BATEMAN (1966) reported positive divergence in 11-week body weight between high and low litter size selected lines. Realized genetic correlations between litter size and body weight have not been obtained from double-selection experiments.

Selection index theory was first developed by SMITH (1936) and HAZEL (1943) as an objective method of selecting for a linear function of several traits defined as the aggregate breeding value. Theoretically, the selection index procedure maximizes the correlation between the aggregate breeding value and the index, and it is never inferior to tandem selection or independent culling levels (HAZEL and LUSH 1942; YOUNG 1961; FINNEY 1962). DOOLITTLE, WILSON and HULBERT (1972) found no differences in the response of litter size plus 3- to 6-week postweaning gain among the selection index, independent culling level and tandem selection procedures. Experimental information is lacking for those situations where the goal defined by the selection index is antagonistic to the genetic correlation between litter size and body weight.

The first objective of the present study was to determine realized heritabilities of litter size and 6-week body weight and the realized genetic correlation between the traits from single-trait selected lines. The second objective was to evaluate the efficacy of antagonistic index selection (RUTLEDGE, EISEN and LEGATES 1973; NORDSKOG *et al.* 1974) in selecting for litter size and 6-week body weight. This method of selection was treated as an example of a "desired gains" index (PESEK and BAKER 1969). Correlated selection responses for a series of traits were evaluated in each line. Preliminary results of this experiment have been reported previously (EISEN 1976b, 1977a).

MATERIALS AND METHODS

Experimental design: Mice used to form the lines in the present study were obtained from the randombred ICR population (EISEN and HANRAHAN 1974). Single-trait selection was established for increased litter size in one line (L+) and increased 6-week body weight in a second line (W+). A selection index was used in two additional lines to select simultaneously, but in opposite directions, for genetic gains in litter size and 6-week body weight. The appropriate economic weights to realize this goal were not apparent. Rather than determining economic weights, desired genetic gains in each trait were calculated first. Then the desired genetic gains index was constructed (PESEK and BAKER 1969; BAKER 1974; YAMADA, YOKOUCHI and NISHIDA 1975). The absolute value of the desired genetic gain in litter size was taken to be the predicted correlated response in litter size based on single-trait selection for 6-week body weight. In a similar manner, the absolute value of the desired genetic gain in 6-week body weight was calculated as the predicted correlated response to single-trait selection for litter size. Genetic and phenotypic parameter estimates used to construct the desired gains index were obtained from previously published data on the ICR line (HANRAHAN and EISEN 1973, 1974). The calculated desired gains index was $I = 0.305P_W - 0.436P_L$, where P_W and P_L are the phenotypic values for 6-week body weight and litter size, respectively. The desired gains index lines were designated L$^-$W+, selected for decreased litter size and increased 6-week body weight, and L+W$^-$, selected for increased litter size and decreased 6-week body weight. A randomly selected control line (K) was used to adjust for possible environmental trends. The present study includes 12 generations of selection with all lines maintained contemporaneously.

Each generation, all available females were mated in each line. Most matings involved one male and two females, but in some cases one or three females were used. Half-sib and full-sib matings were avoided. The aim was to choose the best 20 females in each selected line based on individual selection for the appropriate selection criterion. Litters from the selected females and an additional few used as reserves were kept, while all other litters were discarded.

The control line was maintained by randomly selecting one male and one female from each full-sib family. Individual selection was conducted only for females in each selected line, while males were randomly selected. This procedure resulted in a relatively mild selection intensity but, at the same time, reduced the rate of inbreeding relative to the expectation in selected lines of moderate population size (ROBERTSON 1961). Justification for this approach was based on the desire to avoid the relatively high degree of inbreeding depression for litter size reported in the ICR line (EISEN, HANRAHAN and LEGATES 1973; HAUSCHKA and MIRAND 1973). To be considered as a candidate for selection, a female had to have a score for litter size and 6-week body weight.

At eight to ten weeks of age, males were joined with females in all lines on the same day. Males were discarded after 16 days and females were caged individually and checked daily until parturition (day zero). Still-born pups were removed at this time. At one day of age, the numbers of live and dead young were recorded. Litter size was defined as the total number of pups born, and excluded litter sizes of zero due to infertile matings. The live young were sexed and litters were standardized randomly to eight pups, attempting to obtain two males and six females. Sex ratio was expressed as the percentage of males in the litter. Foster pups needed to augment a litter to eight young were obtained from litters of the same age and line. These pups were discarded at weaning. Percent perinatal survival was based on the frequencies of still-born pups on day zero and dead pups on day one. The interval between joining and parturition was recorded for each female, and the percent of fertile matings was calculated for each line. Mice were permanently identified at 12 days of age by toe-clipping. At three weeks of age, mice were weaned and randomly assigned to cages containing four mice of like sex and line. Mortality from two days to weaning was negligible. Purina Mouse Chow was fed *ad libitum* from joining of the breeders until weaning of the young, and Purina Laboratory Chow was fed *ad libitum* following weaning.

After weaning, females were checked daily for vaginal introitus. Age and weight at vaginal introitus were recorded. Age at vaginal introitus in mice is not as reliable an index of sexual maturation as age at first estrus, and is probably more closely related to overall physical maturation than to sexual maturation (Bakker, Nagai and Eisen 1977). Six-week body weight was obtained on all females and males, and postweaning gain was calculated as 6-week body weight minus 3-week body weight.

Underlying model: The genetic model assumed to control the phenotypic variation of the i^{th} trait (trait subscript is omitted for simplicity unless covariances among two traits are involved) was defined by

$$P_x = \mu + A_{o_x} + A_{m_w} + e_{m_w} + e_{o_x} ,$$

where P_x is the phenotype of individual x, μ is the mean, A_{o_x} is the additive direct genetic effect of individual x, A_{m_w} is the additive maternal genetic effect of dam w, and e_{m_w} and e_{o_x} are corresponding maternal and direct environmental effects (Willham 1963). The phenotypic variance is given by

$$\sigma^2_P = \sigma^2_{A_o} + \sigma^2_{A_m} + \sigma_{A_oA_m} + \sigma^2_C + \sigma^2_E ,$$

where $\sigma^2_{A_o}$ and $\sigma^2_{A_m}$ are additive direct and additive maternal genetic variances, respectively, $\sigma_{A_oA_m}$ is the additive direct-maternal genetic covariance, and σ^2_C and σ^2_E are maternal and direct environmental variances.

Given a second phenotype, P_y, whose dam is z, the covariance between x and y is

$$\text{Cov}(P_x, P_y) = 2r_{xy}\,\sigma^2_{A_o} + 2r_{wz}\,\sigma^2_{A_m} + 2(r_{xz} + r_{yw})\,\sigma_{A_oA_m} + k\sigma^2_C$$

where r is Malecot's coefficient of coancestry. The coefficient k was assumed to be one for individuals reared by the same dam and zero otherwise. All other possible covariances were assumed to be zero.

Estimates of genetic parameters: "Heritabilities" were estimated from the regressions of repeated records of offspring on sire or dam, pooled within generations for each line. For the i^{th} trait, the expectation of twice the regression of offspring on dam is

$$h^2_d = (\sigma^2_{A_o} + \sigma^2_{A_m} + 5/2\,\sigma_{A_oA_m})/\sigma^2_P \tag{1}$$

and the expectation of twice the regression of offspring on sire is

$$h^2_s = (\sigma^2_{A_o} + 1/2\,\sigma_{A_oA_m})/\sigma^2_P \; . \tag{2}$$

In the presence of additive direct-maternal covariance, h^2_s would overestimate or underestimate the usual definition of heritability, $h^2 = \sigma^2_{A_o}/\sigma^2_P$, depending on the sign of $\sigma_{A_oA_m}$. Since individual selection was limited to females only, h^2_d is the expectation of realized heritability (h^2_R) for the appropriate selection criterion in each line.

The "genetic" correlation between two traits was estimated from

$$r^*_G = \frac{1/2\,[\text{Cov}(P_{x_i}, P_{y_j}) + \text{Cov}(P_{x_j}, P_{y_i})]}{[\text{Cov}(P_{x_i}, P_{y_i})\,\text{Cov}(P_{x_j}, P_{y_j})]^{1/2}} \; . \tag{3}$$

The expectation of (3) for dam parents is

$$r^*_{G_d} = \frac{\sigma_{A_{o_{ij}}} + \sigma_{A_{m_{ij}}} + 5/4\,(\sigma_{A_{o_i}A_{m_j}} + \sigma_{A_{o_j}A_{m_i}})}{[(\sigma^2_{A_{o_i}} + \sigma^2_{A_{m_i}} + 5/2\,\sigma_{A_{o_i}A_{m_i}})\,(\sigma^2_{A_{o_j}} + \sigma^2_{A_{m_j}} + 5/2\,\sigma_{A_{o_j}A_{m_j}})]^{1/2}} \tag{4}$$

and the expectation for sire parents is

$$r^*_{G_s} = \frac{\sigma_{A_{o_{ij}}} + 1/4\,(\sigma_{A_{o_i}A_{m_j}} + \sigma_{A_{o_j}A_{m_i}})}{[(\sigma^2_{A_{o_i}} + 1/2\,\sigma_{A_{o_i}A_{m_i}})\,(\sigma^2_{A_{o_j}} + 1/2\,\sigma_{A_{o_j}A_{m_j}})]^{1/2}} \tag{5}$$

where the definitions of all genetic variance terms defined for the i^{th} trait are now extended to covariances between the i^{th} and j^{th} traits. By analogy to the expectation of h^2_d, $r^*_{G_R}$ is the expectation of the realized genetic correlation between litter size and 6-week body weight. Thus, the genetic correlations defined here have a different expectation from the usual definition of the genetic correlation, $r_G = \sigma_{A_{o_{ij}}}/\sigma_{A_{o_i}}\sigma_{A_{o_j}}$ (FALCONER 1960a). Phenotypic correlations (r_p) were calculated as product-moment correlations.

Because economic weights were not involved in arriving at the desired gains index, the index unit *per se* was defined as a trait, and the realized heritability of index units was used to evaluate direct response from index selection, rather than the realized response in the aggregate genotype. The heritability of index units, therefore, was defined as

$$h^2_{d_I} = \frac{b^2_i h^2_{d_i} \sigma^2_{P_i} + b^2_j h^2_{d_j} \sigma^2_{P_j} + 2b_i b_j r^*_{G_d} h_{d_i} h_{d_j} \sigma_{P_i} \sigma_{P_j}}{b^2_i \sigma^2_{P_i} + b^2_j \sigma^2_{P_j} + 2b_i b_j r_P \sigma_{P_i} \sigma_{P_j}} \tag{6}$$

where b_i is the weighting factor for the i^{th} trait in the index.

The effect of "service" sire (the male joined to a female, as opposed to the parental sire of the female) on litter size, the desired gains index, perinatal survival, sex ratio and the interval between joining and parturition was determined from the model $Y_{ijk} = \mu + t_i + v_{j(i)} + e_{ijk}$, where Y_{ijk} is the trait of the k^{th} female joined with the j^{th} service sire in the i^{th} generation, μ is the grand mean, t_i is the i^{th} generation effect, $v_{j(i)}$ is the j^{th} service sire effect and e_{ijk} is the random error; $v_{j(i)}$ and e_{ijk} were assumed to be distributed with zero means and variances σ^2_v and σ^2_e, respectively. The repeatability of service sires was calculated at $t_v = \sigma^2_v/(\sigma^2_v + \sigma^2_e)$. Subsequently, an analysis of full-sib family differences was conducted based on the model $Y_{ijk} = \mu + t_i + f_{j(i)} + w_{ijk}$, where Y_{ijk} is the trait of the k^{th} female sib in the j^{th} full-sib family in the i^{th} generation, $f_{j(i)}$ is the j^{th} full-sib family effect and w_{ijk} is the random error; $f_{j(i)}$ and w_{ijk} were assumed to be distributed with zero means and variances σ^2_f and σ^2_w, respectively. Twice the repeatability of full-sib families was calculated as $h^2_f = 2\sigma^2_f/(\sigma^2_f + \sigma^2_w)$, with expectation

$$h^2_f = (\sigma^2_{A_o} + 2\sigma^2_{A_m} + 2\sigma_{A_oA_m} + 2\sigma^2_C)/\sigma^2_P\ . \tag{7}$$

Inbreeding effects: Individual inbreeding coefficients were calculated from pedigrees to determine the rate of inbreeding within each line. The inbreeding coefficients of all individuals in generation zero were arbitrarily set to zero. Regressions of individual performance on inbreeding coefficients were calculated within generations for sex-limited traits and within generation-sex subclasses for body weights and postweaning gain. This analysis was limited to generations 4 to 12, since earlier generations had accumulated little inbreeding.

Analysis of response to selection: Generation means for each trait were taken as a deviation from the control line mean. Genetic change in each trait was calculated as the regression of the generation mean deviation on generation number. Realized heritability was calculated as direct response in the selection criterion regressed on cumulative selection differential (FALCONER 1960a). Standard errors of the direct and correlated responses and the realized heritabilities were based on formulas presented by HILL (1972a, 1972b). Realized genetic correlations were estimated using the following formulas (RUTLEDGE, EISEN and LEGATES 1973):

$$r^*_{G_R} = (b^*_{G_{ij}} b^*_{G_{ji}})^{1/2} , \tag{8}$$

$$r^*_{G_R} = b^*_{G_{ij}} (h_{d_j} \sigma_{P_j} / h_{d_i} \sigma_{P_i}) \tag{9}$$

where $b^*_{G_{ij}}$ is the realized genetic regression of correlated response in trait i on direct response in trait j. Values of h_d used in (9) were based on realized heritabilities for litter size and 6-week body weight and on formula (1) for the remaining traits, whereas values of σ_P were calculated from the pooled within-generation phenotypic variances in line K. Standard errors of $r^*_{G_R}$ were based on formulas given by HILL (1971).

RESULTS

Estimates of genetic and phenotypic parameters: Means, phenotypic variances and coefficients of variation in the control (K) line are presented in Table 1. These statistics are in general agreement for traits previously reported in the ICR base population (EISEN and HANRAHAN 1974).

Estimates of h^2_d, calculated from formula (1), are presented in Table 2. There was considerable variation among lines in the estimates of h^2_d for some traits. However, the fluctuations do not appear to be associated with any systematic effect of selection. Since the offspring-dam regression coefficients were not biased by selection and the relatively low intensity of selection applied in each line was not expected to cause a significant reduction in genetic variance, the line estimates of h^2_d were pooled for each trait. The heritability of the selection criterion (h^2_d) used in the present study was greater for 6-week body weight (0.42 ± 0.02) than for either litter size (0.17 ± 0.04) or selection index units (0.14 ± 0.04). The estimate of h^2_d for 3-week body weight was also large (0.42 ± 0.02), while

TABLE 1

Means, phenotypic variances and coefficients of variation in the control (K) line†

Trait	Sample size	Mean	Phenotypic variance	Coef. of variation
6-week body wt (g)‡	2302	27.96	5.77	8.59
Litter size	1238	12.47	5.51	18.82
Index units	1238	2.26	1.09	46.19
3-week body wt (g)‡	2302	13.57	3.10	12.97
Postweaning gain (g)‡	2302	14.35	4.00	13.93
Vaginal introitus age (d)	1587	25.93	10.30	12.38
Vaginal introitus wt (g)	1587	16.65	5.25	13.76
Perinatal survival (%)	1238	98.44	28.15	5.39
Sex ratio (%)	1238	50.68	217.64	29.10
Joining to parturition (d)	1238	21.50	2.37	11.02
Fertile matings (%)	1306	95.91	1.98	2.06

† Pooled within generations.
‡ Adjusted to a midsex equivalent.

TABLE 2

Estimates of twice the regression of offspring on dam (h_d^2 ± *S.E.*) *and twice the regression of offspring on sire* (h_s^2 ± *S.E.*)†

Trait	Line					
	K	L^+	W^+	L^-W^+	L^+W^-	Pooled‡
			h_d^2 ± S.E.			
6-week body wt (g)	0.37 ± 0.05	0.41 ± 0.05	0.41 ± 0.09	0.46 ± 0.05	0.45 ± 0.04	0.42 ± 0.02
Litter size	0.09 ± 0.07	0.14 ± 0.14	0.17 ± 0.06	0.18 ± 0.09	0.31 ± 0.09	0.17 ± 0.04
Index units	0.09 ± 0.07	0.34 ± 0.10	0.08 ± 0.06	0.15 ± 0.10	0.38 ± 0.16	0.14 ± 0.04
3-week body wt (g)	0.45 ± 0.05	0.42 ± 0.05	0.18 ± 0.06	0.50 ± 0.05	0.46 ± 0.04	0.42 ± 0.02
Postweaning gain (g)	0.28 ± 0.05	0.27 ± 0.04	0.27 ± 0.06	0.14 ± 0.05	0.27 ± 0.04	0.25 ± 0.02
Vaginal introitus age (d)	0.29 ± 0.05	0.24 ± 0.05	0.48 ± 0.05	0.18 ± 0.06	0.09 ± 0.04	0.24 ± 0.02
Vaginal introitus wt (g)	0.28 ± 0.06	0.15 ± 0.05	0.25 ± 0.05	0.29 ± 0.06	0.27 ± 0.04	0.25 ± 0.02
Perinatal survival (%)	—0.02 ± 0.08	—0.02 ± 0.06	—0.02 ± 0.14	0.10 ± 0.10	0.09 ± 0.06	0.03 ± 0.03
Sex ratio (%)	—0.04 ± 0.06	0.01 ± 0.07	—0.09 ± 0.07	—0.11 ± 0.06	0.00 ± 0.07	—0.05 ± 0.03
Joining to parturition (d)	0.07 ± 0.07	0.03 ± 0.05	0.04 ± 0.06	0.04 ± 0.07	0.06 ± 0.05	0.05 ± 0.03
			h_s^2 ± S.E.			
6-week body wt (g)	0.13 ± 0.04	0.14 ± 0.04	0.16 ± 0.04	0.35 ± 0.04	0.33 ± 0.04	0.22 ± 0.02
3-week body wt (g)	0.06 ± 0.04	0.09 ± 0.04	0.10 ± 0.05	0.14 ± 0.05	0.21 ± 0.04	0.12 ± 0.02
Postweaning gain (g)	0.12 ± 0.04	0.07 ± 0.04	0.20 ± 0.04	0.29 ± 0.04	0.23 ± 0.04	0.18 ± 0.02

† Pooled within generations. Number of offspring-parent pairs per line varied as follows: 3- and 6-week body weight and postweaning gain (2156 to 2361), age and weight at vaginal introitus (1404 to 1814) and remaining traits (1148 to 1289).

‡ Pooled over lines by using the weighted average, where the weighting factor was the reciprocal of the variance of each estimate.

TABLE 3

The intraclass correlation among service sires (t_v ± *S.E.*) *and twice the intraclass correlation among full-sib families* (h_f^2 ± *S.E.*)†

Trait	Line					
	K	L+	W+	L-W+	L+W-	Pooled‡
			t_v ± S.E.			
Litter size	0.10 ± 0.04	0.13 ± 0.04	0.06 ± 0.04	0.07 ± 0.04	0.12 ± 0.03	0.10 ± 0.02
Index units	0.09 ± 0.04	0.09 ± 0.04	—0.05 ± 0.04	0.08 ± 0.04	0.11 ± 0.03	0.08 ± 0.02
Perinatal survival	0.02 ± 0.04	0.01 ± 0.04	0.00 ± 0.04	—0.02 ± 0.04	0.06 ± 0.03	0.02 ± 0.02
Sex ratio	—0.02 ± 0.04	0.05 ± 0.04	0.06 ± 0.04	0.08 ± 0.04	—0.02 ± 0.03	0.03 ± 0.02
Joining to parturition	0.11 ± 0.04	0.19 ± 0.04	0.12 ± 0.04	0.17 ± 0.04	0.08 ± 0.03	0.13 ± 0.02
			h_f^2 ± S.E.			
Litter size	0.11 ± 0.04	0.11 ± 0.04	0.08 ± 0.03	0.17 ± 0.04	0.10 ± 0.03	0.11 ± 0.02
Index units	0.16 ± 0.04	0.19 ± 0.04	0.16 ± 0.04	0.21 ± 0.05	0.20 ± 0.04	0.18 ± 0.02
Perinatal survival	0.12 ± 0.04	0.13 ± 0.04	0.11 ± 0.04	0.04 ± 0.04	0.12 ± 0.04	0.10 ± 0.02
Sex ratio	—0.01 ± 0.03	—0.02 ± 0.03	0.00 ± 0.03	0.08 ± 0.04	0.00 ± 0.03	0.00 ± 0.01
Joining to parturition	—0.07 ± 0.02	—0.02 ± 0.03	—0.03 ± 0.03	0.04 ± 0.04	0.03 ± 0.03	—0.02 ± 0.01

† Pooled within generations. Df among full sib families varied from 251 to 273 for each line and df among service sires varied from 551 to 603 for each line.

‡ Pooled over lines by using the weighted average, where the weighting factor was the reciprocal of the variance of each estimate.

estimates for postweaning gain and age and weight at vaginal opening were intermediate. Perinatal survival, sex ratio and interval from joining to parturition yielded h_d^2 estimates that were not significantly different from zero $(P > 0.05)$.

Twice the regression of offspring on sire (h_s^2) estimated for 3- and 6-week body weight and postweaning gain were less than comparable estimates of h_d^2. This result was anticipated because additive maternal genetic effects are known to influence these traits (HANRAHAN and EISEN 1973). The h_s^2 values probably are underestimates of h^2 since $\sigma_{A_oA_m} < 0$ for these traits (HANRAHAN and EISEN 1973).

The analysis of service sire effects, pooled over lines, indicates that service sires accounted for a significant $(P < 0.01)$ amount of variation in litter size, index units and interval from joining to parturition (Table 3). The service sire effect on index units must be manifested through litter size because 6-week body weight of the female is uncorrelated with the service sire chosen. Service sire effects were not significant for perinatal survival and sex ratio.

Intraclass correlations among full-sib families have been multiplied by two (Table 3). Litter size, index units and perinatal survival yielded pooled estimates of h_f^2 significantly $(P < 0.01)$ different from zero. The consistently higher estimates for index units relative to litter size were due to the influence of the large additive direct maternal component influencing the 6-week body weight portion of index units. Dominance variance was assumed to be zero in the full-sib analysis. It is, of course, not possible to test the validity of this assumption in the present data. Dominance variance may have contributed to the significant $(P < 0.01)$ estimate of h_f^2 for perinatal survival, considering that the pooled estimate of h_d^2 for this trait was only 0.03 ± 0.03. The absence of significant estimates of h_f^2 for sex ratio and interval from joining to parturition, coupled with the low estimates of h_d^2, suggests that total genetic variance for these traits is extremely small, if not zero, when measured as a trait of the dam.

Estimates of genetic correlations varied considerably among lines. This may have been due to the greater sensitivity of genetic covariances than genetic variances to the effects of selection (BOHREN, HILL and ROBERTSON 1966). In addition, there was evidence, to be presented in a later section, that the phenotypic relationship between litter size and 6-week body weight changed with selection in some of the lines. For these reasons, genetic and phenotypic correlations are given for the control line only (Table 4). Genetic correlations involving perinatal survival, sex ratio and interval from joining to parturition were assumed to be zero because estimates of h_d^2 for these traits were relatively small and did not differ significantly from zero in the control line and the pooled analysis. The phenotypic correlations involving these traits were generally small and not considered important.

Genetic and phenotypic correlations for a given pair of traits generally had the same sign. Pairs of traits that could be measured in both sexes (3- and 6-week body weight and postweaning gain) had genetic correlations of similar magni-

TABLE 4

Genetic correlations estimated from offspring-dam pairs ($r^*_{G_d}$) *and offspring-sire pairs* ($r^*_{G_s}$) *and phenotypic correlations* (r_p) *in the control (K) line*†

Trait	1	2	3	4	5	6	7	8	9
1 6-week body wt	—	0.63 ± 0.14	0.63 ± 0.14	(0.65 ± 0.05) 0.67 ± 0.05	(0.79 ± 0.02) 0.71 ± 0.05	—0.59 ± 0.07	0.06 ± 0.12	—	—
2 Litter size	0.27	—	—0.30 ± 0.20	0.54 ± 0.15	0.11 ± 0.26	—0.59 ± 0.07	—0.06 ± 0.12	—	—
3 Index units	0.33	—0.82	—	0.04 ± 0.21	0.79 ± 0.10	—0.11 ± 0.25	0.11 ± 0.28	—	—
4 3-week body wt	0.60	0.23	0.12	—	(0.04 ± 0.10) 0.12 ± 0.10	—0.50 ± 0.07	0.37 ± 0.09	—	—
5 Postweaning gain	0.68	0.12	0.29	—0.22	—	—0.29 ± 0.11	—0.31 ± 0.13	—	—
6 Vaginal introitus age	—0.31	—0.12	—0.06	—0.42	0.00	—	0.62 ± 0.08	—	—
7 Vaginal introitus wt	0.19	0.06	0.06	0.27	—0.02	0.66	—	—	—
8 Perinatal survival	0.10	0.02	0.04	0.14	—0.01	—0.05	0.06	—	—
9 Sex ratio	—0.01	—0.02	0.01	—0.03	0.01	0.05	0.05	—0.02	—
10 Joining to parturition	—0.01	0.09	—0.09	—0.01	0.00	0.02	0.02	0.00	—0.05

† Genetic correlations ($r^*_{G_s}$, $r^*_{G_d}$) pooled within generations are above the diagonal, with estimates of $r^*_{G_s}$ given in parentheses. Approximate standard errors of the genetic correlations are given by FALCONER (1960a). Genetic correlations ($r^*_{G_d}$) involving perinatal survival, sex ratio and joining to parturition were assumed to be zero because h^2_d values for these traits were not significantly different from zero. Phenotypic correlations (r_p) pooled within generations are below the diagonal; $r_p \geq |0.06|$ is significant at $P < 0.05$ and $r_p \geq |0.07|$ is significant at $P < 0.01$.

tude when estimated from progeny-dam pairs ($r^*_{G_d}$) or progeny-sire pairs ($r^*_{G_s}$), and they agreed with paternal half-sib estimates (r_G) (HANRAHAN and EISEN 1973; EISEN 1977b). The genetic correlation between litter size and 6-week body weight (0.63 ± 0.14) was higher than the phenotypic correlation (0.27; $P < 0.01$). Index units were genetically positively correlated with 6-week body weight and postweaning gain and negatively correlated with litter size, which agrees with the definition of the index. The genetic correlation between 6-week body weight and age at vaginal introitus was negative. Litter size was genetically positively correlated with 3-week body weight and to a lesser degree with postweaning gain, but negatively correlated with age at vaginal introitus. There was a negative genetic correlation between 3-week body weight and age at vaginal introitus, whereas the correlation between 3-week body weight and weight at vaginal introitus was positive. Postweaning gain was negatively correlated with age and weight at vaginal opening, while age and weight at vaginal opening were positively correlated.

Selection differentials and inbreeding: The summary of data on population size, selection intensity and inbreeding coefficients is presented in Table 5. Mean number of females scored per generation was less in L^-W^+ compared to the other lines because fewer females were available from selected litters. Mean numbers of sires and dams were close to the intended value of 20 for each sex. A comparison of cumulative selection differentials weighted and unweighted by the number of progeny reaching six weeks of age revealed negligible differences for the four selected lines, so that only the latter selection differentials are presented. The close agreement between the weighted and unweighted values suggests that natural selection played a negligible role in the selected lines. The

TABLE 5

Summary of data on population size, selection intensity and inbreeding in each line

	Line				
Item	L^+	W^+	L^-W^+	L^+W^-	K
Males scored/gen.	45.3	47.8	63.8	48.4	54.4
Females scored/gen.	101.8	100.4	88.5	105.3	97.4
Sires/gen.	17.6	19.3	17.8	17.8	18.7
Dams/gen.	20.4	20.3	21.8	20.4	20.4
Cum. sel. diff.	20.25†	16.97‡	9.39§	—8.49§	——
Sel. intensity/gen. (i)	0.61	0.67	0.62	—0.61	——
Sec. sel. int. (litter size)/gen.	——	0.14	—0.52	0.47	——
Sec. sel. int. (6-week body wt)/gen.	0.18	——	0.24	—0.25	——
Cum. inbreeding coef. F_{12} (%)	11.03	11.61	10.55	11.63	9.51
Effective size—N_e‖	51.6	48.8	54.1	48.8	60.3

† Litter size.
‡ 6-week body wt (g).
§ Index units.
‖ Calculated from $\bar{F}_{12} = 1 - (1 - \Delta F)^{12}$ where $\Delta F = \frac{1}{2N_e}$.

TABLE 6

Regression coefficient ± S.E. of traits on individual inbreeding coefficients†,‡

Trait	Line				
	L^+	W^+	L^-W^+	L^+W^-	K
6-week body wt (g)	—0.039 ± 0.031	—0.019 ± 0.024	0.031 ± 0.030	—0.076 ± 0.028**	0.009 ± 0.036
Litter size	0.091 ± 0.051	0.039 ± 0.038	0.034 ± 0.046	—0.003 ± 0.036	0.053 ± 0.048
Index units	—0.058 ± 0.024*	—0.018 ± 0.018	—0.001 ± 0.020	—0.006 ± 0.017	—0.021 ± 0.022
3-week body wt (g)	—0.071 ± 0.019**	—0.005 ± 0.017	0.019 ± 0.020	0.039 ± 0.020*	0.043 ± 0.025
Postweaning gain (g)	—0.031 ± 0.025	—0.014 ± 0.021	0.012 ± 0.024	—0.111 ± 0.023**	—0.034 ± 0.031
Vaginal introitus age (d)	0.094 ± 0.054	—0.003 ± 0.036	—0.013 ± 0.048	—0.016 ± 0.051	—0.144 ± 0.071*
Vaginal introitus wt (g)	—0.056 ± 0.042	0.029 ± 0.032	—0.004 ± 0.040	—0.003 ± 0.035	—0.065 ± 0.045
Perinatal survival (%)	0.000 ± 0.001	—0.001 ± 0.001	0.001 ± 0.001	—0.001 ± 0.001	0.000 ± 0.001
Sex ratio (%)	0.000 ± 0.002	0.001 ± 0.002	—0.001 ± 0.002	0.000 ± 0.002	—0.003 ± 0.003
Joining to parturition (d)	—0.033 ± 0.052	0.025 ± 0.041	0.078 ± 0.049	0.007 ± 0.040	0.048 ± 0.047

* $P < 0.05$.

** $P < 0.01$.

† Pooled within generations for sex limited traits and within generation by sex subclasses for other traits, using data from generations four to 12. Degrees of freedom for sex-limited (other) traits are: 918 (1401) for L^+, 893 (1386) for W^+, 771 (1410) for L^-W^+, 938 (1392) for L^+W^- and 846 (1394) for K.

‡ Regression coefficients are expressed per one percent increase in inbreeding coefficient.

cumulative selection differential for the desired gains index was higher in L$^-$W$^+$ than in L$^+$W$^-$, which was due to a larger variance of index units in the former line. The absolute values of the standardized selection differentials (i) were similar for the four lines. The absolute values of the secondary selection intensities in the index lines were about twice as great for litter size as for 6-week body weight. The intended ratio of absolute index weights of litter size to 6-week body weight was 1/0.70. The realized ratios of index weights (Dickerson *et al.* 1954) were —1/0.80 and 1/—0.76 for L$^-$W$^+$ and L$^+$W$^-$, respectively, indicating that slightly less relative weight was placed on litter size than was intended. The mean cumulative inbreeding coefficient ($\bar{F}_{12}$) at generation 12, calculated from pedigrees, was slightly less in the K line compared with the selected lines. Effective population size was highest in line K and lowest in the W$^+$ and L$^+$W$^-$ lines.

Regression coefficients of each trait on individual inbreeding coefficients are given in Table 6. There were several significant effects due to inbreeding depression, but no systematic trends. Previous studies have indicate that litter size is sensitive to inbreeding depression (Roberts 1960). Also, perinatal survival had a suggestion of dominance variance in the present study and, therefore, might be expected to show a decline with inbreeding. Yet, neither trait exhibited a decline in the mean at the levels of inbreeding reached in the five lines. Falconer

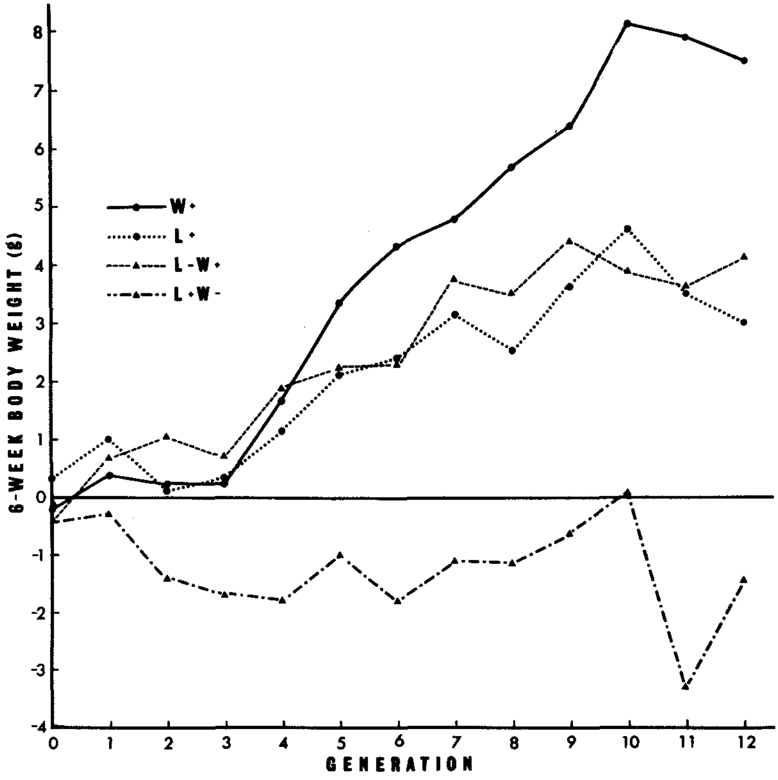

Figure 1.—Generation mean deviations for 6-week body weight.

(1960b) noted no reduction in litter size in an outbred stock that had accumulated inbreeding slowly over 31 generations. None of the traits evinced a significant effect of inbreeding in the W+ and L-W+ lines, and only age at vaginal introitus declined significantly in the K line. Index units and 3-week body weight exhibited a significant decline due to inbreeding in L+, whereas 3-week body weight increased ($P < 0.05$) and 6-week body weight and postweaning gain decreased ($P < 0.01$) in L+W-. Inbreeding effects were not considered to be an important factor in the present study, and no attempt was made to adjust generation means for inbreeding effects.

Single-trait selection: Generation mean deviations for 6-week body weight and litter size are plotted in Figures 1 and 2, respectively, and linear regression coefficients of each trait on generation number are given in Table 7. No significant nonlinear effects were found, although it appears that there was a lag of several generations before selection responses were clearly apparent. The K line declined ($P < 0.05$) in 6-week body weight and had a nonsignificant decline in litter size. Possible causes of the generation trend are inbreeding depression, unintended selection pressure, random genetic drift or environmental effects peculiar to the laboratory. Six-week body weight showed no inbreeding depression (Table 6) and the cumulative selection differential was negligible (—0.62 *g*).

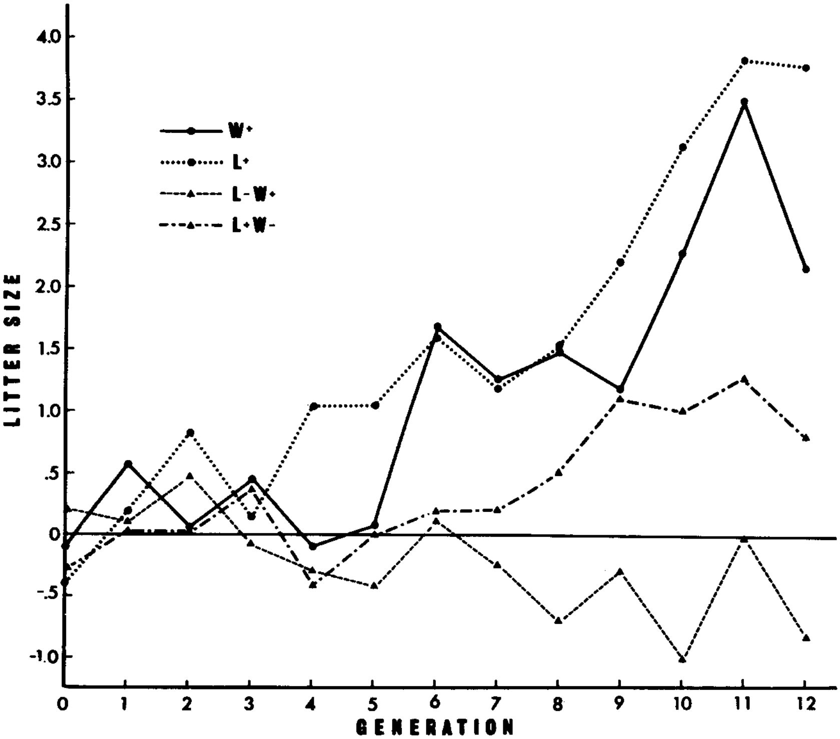

FIGURE 2.—Generation mean deviations for litter size.

TABLE 7

Regression coefficients ± S.E. of responses in 6-week body weight, litter size and index units on generation number, realized heritabilities, drift and error variances and sampling erors of realized heritabilities†

Item	Line					
	L^+	W^+	L^-W^+	L^+W^-	Divergence‡	K
6-week body wt response (g)	0.33 ± 0.10**	0.78 ± 0.09**	0.39 ± 0.04**	—0.06 ± 0.09	0.46 ± 0.10**	—
	0.18 ± 0.08*	0.62 ± 0.10**	0.24 ± 0.10*	—0.22 ± 0.10*	—	—0.15 ± 0.07*
Litter size response	0.33 ± 0.09**	0.24 ± 0.07**	—0.08 ± 0.03*	0.12 ± 0.05*	—0.19 ± 0.07*	—
	0.28 ± 0.06**	0.19 ± 0.07*	—0.13 ± 0.05*	0.06 ± 0.05	—	—0.05 ± 0.04
Index units response	—0.05 ± 0.02*	0.11 ± 0.03**	0.15 ± 0.03**	—0.06 ± 0.02*	0.21 ± 0.01**	—
	—0.06 ± 0.02*	0.09 ± 0.02**	0.13 ± 0.02**	—0.08 ± 0.02**	—	—0.02 ± 0.02
Realized heritability (h_R^2)§	0.19 ± 0.04**	0.55 ± 0.07**	0.19 ± 0.04**	0.09 ± 0.03*	0.14 ± 0.02**	
	0.16 ± 0.03**	0.44 ± 0.07**	0.16 ± 0.03**	0.12 ± 0.03**	—	
Drift variance§	42.51	82.51	7.83	3.86	7.37	
($\times 10^3$)	19.79	37.28	3.69	2.83	—	
Error variance§	12.63	3.84	2.59	2.33	2.60	
($\times 10^2$)	34.73	11.78	2.99	3.72	—	
Biased variance of h_R^2§	3.67	17.46	3.87	4.43	0.81	
($\times 10^4$)	6.89	33.71	2.71	3.94	—	
Nearly unbiased variance of h_R^2§	13.23	42.42	14.44	9.00	3.61	
($\times 10^4$)	11.49	51.39	8.27	8.59	—	

* $P < 0.05$.

** $P < 0.01$.

† Upper values are based on deviations from control (K) line means (method 1) and lower values are based on actual generation means (method 2).

‡ L^-W^+ minus L^+W^-.

§ Refers to litter size for $L+$, 6- week body weight for $W+$, and index units for L^-W+, $L+W^-$ and divergence, respectively. Nearly unbiased variance of h_R^2 obtained by methods of HILL (1972a,b). Error and drift variances were calculated by modification of formulas (18) in HILL (1972b), as required.

Over t generations, the expected drift variance ($\sigma^2_{d_t}$) was approximated by $t\,\sigma^2_A/N_e$, where σ^2_A = additive genetic variance and N_e = effective population size (HILL 1972c). In the present study, σ^2_A for 6-week body weight was defined as the regression of offspring on midparent (0.32) times the phenotypic variance $(5.77) = 1.85$, $N_e = 60.3$ and $\sigma_{d_{12}} = 0.61$. Thus, the trend in the control line was three times the standard deviation expected in generation 12 from genetic drift alone (*i.e.*, 3 × 0.61). It is still not possible from the present design to determine if the reduction in 6-week body weight was due to genetic drift or to an environmental trend in the laboratory, or both. Since the decline in 6-week body weight might be large enough to affect the magnitude of the realized responses, regression coefficients were calculated on the actual generation means (method 2) of the selected lines for purposes of comparison with generation mean deviations from the control line (method 1).

The realized direct response in litter size in the L+ line was significant ($P < 0.01$) for both methods, amounting to an increase of about 0.3 pups per generation or a total response of 1.5 phenotypic standard deviations. Both methods 1 and 2 yielded similar realized heritabilities (0.19 ± 0.04 and 0.16 ± 0.03), which agreed with the pooled estimate of h^2_d (0.17 ± 0.04). Correlated response in 6-week body weight was significant, but obviously reduced when estimated by method 2. A large ($P < 0.01$) direct response in 6-week body weight of 0.6 to 0.8 grams per generation, depending on the method used to estimate response, was observed in the W+ line. The cumulative response was 3.1 to 3.9 phenotypic standard deviations. The realized heritabilities of 6-week body weight were 0.55 ± 0.07 and 0.44 ± 0.07 as calculated by methods 1 and 2, respectively, which were not significantly different from the pooled base population estimate of 0.42 ± 0.02. Correlated responses in litter size in W+ were 0.24 ± 0.07 ($P < 0.01$) and 0.19 ± 0.07 ($P < 0.05$) pups per generation by methods 1 and 2, respectively. The nearly unbiased variances of h^2_R (HILL 1972a, 1972b) for litter size and 6-week body weight were always larger than the variances of the regression coefficients calculated by least squares. Drift variances were larger than error variances except in the case of litter size calculated by method 2.

The realized genetic correlations between litter size and 6-week body weight calculated by (8) were 0.52 ± 0.10 (method 1) and 0.52 ± 0.13 (method 2). Using formula (9), $r^*_{G_R}$ was 0.50 ± 0.10 (method 1) and 0.46 ± 0.13 (method 2) in the L+ line and 0.53 ± 0.10 (method 1) and 0.59 ±0.12 (method 2) in the W+ line. There was no effect of the method used on the realized genetic correlations. The $r^*_{G_R}$ values showed no asymmetry when estimated from L+ and W+ separately. The realized genetic correlation was not significantly different from the base population estimate ($r^*_{G_d} = 0.63 \pm 0.14$). HANRAHAN and EISEN (1974) obtained a paternal half-sib genetic correlation estimate of 0.36 from the ICR base population.

The realized genetic regressions of litter size on 6-week body weight obtained by methods 1 and 2 were 0.31 ± 0.05 and 0.34 ± 0.04 pups per gram, respec-

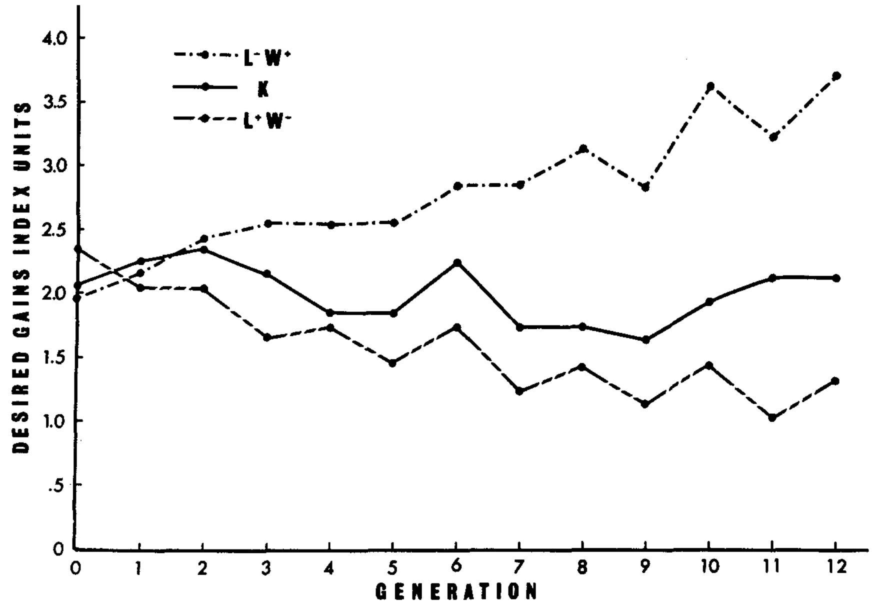

FIGURE 3.—Generation means in desired gains index units.

tively, which was not significantly different from the estimate in the control line of 0.36 ± 0.08. The phenotypic regression of litter size on 6-week body weight was 0.31 ± 0.03 pups per gram.

Antagonistic index selection: Figure 3 gives generation means for the desired gains index. The regression coefficient of index units on generation number was not significant in the control line (Table 7). The desired gains index showed significant responses in the intended direction for L^-W^+ and L^+W^- when calculated by either method 1 or 2. The L^-W^+ line exhibited a greater index response than did L^+W^-. The divergence between the index selected lines was 0.21 ± 0.01 index units per generation for a cumulative divergence of 2.4 phenotypic standard deviation units. The realized heritabilities of index units calculated by method 1 were 0.19 ± 0.04 and 0.09 ± 0.03 in the L^-W^+ and L^+W^- lines, respectively, and the corresponding realized heritabilities calculated by method 2 were 0.16 ± 0.03 and 0.12 ± 0.03. The results suggest a greater h^2_R in index units in the L^-W^+ line, particularly when calculated by method 1. Realized heritability obtained by divergence was 0.14 ± 0.02, which is identical to the pooled estimate of 0.14 ± 0.04 obtained from daughter-dam regression. The heritability of index units based on paternal half-sib covariance in the ICR base population was 0.26 ± 0.12. The nearly unbiased variances of h^2_R (HILL 1972a,b) were consistently larger than the usual least-squares variances.

Generation mean deviations in the index lines for 6-week body weight and litter size are plotted in Figures 1 and 2, respectively. Divergence in 6-week body weight was 0.46 ± 0.10 g. The regressions of 6-week body weight on generation number calculated by method 1 showed an asymmetric correlated response. The

L^-W^+ line exhibited an increased 6-week body weight of 0.39 g per generation ($P < 0.01$), but 6-week body weight declined in the L^+W^- line by only −0.06 g per generation ($P > 0.05$). However, it is clear from Figure 1 that after generation two, 6-week body weight in L^+W^- was consistently below the control line, except in generation ten. Omitting generation ten from the analysis yielded a regression of 6-week body weight on generation number of −0.11 g ($P > 0.05$). The correlated responses in 6-week body weight presented a different picture when calculated by method 2. The absolute values of the regressions were very similar; 0.24 ± 0.10 g for L^-W^+ and −0.22 ± 0.10 g for L^+W^-, so that no asymmetry in the correlated response was apparent using this procedure.

The correlated response in litter size was −0.19 ± 0.07 when calculated by divergence. Litter size showed significant ($P < 0.05$) correlated responses in the intended direction in both index lines when calculated by method 1. In contrast, correlated responses in litter size obtained by method 2 were about twice as great in L^-W^+ (−0.13 ± 0.05) as in L^+W^- (0.06 ± 0.05).

The desired gains index was based on heritabilities of 0.45 for 6-week body weight, 0.28 for litter size and a genetic correlation of 0.45. Considering the realized genetic parameters obtained from the present single-trait selection study, only the heritability of litter size appeared to be overestimated. Based on the desired gains index, the absolute values of expected correlated responses per unit selection intensity were 0.42 g for 6-week body weight and 0.38 for litter size. These can be compared with realized correlated responses per unit selection intensity in the present study:

Trait	Single-trait selection	L^-W^+	L^+W^-	½(Divergence)
6-week body wt	0.52±0.16, 0.29±0.13, 0.41	0.63±0.07, 0.39±0.16, 0.51	−0.10±0.15, −0.36±0.16, −0.23	0.37±0.08
Litter size	0.36±0.11, 0.28±0.11, 0.32	−0.13±0.05, −0.21±0.10, −0.17	0.20±0.08, 0.10±0.08, 0.15	−0.16±0.06

where the first, second and third values in columns 2 to 4 were based on method 1, method 2 and the mean of both, respectively. For the single-trait correlated responses, 6-week body weight is in agreement with expectation, and if the heritability of litter size is adjusted downward, the expectation for the correlated response in litter size also was realized. The expected correlated response in 6-week body weight in the index lines appears to have been realized if method 2 or divergence are used as criteria. However, the correlated response in litter size was only about one-half its expected value.

Realized genetic correlations involving index units with litter size and 6-week body weight were calculated by method 1 and formulas (8) and (9). Divergence between L^-W^+ and L^+W^- was used in all cases. The realized genetic correlations between index units and litter size were −0.39 ± 0.13, based on the double-selection method [formula (8)], −0.39 ± 0.13 based on the correlated response for index units in L^+ [formula (9)] and −0.38 ± 0.13, based on the correlated divergence for litter size in the index lines [formula (9)]. The corresponding values calculated for $r^*_{G_R}$ between index units and 6-week body weight were

TABLE 8

Regression coefficients ± S.E. of selection differentials and phenotypic statistics on generation number

Item	Line				
	L^+	W^+	L^-W^+	L^+W^-	K
Selection differential†	0.083 ± 0.033*	0.055 ± 0.034	0.038 ± 0.015*	0.023 ± 0.015	—
Phenotypic variance					
6-week body wt (g^2)	—0.10 ± 0.08	0.07 ± 0.09	0.14 ± 0.10	0.05 ± 0.11	—0.19 ± 0.05**
Litter size	0.28 ± 0.13*	0.35 ± 0.08**	0.27 ± 0.12*	0.03 ± 0.13	—0.15 ± 0.09
Index units (×10)	—	—	0.62 ± 0.25*	0.15 ± 0.29	—0.19 ± 0.15
Coef. of variation (%)					
6-week body wt	—0.14 ± 0.06*	—0.10 ± 0.23	0.03 ± 0.07	0.12 ± 0.11	—0.12 ± 0.05*
Litter size	—0.04 ± 0.22	0.20 ± 0.17	0.64 ± 0.20**	—0.06 ± 0.19	—0.19 ± 0.15
Phenotypic regression (×10)‡	—0.21 ± 0.10*	—0.26 ± 0.11*	0.06 ± 0.07	—0.09 ± 0.07	—0.07 ± 0.08
Phenotypic correlation (×10)§	—0 23 ± 0.06**	—0.26 ± 0.10*	0.05 ± 0.05	—0.05 ± 0.07	—0.08 ± 0.09

* $P < 0.05$.
** $P < 0.01$.
† Litter size for $L+$, 6-week body weight for $W+$, and index units for L^-W+ and $L+W^-$.
‡ Regression of litter size on 6-week body weight.
§ Correlation between litter size and 6-week body weight.

0.54 ± 0.11, 0.64 ± 0.10 and 0.46 ± 0.14. The values of $r^*_{G_R}$ are in agreement with estimates of $r^*_{G_d}$ of -0.30 ± 0.20 between index units and litter size and 0.63 ± 0.14 between index units and 6-week body weight obtained in the control line.

Trends in selection differentials and other statistics: Regression coefficients of selection differentials and phenotypic statistics on generation number are given in Table 8. The selection differentials for litter size in L^+ and index units in L^-W^+ increased significantly ($P < 0.05$), which likely was due to the increased ($P < 0.05$) phenotypic variances for these respective traits in L^+ and L^-W^+. The phenotypic variance and coefficient of variation of 6-week body weight decreased significantly in the K line, while the coefficient of variation in 6-week body weight declined in L^+. Phenotypic variance of litter size increased in L^+, W^+ and L^-W^+. This could be explained by a scaling effect in L^+ and W^+ due to the increase in mean litter size, since the coefficients of variation for litter size were not altered. However, the increased phenotypic variance of litter size in

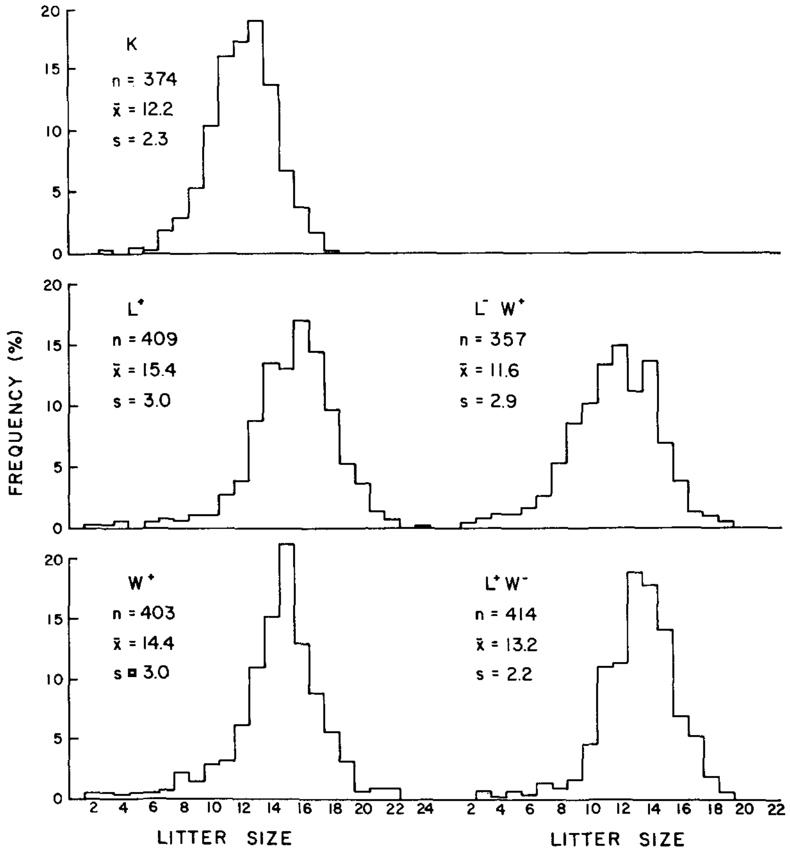

FIGURE 4.—Relative frequency distributions of litter size pooled over generations 9 to 12.

L^-W^+ may be a true indication of increased variability, since the coefficient of variation also showed a positive trend.

Relative frequency distributions of litter size pooled over generations 9 to 12 are presented in Figure 4. The distributions emphasize the changes in mean and variance observed in each line. The distribution of litter size for each line, adjusted for generation effects, differed significantly ($P < 0.01$) from a normal distribution, as determined by the Kolmogrov test. Significant ($P < 0.01$) negative skewness was detected in all selected lines, but not in the control line. Kurtosis was significant ($P < 0.01$) in all lines except for L^-W^+. The kurtosis appeared to be due to an excess of litter sizes at the center of the distributions.

The L^+ and W^+ lines showed a decline ($P < 0.05$) in the phenotypic regression of litter size on 6-week body weight and the corresponding phenotypic correlation whereas the index lines and the control line showed no change in these statistics (Table 8). The pooled within generation regressions of 6-week body weight on litter size were 0.20 ± 0.04, 0.20 ± 0.04, 0.28 ± 0.04, 0.26 ± 0.03 and 0.31 ± 0.03 (all $P < 0.01$) in the L^+, W^+, L^-W^+, L^+W^- and K lines, respectively. The data from generations 9 to 12 were pooled in the L^+ and W^+ line, and regressions of 0.046 ± 0.065 ($df = 404$, $P > 0.05$) and 0.026 ± 0.070 ($df = 398$, $P > 0.05$) were obtained with no significant quadratic terms.

Correlated responses to selection: Selection can result in changes in unselected traits as a result of pleiotropic effects. Correlated responses for a series of traits are presented as regression coefficients of response on generation number (Table 9). The control (K) line decreased ($P < 0.05$) in postweaning gain and increased ($P < 0.05$) in perinatal survival. Thus, the decline noted earlier in 6-week body weight of the K line was due to a decrease in postweaning gain and not 3-week body weight. Therefore, the correlated response in postweaning gain also was expressed as both a deviation from control line means (method 1) and not deviated from the control line (method 2). Correlated responses in all other traits were expressed as deviations from control.

There were significant positive correlated responses in 3-week body weight and postweaning gain (method 1) in the L^+ line. Significant positive correlated responses in the W^+ line were found for 3-week body weight, postweaning gain (methods 1 and 2) and weight at vaginal introitus, whereas a negative correlated response was obtained for age at vaginal introitus. The L^-W^+ line increased significantly in 3-week body weight, postweaning gain (method 1) and weight at vaginal introitus, while decreasing in age at vaginal introitus. The L^+W^- line decreased significantly in postweaning gain (method 2) and weight at vaginal introitus. There were no significant correlated responses in perinatal survival, sex ratio, interval from joining to parturition and percent of fertile matings in any of the selected lines.

Realized genetic correlations ($r^*_{G_R}$) involving the selected traits, litter size, 6-week body weight and index units, with several other traits were calculated from formula (9) (Table 10). Realized genetic correlations involving the selected traits with perinatal survival and interval from joining to parturition were not

TABLE 9

Regression coefficients ± S.E. of correlated traits on generation number

Trait	Line				
	L^+	W^+	L^-W^+	L^+W^-	K
3-week body wt (g)	0.11 ± 0.04*	0.39 ± 0.06**	0.15 ± 0.07*	—0.09 ± 0.07	0.03 ± 0.04
Postweaning gain (g)					
Method 1	0.22 ± 0.05**	0.39 ± 0.07**	0.24 ± 0.06**	0.03 ± 0.06	—
Method 2	0.04 ± 0.05	0.21 ± 0.07*	0.06 ± 0.08	—0.15 ± 0.07*	—0.17 ± 0.06*
Vaginal introitus age (d)	—0.09 ± 0.09	—0.30 ± 0.10*	—0.19 ± 0.09*	—0.06 ± 0.09	0.07 ± 0.10
Vaginal introitus wt (g)	0.10 ± 0.06	0.19 ± 0.07*	0.09 ± 0.04*	—0.13 ± 0.05*	0.01 ± 0.09
Perinatal survival (%)	0.05 ± 0.06	—0.09 ± 0.08	—0.17 ± 0.09	—0.17 ± 0.09	0.14 ± 0.06*
Sex ratio (%)	0.12 ± 0.15	0.30 ± 0.17	0.17 ± 0.16	0.20 ± 0.16	—0.26 ± 0.15
Joining to parturition (d)	0.05 ± 0.06	0.05 ± 0.07	0.05 ± 0.07	0.14 ± 0.07	—0.02 ± 0.02
Fertile matings (%)	—0.31 ± 0.23	—0.14 ± 0.41	0.26 ± 0.26	—0.31 ± 0.24	0.22 ± 0.18

* $P < 0.05$.
** $P < 0.01$.

TABLE 10

Realized genetic correlations ($r^*_{G_R}$) ± *S.E. between correlated traits and litter size, 6-week body weight and index units*

Trait	Trait†		
	Litter size	6-week body wt	Index units
3-week body wt	0.23 ± 0.08*	0.75 ± 0.05**	0.38 ± 0.05**
Postweaning gain			
Method 1	0.59 ± 0.08**	0.89 ± 0.04**	0.37 ± 0.07**
Method 2	0.37 ± 0.10**	0.73 ± 0.08**	—
Vaginal introitus age	—0.10 ± 0.10	—0.45 ± 0.09**	—0.11 ± 0.08
Vaginal introitus wt	0.27 ± 0.10*	0.30 ± 0.09**	0.34 ± 0.07**
Perinatal survival	—0.09 ± 0.32	—0.17 ± 0.29	0.04 ± 0.28
Joining to parturition	0.39 ± 0.24	0.36 ± 0.21	0.34 ± 0.20

* $P < 0.05$.
** $P < 0.01$.
† Calculated from correlated responses in the L+ line for litter size, the W+ line for 6-week body weight and divergence (L-W+ minus L+W-) for index units.

significant, in agreement with estimates of $r^*_{G_d}$. The realized genetic correlations involving sex ratio with the selected traits were assumed to be zero because the estimate of h^2_d for sex ratio was less than zero.

The realized genetic correlation between litter size and 3-week body weight was 0.23 ± 0.08, which was smaller than, but not significantly different from, the base population estimate of 0.54 ± 0.15. The realized genetic correlations between postweaning gain and litter size were 0.59 ± 0.08 and 0.37 ± 0.10 (methods 1 and 2, respectively), which were not significantly larger than the estimate of 0.11 ± 0.26 obtained from $r^*_{G_d}$. Litter size and age at vaginal introitus had an $r^*_{G_R}$ of —0.10 ± 0.10, which was smaller than the $r^*_{G_d}$ estimate of —0.59 ± 0.07. The realized genetic correlation between litter size and weight at vaginal introitus was positive (0.27 ± 0.10) in contrast to a small negative (—0.06 ± 0.12) base population estimate.

Realized genetic correlations of 6-week body weight with 3-week body weight, postweaning gain, and age and weight at vaginal opening were in fairly close agreement with $r^*_{G_d}$ estimates. The realized genetic correlation between index units and 3-week body weight of 0.38 ± 0.05 was larger than the $r^*_{G_d}$ estimate (0.04 ± 0.21), and the opposite was found for index units and postweaning gain (0.37 ± 0.07 *vs.* 0.79 ± 0.10). The realized genetic correlations of index units with age or weight at vaginal introitus agree in sign with estimates of $r^*_{G_d}$.

DISCUSSION

Response to individual selection within a population can be predicted from estimates of the fractions of additive direct and additive maternal genetic variances in addition to additive direct-maternal genetic covariances. Fractions of additive by additive epistatic variances can also influence selection response (GRIFFING 1960), but these were assumed to be negligible in the present study. Since phenotypes were tested under only a single set of environmental conditions, any genotype by environment interactions that might affect the estimates of genetic parameters and selection responses cannot be detected. Inbreeding depression can have an effect on fitness traits such as litter size (ROBERTS 1960). However, FALCONER (1960b) found that a slow accumulation of inbreeding due to restricted population size had little effect on litter size, in agreement with the present results. Genetic drift and inbreeding depression may reduce realized direct and correlated responses and selection limits from that expected based on large sample theory (ROBERTSON 1960, 1961; BOHREN 1975). This theoretical expectation has been verified experimentally in several studies (JONES, FRANKHAM and BARKER 1968; FRANKHAM, JONES and BARKER 1968; HANRAHAN, EISEN and LEGATES 1973; EISEN, HANRAHAN and LEGATES 1973; EISEN 1975). Thus, individual selection in the present study was designed to be conducted with a reasonably large effective population size (N_e) of about 50. The range of N_e in the selected lines was 48.8 to 54.1. Even though the control line had an N_e of 60.3, there was a significant decline in 6-week body weight in this line. Inbreeding depression and unintentional selection were found not to be likely causes for this trend. While inconclusive, the trend appeared to be due to a combination of genetic drift and environmental effects in the laboratory.

Increased selection intensity can reduce effective population size (ROBERTSON 1961). Since it was desirable for purposes of interpretation of realized genetic parameters to have similar and large effective population sizes in all selected lines, and since one of the key traits in this study was litter size, a sex-limited trait, it was decided to select only on the basis of female performance in each line and to select males randomly. It was felt that the disadvantage of the reduced selection intensity was more than offset by the minimal level of inbreeding expected. The results indicated that the effects of inbreeding on traits in the selected lines were negligible and could reasonably be ignored in interpretation of the data. An additional advantage of following a similar selection procedure in all lines is that the coefficients of the genetic variances and covariances in the realized responses are identical for all traits. This is particularly important when maternal genetic effects are involved, as they were in the present study.

Selection for litter size, postweaning body weight or an index involving these traits presents several specific problems. If litter size is not standardized shortly after parturition, a negative environmental maternal effect results such that individuals born and reared in large litters tend to be smaller at time of mating and hence have smaller litters, and *vice versa* (FALCONER 1955, 1963). Standardizing litter size at five days of age eliminated the negative maternal effect (EISEN 1970). Other environmental factors that affect body weight, such as age or parity, are positively associated with ovulation rate, a component of litter size in mice (KENNEDY and KENNEDY 1972). Based on these observations from the literature, it was decided to standardize litters to eight mice at one day of age.

Realized heritabilities and genetic correlations obtained in this selection study pertain only to litters standardized to eight mice.

A second difficulty peculiar to litter size concerns the assumption that the service sire has no effect on litter size. It was observed that the service sire accounted for 6% to 13% of the variance in litter size. Previous studies indicated that the service sire had no effect on litter size (Falconer 1955; Bateman 1966; Hanrahan and Eisen 1974), yet others reported significant service-sire effects (Falconer 1960b; Finn 1964; Schilling, North and Bogart 1968). The variance due to service sires did not appear to be large enough to bias seriously realized genetic parameters.

Single-trait selection: Realized genetic parameters in the single-trait selected lines were in excellent agreement with base population estimates. Individual selection was used without any detrimental effects due to inbreeding. The realized heritabilities of litter size were 0.19 ± 0.04 and 0.16 ± 0.03 by methods 1 and 2, respectively, in agreement with the pooled estimate of 0.17 ± 0.04 calculated by daughter-dam regression. In an earlier study with the ICR population, Hanrahan and Eisen (1974) reported a comparable daughter-dam regression estimate of heritability (0.23 ± 0.08); it was also found that $\sigma^2_{A_m} \doteq -\sigma_{A_oA_m}$. This may help explain the relatively low full-sib estimate of heritability (0.11 ± 0.02) since $\sigma^2_{A_m}$ and $\sigma_{A_oA_m}$ would be cancelled out. The low estimate of h^2_f also suggests that neither common environmental variance (σ^2_C) nor dominance variance were particularly important for litter size in the ICR population. Falconer (1963) reported similar findings, whereas others reported that dominance and/or common environmental variance were important (Rahnefeld, Boylan and Comstock 1962; Miller, Legates and Cockerham 1963). Bowman (1962) was unable to exploit any nonadditive variance for litter size by means of recurrent selection. The absence of detectable nonadditive variance for litter size in several cases, together with clear evidence of heterosis and inbreeding depression (Roberts 1960; McCarthy 1965), presents somewhat of an enigma, as pointed out by Roberts (1965b). Additive genetic variance for ovulation rate, a major component of litter size, is sizeable (Land and Falconer 1969; Land 1970). Therefore, nonadditive genetic effects in litter size may be due to embryo mortality. The extremely high mean litter size in the ICR population may make detection of nonadditive genetic variance difficult.

Realized heritability for increased litter size at birth in the present experiment was similar to other studies: 0.15 (Falconer 1960b), 0.13 ± 0.07, 0.22 ± 0.06, 0.25 ± 0.08 (Bradford 1968), 0.17 ± 0.09, 0.03 ± 0.04 (Doolittle, Wilson and Hulbert 1972), 0.16 ± 0.06 (Eklund and Bradford 1977) and 0.13 ± 0.01 (Bakker, Wallinga and Politiek 1978). Bateman (1966) reported a divergence of 5.6 ± 0.4 pups between lines selected for high and low litter size at birth. Selection for increased litter size at weaning yielded no significant response (Dalton and Bywater 1963). The conclusion is clear that additive genetic variability in litter size at birth is sufficiently large in mice to yield significant genetic progress. Comparing the various selection studies, there is no evidence that the realized heritability of litter size at birth is affected by standardizing litter size to a constant number, as was done in our experiment or partially as in Bradford's (1968) study. However, since no litter size selection studies have been done concurrently with standardized and unstandardized litters, this conclusion remains tentative.

The significant decline in body weight of the control line indicates the necessity of caution in interpreting the responses and correlated responses in 6-week body weight. As an alternative to using deviations from control, responses in 6-week body weight were calculated ignoring the control. The respective realized heritabilities of 0.55 ± 0.07 and 0.44 ± 0.07 were not sufficiently different to cause too much concern, and agree with the daughter-dam regression heritability of 0.42 ± 0.02. The realized heritability was generally higher than previous values for postweaning body weights or gains (Roberts 1965a; Eisen 1974). Individual selection was based on female performance only, so that the expected heritability includes additive maternal genetic variance and additive direct-maternal genetic covariance in addition to additive direct genetic variance. It is not possible to say what the relative contribution of each component has been to the total response. However, the close agreement between h^2_R and h^2_d suggests that $\sigma^2_{A_m}$ contributed to the high realized heritability.

The realized genetic correlations between litter size and 6-week body weight of 0.52 ± 0.10 (method 1) and 0.52 ± 0.13 (method 2) obtained from the double selection experiment were similar to the base population estimate of 0.63 ± 0.14. No asymmetry of the realized genetic correlation was detected, nor was there any significant effect of method 1 *vs.* 2 on the realized genetic correlation. Land (1970) found a realized genetic correlation of 0.4 between body weight and natural ovulation rate in mice. The realized genetic regression of natural ovulation rate on body weight of approximately 0.4 eggs per gram (Land 1970) was similar to the realized genetic regression of litter size on 6-week body weight obtained herein (0.31 ± 0.05, 0.34 ± 0.04 by methods 1 and 2, respectively). The similarity of both $r^*_{G_R}$ and $b^*_{G_{ij}}$ for body weight and natural ovulation rate with body weight and litter size is not surprising since ovulation rate is a major component of litter size. The evidence is clear that there exists a number of segregating loci in the ICR line that exhibit positive pleiotropy for litter size and body weight. However, the reduction of the phenotypic correlation between litter size and 6-week body weight in the later generations of selection in the L+ and W+ lines indicates that many of these positive pleiotropic loci may be approaching fixation for the desirable allele. Similar effects of selection for ovulation rate were reported on the phenotypic regression of ovulation rate on body weight (Land 1970).

Selection for litter size in unstandardized litters yielded a negligible realized genetic correlation between litter size and 8-week body weight (Bakker, Wallinga and Politiek 1978). These authors attributed the lack of a correlated response in body weight to the failure of standardizing litters and thus removing the environmental maternal effect causing the negative regression of daughter's body weight on mother's litter size (FALCONER 1963). This regression was not significant ($P > 0.05$) in the L+ and W+ lines (0.009 ± 0.043 and 0.033 ± 0.022 grams per pup, respectively) and should not mask the expression of positive pleiotropic loci influencing body weight and litter size.

Antagonistic index selection: Bi-directional selection, using the desired gains index, yielded significant divergence in index units (0.21 ± 0.01) and virtually the same realized heritability of index units (0.14 ± 0.01) as twice the regression of daughter on dam (0.14 ± 0.04). Divergence in litter size (-0.19 ± 0.07) and 6-week body weight (0.46 ± 0.10) was in the expected direction. Index unit response was slightly asymmetric, with L^-W^+ showing the greater response. The interpretation of results in the index lines is partly dependent on whether or not deviations from control are used. Based on method 1, L^-W^+ resulted in a greater selection response in the desired gains index and 6-week body weight than did selection for L^+W^-. However, using method 2 yielded similar absolute responses for 6-week body weight and reduced the apparent asymmetry in index units. A similar difficulty arises when considering litter size. Using divergence as the criterion, the response in litter size is about one-half its expected value, while the response in 6-week body weight was slightly less than expected.

Several factors could be responsible for a realized response lower than that predicted for the components of the selection index. Incorrect estimates of base population genetic parameters are a possible explanation (HARRIS 1963). BOHREN, HILL and ROBERTSON (1966) demonstrated that the genetic covariance between two traits is subject to asymmetry due to change in gene frequency, and asymmetry in correlated responses would be prevalent. They concluded that prediction of correlated responses would be valid over fewer cycles of selection than it would for direct response. The influence of multi-trait selection on the genetic covariance between traits may cause similar difficulties in predicting the correlated responses in component traits of a selection index. The antagonistic selection index further complicates the situation since physiological or anatomical incompatibilities between traits can be introduced after a few generations of selection. EISEN (1977a) reviewed other antagonistic selection index experiments where realized genetic gains in the component traits differed from expectation (RUTLEDGE, EISEN and LEGATES 1973; NORDSKOG *et al.* 1974; BERGER and HARVEY 1975; MOLL, STUBER and HANSON 1975). The discrepancy between realized and expected response has been attributed to maternal effects involving preweaning gain and postweaning body weight in mice (BERGER and HARVEY 1975) and to a nonlinear relationship between yield and ear height in corn (MOLL, STUBER and HANSON 1975). Neither maternal effects nor nonlinearity appear to be an explanation in the present study. Studies involving antagonistic selection have demonstrated reasonable success in Tribolium (BELL and BURRIS 1973), Drosophila (SHERIDAN and BARKER 1974) and tobacco (MATZINGER, COCKERHAM and WERNSMAN 1977).

Correlated responses: In agreement with previous studies (see reviews by EISEN 1974, 1976a), selection for 6-week body weight yielded positive realized genetic correlations with postweaning gain and 3-week weight. The realized genetic correlations of litter size with 3-week body weight and postweaning gain were also positive but of a lower magnitude, which was expected because of the positive genetic correlation between litter size and 6-week body weight. Positive realized genetic correlations between litter size and postweaning gain have been found by DOOLITTLE, WILSON and HULBERT (1972), WILSON (1973) and EISEN (1975). The positive realized genetic correlations of index units with 3-week body weight and postweaning gain were again expected because of the positive genetic correlation between index units and 6-week body weight.

The negative realized genetic correlation between age at vaginal opening and 6-week body weight and the positive realized genetic correlation between weight at vaginal opening and 6-week body weight are in agreement with the study by BAKKER, NAGAI and EISEN (1977). Selection for litter size and the index did not yield a significant reduction in age at vaginal opening, though weight at vaginal opening was increased. The decrease in age at vaginal opening due to selection for 6-week body weight suggests an acceleration in overall development, but not necessarily earlier puberty. BAKKER, NAGAI and EISEN (1977) reported that one line selected for increased 6-week body weight had a nonsignificantly earlier age at first estrus, while a line selected for increased postweaning gain had a nonsignificantly later age at first estrus. The phenotypic correlation between age at vaginal opening and age at first estrus was only 0.23.

Sex ratio did not exhibit a significant correlated response to selection in any of the lines. The genetic variance in sex ratio was essentially zero. FALCONER (1954) found no response to selection for high or low sex ratio and no evidence of any genetic variation in sex ratio.

Correlated responses may occur in characters even though they are not correlated genetically with the selected trait, because they form a component of fitness (LERNER 1954). Perinatal survival, interval from joining to parturition and percent fertile matings are considered to be traits of this type. None of these fitness related traits evinced any decline in the selected lines. The relatively mild selection pressure coupled with a fairly large effective population size probably contributed to the avoidance of any measurable decline in fitness.

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