

# EFFECTS OF POPULATION SIZE AND SELECTION INTENSITY ON CORRELATED RESPONSES TO SELECTION FOR POSTWEANING GAIN IN MICE<sup>1</sup>

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## ABSTRACT

Correlated responses to selection for postweaning gain in mice were studied to determine the influence of population size and selection intensity. Correlated traits measured were three-, six- and eight-week body weights, litter size, twelve-day litter weight, proportion infertile matings and two indexes of reproductive performance. In general, the results agreed with observations made on direct response: correlated responses in the body weight traits and litter size increased as (1) selection intensity increased and (2) effective population size increased. Correlated responses in the body weight traits and litter size were positive in the large population size lines (16 pairs), as expected from the positive genetic correlation between these traits and postweaning gain. However, several negative correlated responses were observed at small population sizes (one and two pairs). Within each level of selection intensity, traits generally associated with fitness tended to decline most in the very small populations (one and two pairs) and in the large populations (16 pairs) for apparently different reasons. The fitness decline at the small effective population sizes was attributable to inbreeding depression. In contrast, it was postulated that the fitness decline at the large effective population size was due to selection moving the population mean for body weight and a trait positively correlated genetically with body weight (i.e., percent body fat) away from an optimum.

RECENT studies have focused on the effects of population size and selection intensity on direct response to selection for a quantitative character. Smaller effective population sizes tend to decrease selection response and realized heritability, and to increase replicate variability (TANTAWY 1956; FRANKHAM, JONES and BARKER 1968; RUMBALL and RAE 1968; HANRAHAN, EISEN and LEGATES 1973). These observations may be partly attributed, at the locus level, to genetic drift (KERR and WRIGHT 1954; ROBERTSON 1960, 1961). Reduced selection intensities invariably yield decreased selection response per generation (CLAYTON, MORRIS and ROBERTSON 1957; FRANKHAM, JONES and BARKER 1968; HANRAHAN, EISEN and LEGATES 1973), as expected from large sample selection theory.

Little information is available regarding the effects of population size and

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selection intensity on correlated responses to selection. The present study considers influences of these factors on several correlated traits, where selection was practiced for increased postweaning gain in mice (HANRAHAN, EISEN and LEGATES 1973).

MATERIALS AND METHODS

The ICR base population of mice used in the present experiment has been described by HANRAHAN and EISEN (1973). The design of the selection experiment for postweaning gain (six-minus three-week body weight) reported by HANRAHAN, EISEN and LEGATES (1973) is given in Table 1. Selection was practiced exclusively within full-sib families for fourteen generations. Pair-matings were made at random at eight to ten weeks of age except that full-sib matings were avoided where possible. Females were placed in separate cages sixteen days after exposure to males. Litters were standardized to eight mice (4♂:4♀) whenever possible at day five postpartum. Litters with less than eight young were augmented by foster mice of the same line and age. Mice were weaned at three weeks of age, at which time foster young were discarded. Further details of the experimental design are given by HANRAHAN, EISEN and LEGATES (1973).

Correlated traits measured were individual body weights at three, six and eight weeks of age, litter size (number of live young born per litter), twelve-day litter weight and proportion infertile matings. Body weights were recorded to the nearest 0.1 g. In addition, two indexes of reproductive performance were calculated each generation to determine changes in overall fitness at the various selection intensity-population size combinations. Although a direct measure of total fitness is difficult to define, a useful indicator is mean litter size per mating. This was defined as Index-1 = (1 - p<sub>1</sub>)  $\bar{L}$ , where p<sub>1</sub> equals proportion of infertile matings and  $\bar{L}$  equals mean litter size for the particular generation and line. The ability of the dam to maintain a well-nourished litter also may be considered a useful component of fitness. Since litter size was standardized to eight young in the present study, it need not be considered further. Thus the second measure of fitness was defined as Index-2 = (1 - p<sub>1</sub> - p<sub>2</sub>)  $\bar{W}$ , where p<sub>2</sub> = proportion of dams losing their entire litter prior to day twelve postpartum and  $\bar{W}$  = mean twelve-day litter weight.

HANRAHAN, EISEN and LEGATES (1973) have given formulas for the expected direct response to within-family selection in the presence of maternal effects and a genetic correlation less than unity between additive genetic effects in males and females. The expected correlated response in the j<sup>th</sup> sex of trait X due to within-family selection for trait Y is

$$\Delta G_{x_j,y} = \frac{1}{4} i_j [h_{x_o_j} h_{y_o_1} r_{x_o_j y_o_1} + h_{x_m_j} h_{y_o_1} r_{x_m_j y_o_1} + h_{x_o_j} h_{y_o_2} r_{x_o_j y_o_2} + h_{x_m_j} h_{y_o_2} r_{x_m_j y_o_2}] \sigma_{p_x} K_j,$$

TABLE 1

Design of the selection experiment

Population size*	Number of replicates for each selection intensity†	Selection intensity codes‡		
		Control (C)	Intermediate (I)	Maximum (M)
1	16	C1	I1	M1
2	8	C2	I2	M2
4	4	C4	I4	M4
8	2	C8	I8	M8
16	2	C16	I16	M16

\* Population size is expressed as the number of pairs of selected parents mated each generation.  
 † Replicate lines within treatments are referred to as, for example, M16-1, M16-2. The replicate designation is omitted when data are pooled and reference is then made to the M16 line.  
 ‡ Selection intensities of 100% (C), 50% (I) and 25% (M).

where

$h_{k_s}^2$  = heritability of  $s$  effects in the  $k^{\text{th}}$  trait of the  $j^{\text{th}}$  sex;  $s$  = direct ( $o$ ) or maternal ( $m$ ) effects,  $k$  = trait  $X$  or  $Y$  and  $j$  = males (1) or females (2),

$r_{x_s y_{s'j}}$  = genetic correlation between the  $s$  effects in trait  $X$  of the  $j^{\text{th}}$  sex and the  $s'$  effects in trait  $Y$  of the  $j^{\text{th}}$  sex,

$\sigma_{p_x j}$  = phenotypic standard deviation for trait  $X$  in the  $j^{\text{th}}$  sex,

$\bar{i}_j$  = standardized selection differential in the  $j^{\text{th}}$  sex,

$K_j = \sqrt{(n_j - 1) / n_j (1 - t_{x_j})}$ ,  $n_j$  is progeny number and  $t_{x_j}$  is the intraclass correlation among full sibs of the  $j^{\text{th}}$  sex for trait  $X$ .

Assuming that  $r_{x_o j y_{o j'}}$  are equal for all  $j, j' = 1, 2$  and similarly for  $r_{x_m j y_{o j'}}$ , the response becomes

$$\Delta G_{x_j y} = \frac{1}{4} \bar{i}_j (h_{x_o j} r_{x_o j y_{o j'}} + h_{x_m j} r_{x_m j y_{o j'}}) (h_{y_{o_1}} + h_{y_{o_2}}) \sigma_{p_x j} K_j.$$

The estimated genetic parameters in the ICR base population (HANRAHAN and EISEN 1973) are presented in Table 2. These values were substituted into the above formula to predict the correlated selection responses.

RESULTS

*Correlated responses in body weight:* The regressions of correlated responses on generations of selection, expressed as a deviation from the mean of the two control line replicates of the largest population size (C16), are presented in Table 3 for three-, six- and eight-week body weights. Plots of male generation mean deviations for three- and six-week body weights for several of the selected lines are given in Figure 1. The observed correlated responses were generally similar between the sexes for each body weight trait. As expected, significantly ( $P < .01$ ) greater correlated responses were observed in the maximum selection intensity lines (M) than in the intermediate intensity lines (I) of the same population size.

Correlated responses decreased as population size decreased, when comparisons are made within levels of selection intensity. The selection differential for postweaning gain did not differ sufficiently among the various population sizes (HANRAHAN, EISEN and LEGATES 1973) to account for this result. Since the correlated responses were measured as a deviation from the C16 reference line, the trends reflect the additional effect of inbreeding depression and possibly genetic drift. Correlated responses in the one- and two-pair lines are biased since

TABLE 2

*Estimates of genetic parameters\* and predicted correlated responses†*

Trait	$h_{y_{o_1}}^2$	$h_{y_{o_2}}^2$	$h_{y_{m_1}}^2$	$h_{y_{m_2}}^2$	$r_{x_o j y_{o j'}}$	$r_{x_m j y_{o j'}}$	$\Delta G_{x.y}$
Postweaning gain (g)	0.29	0.38	—	—	—	—	—
three-week weight (g)	0.34	0.45	0.27	0.06	— .04	0.20	0.06
six-week weight (g)	0.39	0.51	0.75	0.31	0.65	— .08	0.33
eight-week weight (g)	0.44	0.51	0.13	0.01	0.83	— .63	0.38
Litter size	—	0.28	—	0.14	0.74	— .64	0.11

\* Parameters are defined in the text.

† Predicted mean correlated response per generation of males and females in the M lines. Predicted correlated responses in the I lines are slightly less than one-half of the values shown.

TABLE 3

*Regressions of correlated responses, expressed as deviations from C16, on generation number (g) for the body weight traits, pooled over replicates†*

Line	Three-week weight		Six-week weight		Eight-week weight	
	Male	Female	Male	Female	Male	Female
I1	— .31**	— .26**	— .33**	— .23**	— .31**	— .23**
I2	— .13**	— .15**	— .06	— .06	— .04	— .01
I4	— .04	— .01	0.10*	0.12**	0.15**	0.15**
I8	0.09**	0.08*	0.25**	0.22**	0.30**	0.23**
I16	0.04	0.04	0.35**	0.35**	0.39**	0.39**
M1	— .05	— .01	0.23*	0.33**	0.23*	0.32**
M2	— .07	— .07	0.14*	0.25**	0.27**	0.34**
M4	0.02	0.06	0.40**	0.39**	0.45**	0.41**
M8	0.12*	0.16**	0.41**	0.41**	0.53**	0.49**
M16	0.13**	0.14**	0.69**	0.67**	0.80**	0.77**

\* P < .05, \*\* P < .01.

† Regression coefficients for I1, M1, I2 and M2 in this and subsequent tables are biased because of extinction of replicates.

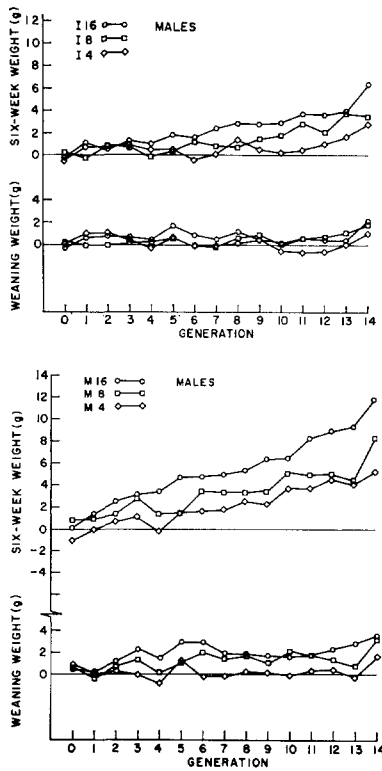


FIGURE 1.—Correlated responses of three- and six-week body weights to selection for increased postweaning gain, expressed as a deviation from the C16 line means.

TABLE 4

*Pooled regressions of correlated responses on cumulative selection differentials in postweaning gain, pooled over replicates*

Line	Three-week weight		Six-week weight		Eight-week weight	
	Male	Female	Male	Female	Male	Female
I1	— .28**	— .27**	— .23*	— .22**	— .19*	— .19*
I2	— .02	— .06	0.24**	0.15**	0.34**	0.25**
I4	0.13**	0.15**	0.37**	0.29**	0.45**	0.35**
I8	0.34**	0.32**	0.66**	0.51**	0.76**	0.57**
I16	0.22**	0.18**	0.70**	0.58**	0.77**	0.66**
M1	— .01	0.01	0.28**	0.30**	0.26**	0.30**
M2	0.13**	0.11**	0.35**	0.33**	0.46**	0.42**
M4	0.12**	0.13**	0.44**	0.38**	0.50**	0.41**
M8	0.18**	0.19**	0.43**	0.35**	0.51**	0.42**
M16	0.16**	0.15**	0.54**	0.48**	0.62**	0.56**

\*  $P < .05$ , \*\*  $P < .01$ .

several replicates became extinct during the course of the experiment. However, even with the omission of these lines, a lowered correlated response was noted as population size decreased.

The predicted correlated responses in the body weight traits were compared with the observed responses in the M16 and I16 lines, where the influence of genetic drift should be minimal. The observed correlated responses for each trait were consistently greater than the predicted values. The importance of this outcome is difficult to evaluate because of the large sampling errors of the predicted values.

Correlated responses in the body weight traits were regressed on the cumulative selection differentials for postweaning gain, according to the method of RICHARDSON, KOJIMA and LUCAS (1968). This procedure permits simultaneous estimates of genetic trends in correlated responses per unit selection differential of the primary trait, adjusted for environmental effects. These regression coefficients, pooled over replicates, are presented in Table 4. The analyses of variance (Table 5) indicated a significant increase of the correlated responses per unit selection differential in all three traits as population size increased. This trend tended to be quadratic. On the average, no significant effect of selection intensity on the correlated responses was observed. However, significant interactions between population size and selection intensity were present, with M exceeding I intensity at small population sizes and *vice versa* at larger sizes. The interpretation of this interaction has been discussed previously since it was observed for the direct response in postweaning gain (HANRAHAN, EISEN and LEGATES 1973).

The analyses of variance to test for homogeneity of correlated responses among replicates is given in Table 6. Considerable heterogeneity of replicate responses occurred. The replicate variability was comparable to that observed for the primary trait (HANRAHAN, EISEN and LEGATES 1973).

*Correlated responses in litter traits:* Regressions of litter size at birth and

TABLE 5

*Effect of population size and selection intensity on correlated responses per unit primary selection differential*

Source	d.f.	Three-week weight		Mean squares Six-week weight		Eight-week weight	
		Male	Female	Male	Female	Male	Female
Population size (P)	4						
Linear (PL)	1	333.06**	632.74**	909.62**	1366.20**	711.03**	1573.67**
Quadratic (QL)	1	153.21**	141.91**	141.43*	32.65	324.48**	63.16*
Selection intensity (I vs M)	1	25.79	8.17	11.11	3.37	0.95	1.12
P × (I vs M)	4						
PL × (I vs M)	1	871.68**	194.34**	2157.47**	455.17**	2385.93**	436.96**
PQ × (I vs M)	1	27.29	35.50	87.23*	163.02**	87.93	233.29**
Error	563	12.80	9.94	21.83	11.98	24.09	15.06

\* P < .05, \*\* P < .01.

twelve-day litter weight, expressed as deviations from the C16 line, on generations of selection are presented in Table 7. Only the M16 and I16 lines showed a significant positive correlated response in litter size. As was the case for the body weight traits, the correlated responses in these two lines were greater than pre-

TABLE 6

*Analysis of replicate differences in correlated response per unit primary selection differential*

Source	d.f.	Mean squares		
		Three-week weight	Six-week weight	Eight-week weight
		Males		
I2	7	25.77*	50.01*	46.43
M2	7	14.21	19.55	35.11
I4	3	81.55**	105.21**	78.02*
M4	3	17.28	47.90	50.23
I8	1	20.95	37.04	61.40
M8	1	64.06*	14.17	0.93
I16	1	138.53**	231.04**	150.65**
M16	1	0.15	185.77**	262.81**
Error	563	12.80	21.83	24.09
		Females		
I2	7	18.62	25.59*	26.80
M2	7	8.20	35.53**	41.75**
I4	3	76.64**	136.52**	124.94**
M4	3	15.25	16.02	21.82
I8	1	0.03	0.16	7.78
M8	1	7.37	3.17	14.95
I16	1	41.82**	127.96**	139.88**
M16	1	5.85	70.71*	196.08**
Error	563	9.94	11.98	15.06

\* P < .05, \*\* P < .01.

TABLE 7

*Regressions of litter size and twelve-day litter weight, expressed as mean deviations from C16, on generations of selection, pooled over replicates*

Line	Litter size	Twelve-day litter weight (g)
I1	— .08	— .19
I2	0.07	— .70**
I4	0.07	— .18
I8	0.08	0.23†
I16	0.12*	0.18†
M1	— .18*	0.37
M2	0.01	— .13
M4	— .02	0.20
M8	0.07	0.51**
M16	0.23**	0.31†

\*  $P < .05$ , \*\*  $P < .01$ .

† Approaching statistical significance ( $.05 < P < .10$ ).

dicted. There was a general tendency for litter size response to increase as population size increased. Litter size in the M16 line responded twice as much as in I16, which was expected on the basis of the difference in the primary selection differentials. However, there was no consistent difference in correlated response between the I and M lines at the smaller population sizes. This result may have been due to the effects of inbreeding depression.

Correlated responses for twelve-day litter weight were very erratic. There was a general tendency for response to be greater as selection intensity increased and as population size increased.

*Correlated responses in proportion of infertile matings and fitness indexes:* A high proportion of infertile matings led to extinction of several one- and two-pair lines (HANRAHAN, EISEN and LEGATES 1973). The number of surviving replicates and mean survival time in these lines are given in Table 8. Their mean fitness was extremely low. Mean survival time was lower in the full-sib mated lines than in the two-pair lines.

The regressions of the fitness traits, as a deviation from C16, on generations of

TABLE 8

*Surviving replicates and mean survival time through fourteen generations*

Line	Surviving replicates*	Percent surviving	Mean survival time (gen.)†
C1	2	12.5	6.25 (1.75)
I1	3	18.7	6.94 (2.50)
M1	1	6.3	6.75 (2.63)
C2	4	50.0	11.38 (10.63)
I2	4	50.0	10.50 (8.75)
M2	1	12.5	9.38 (6.63)

\* All replicates of size four-pair or more survived.

† Values in parentheses are mean survival times if no reserve matings had been maintained.

TABLE 9

*Regressions of proportion infertile matings, Index-1 and Index-2, expressed as a deviation from C16, on generations of selection, averaged over replicates†*

Line	Proportion infertile matings	Index-1	Index-2(g)
I4	0.005	0.05	— .76
I8	0.004	0.00	0.12
I16	— .019 (0.0029**)	0.36* (— .039**)	2.06* (— .23**)
M4	0.011*	— .14	— .79
M8	0.005	0.04	— .15
M16	— .018 (0.0030**)	0.49* (— .045**)	2.67** (— .30**)

\* P < .05, \*\* P < .01.

† Where quadratic effects contributed significantly to the model, the quadratic regression coefficients are given in parentheses.

selection are shown in Table 9. The generation means for these traits are presented in Figure 2 for the C16, I16 and M16 lines. The C16 line showed no significant response in Index-1 ( $b = -.02 \pm .06$ ), Index-2 ( $b = 0.38 \pm .27$ ) or proportion infertile matings ( $b = -.004 \pm .003$ ). The I16 and M16 lines exhibit

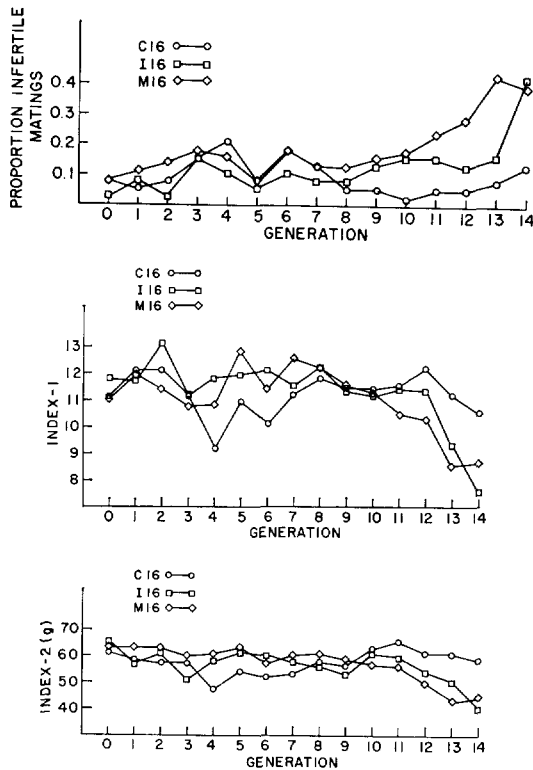


FIGURE 2.—Generation means of proportion infertile matings, Index-1 and Index-2 for the C16, I16 and M16 lines.



ed a significant ( $P < .01$ ) negative quadratic trend for all three fitness traits. This trend was primarily due to a sharp increase in the proportion of infertile matings in these lines beginning at generation nine. Thus, although two components of the fitness indexes, litter size and twelve-day litter weight, showed increased correlated responses to selection for postweaning gain, the fitness indexes still declined significantly. The four- and eight-pair lines did not change significantly in fitness traits except for a significant ( $P < .05$ ) increase in proportion of infertile matings in the M4 line.

#### DISCUSSION

There generally was an increase in all of the body weight traits except for three-week weight in the I1, I2 and M1 lines. These positive correlated responses are a reflection of the sizeable positive genetic correlations among body weights at different ages on the growth curve (EISEN, LANG and LEGATES 1969). The observed correlated responses in three-, six- and eight-week body weights due to selection for increased postweaning gain in the M16 and I16 lines were larger than predicted from base population estimates of genetic parameters. Direct response to selection for postweaning gain in these lines also was greater than that predicted (HANRAHAN, EISEN and LEGATES 1973).

Increased litter size in the M16 and I16 lines was expected based on the positive genetic correlation between litter size and adult body weight in the mouse (RAHNEFELD *et al.* 1966; EISEN, LEGATES and ROBISON 1970). The positive increment in litter size has been observed in previous lines selected for increased adult body weight (MACARTHUR 1944; FALCONER 1953; RAHNEFELD *et al.* 1963; LEGATES 1969). An exception was reported by BRADFORD (1971), who observed no correlated response in litter size due to selection for increased postweaning gain. Evidence from several high body weight selected lines clearly indicates that increased ovulation rate was responsible for the positive response in litter size (MACARTHUR 1949; FALCONER 1960; FOWLER and EDWARDS 1960; ELLIOTT, LEGATES and ULBERG 1968).

Weight of the litter at twelve days increased somewhat in the M16 and I16 lines, although the correlated response did not reach statistical significance ( $P > .05$ ). FALCONER (1953) and LEGATES (1969) reported an initial slight increase in twelve-day litter weight when selection was practiced for six-week body weight. EISEN, LEGATES and ROBISON (1970) found that selection for twelve-day litter weight led to an increase in six-week body weight.

The previous report on selection for increased postweaning gain in mice showed that the response declined as effective population size decreased within a given level of selection intensity (HANRAHAN, EISEN and LEGATES 1973). The present study provides similar findings for correlated responses in body weight and litter size in these lines. This result is particularly striking when litter size is considered since only the M16 and I16 lines showed a significant positive correlated response. In addition, several negative correlated responses were observed at population sizes of one, two and four pairs. Thus, the effects of inbreeding and genetic drift on correlated response are similar to those observed on direct

response, viz. a reduction in effective directional selection response per unit selection differential.

Genetic drift in small populations results in a lower response than predicted from infinite population size theory by increasing the probability of fixation of undesirable alleles during the course of selection (ROBERTSON 1960). The presence of nonadditive gene action would be expected to further depress mean response as inbreeding increases. The following procedure was used to estimate the cumulative effects of effective population size on response for the primary and secondary traits. The mean effective population sizes varied from 2.00 to 48.28 in the I lines and from 2.00 to 40.85 in the M lines (HANRAHAN, EISEN and LEGATES 1973). The mean response per generation for each line, pooled over replicates and sexes (where applicable), was regressed on mean 10% increase in inbreeding of the line, within each level of selection intensity. A critical assumption for this analysis to be valid is that the cumulative selection differentials for each line are similar within levels of selection intensity.

Since the regressions did not differ significantly between levels of selection intensity, pooled values only are presented in Table 10. No significant deviations from linearity were obtained. All traits showed a significant decline with inbreeding except that for twelve-day litter weight. The latter value, however, was in the expected direction and approached statistical significance. The influence of inbreeding on the correlated responses in these traits may be illustrated by taking litter size as an example. For a ten percent increase in inbreeding within the range considered (approximately 12% to 95%), the correlated response over ten generations of selection would be expected to be reduced by 0.28 pups for the same intensity of selection.

A computer simulation study by BERESKIN (1972) considered positive selection for an index at effective population sizes of approximately 4.2, 7.8 and 15.1, respectively. The respective realized heritabilities of the aggregate genotype were  $-.02$ ,  $0.18$  and  $0.35$ . Genetic drift clearly reduced the selection response and even resulted in a negative response at the smallest effective population size, which is in agreement with the present findings.

TABLE 10

*Regressions of mean direct and correlated responses per generation, pooled over replicates and sexes, on mean 10% increase in level of inbreeding†*

Trait	b‡	S.E.
Postweaning gain (g)	—0.025**	0.008
Three-week weight (g)	—0.034**	0.006
Six-week weight (g)	—0.058**	0.009
Eight-week weight (g)	—0.063**	0.008
Litter size	—0.028**	0.007
Twelve-day litter weight (g)	—0.054*	0.027

\* Approaching statistical significance ( $.05 < P < .10$ ).

\*\*  $P < .01$ .

† Pooled over intensities of selection.

‡ One-tail *t*-test.

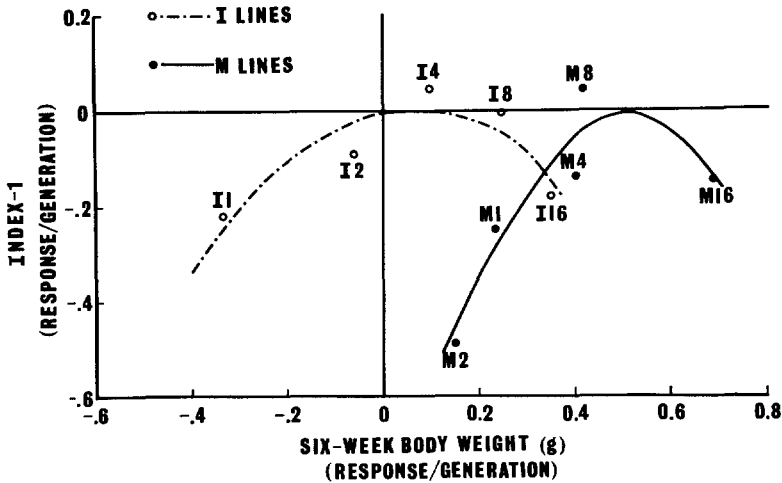


FIGURE 3.—Plot of Index-1 against six-week body weight in terms of linear response per generation for the I and M lines, and least squares regression curves relating Index-1 to six-week body weight responses/generation.

The joint effects of genetic drift and inbreeding depression in selected lines has considerable bearing on the choice of a control line. If a control line with an effective population size very much larger than the selected line is chosen, then the deviation from control over many generations will include drift effects as well as selection. Thus, a more suitable experimental design would be to maintain selected and control lines of the same effective population size, which are also large enough so that drift will be of little consequence over the course of selection.

The relationship between fitness response per generation as measured by Index-1 and six-week body weight response for the I and M lines is plotted in Figure 3. A quadratic relationship between fitness response and body weight response is apparent within each level of selection intensity. It is postulated that the reduction in mean fitness at low body weight responses (small population size) and at high body weight responses (large population size) are a consequence of quite different genetic mechanisms.

The reduction in mean fitness of the one- and two-pair lines selected for increased postweaning gain was due to a high frequency of infertile matings. This led to extinction of many replicates, a phenomenon also observed in the C1 and C2 lines. The mean inbreeding coefficients in all of these lines increased rapidly as selection progressed. Thus, those lines surviving to generation 14 had pedigree inbreeding coefficients of 0.95 in the full-sib mated lines and 0.76, 0.73 and 0.84 in the C2, I2 and M2 lines, respectively (HANRAHAN, EISEN and LEGATES 1973). These findings point to inbreeding depression (FALCONER 1960) as the major cause of the fitness decline in these extremely small effective population size lines. BOWMAN and FALCONER (1960) indicated that selection for litter size under full-sib mating resulted in extinction of 17 of the original 20 lines due to sterility when the inbreeding coefficient reached 0.76.

In contrast, the decrease in fitness traits in the I16 and M16 lines appeared mainly to be a direct consequence of selection for increased postweaning gain. This conclusion is based on the fact that (a) the C16 line showed no change in fitness traits during the course of the experiment and (b) the cumulative inbreeding coefficients of the C16, I16 and M16 lines were not greatly different (0.12, 0.12 and 0.13, respectively). Thus, any contribution of inbreeding to a reduction in mean fitness in these lines was probably small. The major fitness component affected in the I16 and M16 lines was proportion infertile matings, which was combined with two other components of fitness, litter size and twelve-day litter weight, to form two indexes of reproductive fitness. These indexes provided similar evidence for a reduction in fitness, despite the fact that litter size and twelve-day litter weight responded positively to selection for postweaning gain.

The findings for the M16 line are in general agreement with previous reports in the literature, but there are exceptions. BRADFORD (1971) reported a similar increase in proportion infertile matings beginning at about generation ten of selection for increased postweaning gain. However, no increase in litter size at birth was recorded. FALCONER (1955) observed a reduction in proportion fertile matings, after twenty generations of selection for increased six-week body weight, which was later shown to be due to reduced male libido (FOWLER and EDWARDS 1960). The influence of inbreeding cannot be discounted in FALCONER's (1955) study since the effective population size was quite small. In contrast, ELLIOTT, LEGATES and ULBERG (1968) found no decrease in proportion fertile matings in the line selected by LEGATES (1969) for increased six-week body weight, whereas the line selected for small body weight decreased in fertility due to a lowered libido of breeding males.

LERNER (1954) has reviewed several selection experiments showing that fitness generally declines during directional selection for a metric trait. VERGHESE and NORDSKOG (1968) found reduced reproductive fitness in lines of chickens selected for body weight and for egg weight.

It has been postulated that the decline in fitness due to selection for a metric trait may be due to the homeostatic model or the metric deviation model. The homeostatic model assumes that the decline in fitness as a correlated response to selection is due to increased homozygosity at loci affecting the quantitative trait (LERNER 1954). The metric deviation model argues that extreme phenotypes are intrinsically less fit (ROBERTSON 1956). These models have been discussed further by LATTER (1960) and by JAMES (1962). Under these models it may be assumed that there is an optimum phenotype for body weight (or a character highly correlated genetically with body weight) and that deviations from this optimum lead to fitness decline.

Percent body fat has increased significantly as a result of selection for increased postweaning gain in the M16 line (TIMON, EISEN and LEATHERWOOD 1970) and for selection for six-week body weight in FALCONER's (FOWLER 1958) and BRADFORD's (ROBINSON and BRADFORD 1969) lines, whereas LANG and LEGATES (1969) found no increase in percent fat in LEGATES' (1969) line selected for increased six-week body weight. It has already been noted that the first three lines cited

decreased in fertility whereas the fourth line did not. Obesity, manifested in several single gene mutant conditions of mice, is generally accompanied by increased sterility (see BRAY and YORK 1971 for review). Thus, the excessive accumulation of body fat in the M16 line (TIMON, EISEN and LEATHERWOOD 1970) may, in part, be responsible for the decreased fitness in this line. This interpretation would favor the metric deviation model whereby selection has moved the population mean for body weight and percent body fat away from an optimum.

In absolute terms, the fitness decline in the I16 line would not have been expected to be as great as in the M16 line since the six-week body weight response in I16 was only about one-half that of M16. However, the relative fitness decline in the I16 line is compatible within the intermediate level of selection intensity.

In contrast to the M16 and I16 lines, there was no decline in fitness due to directional selection in the M8 and I8 lines. Inbreeding coefficients in these lines of 0.27 and 0.26, respectively, were similar to levels of inbreeding reached in short-term artificial selection studies with mice (ROBERTS 1966). The level of inbreeding may not have been sufficiently high to cause any appreciable inbreeding depression, particularly since it accumulated slowly over fourteen generations. In addition, the M8 and I8 lines had not responded to selection for weight gain to the same degree as their larger population size counterparts. Thus it is hypothesized that the frequency of extremely large body weight phenotypes was not sufficiently high to cause a reduction in mean fitness of these lines.

## LITERATURE CITED

- BERESKIN, B., 1972 Monte Carlo studies of selection and inbreeding in swine. IV. Selection response. *J. Anim. Sci.* **34**: 726-736.
- BOWMAN, J. C. and D. S. FALCONER, 1960 Inbreeding depression and heterosis of litter size in mice. *Genet. Res.* **1**: 262-274.
- BRADFORD, G. E., 1971 Growth and reproduction in mice selected for rapid body weight gain. *Genetics* **69**: 499-512.
- BRAY, G. A. and D. A. YORK, 1971 Genetically transmitted obesity in rodents. *Physiol. Rev.* **51**: 598-646.
- CLAYTON, G. A., J. A. MORRIS and A. ROBERTSON, 1957 An experimental check on quantitative genetic theory. I. Short-term response to selection. *J. Genetics* **55**: 131-151.
- EISEN, E. J., B. J. LANG and J. E. LEGATES, 1969 Comparison of growth functions within and between lines of mice selected for large and small body weight. *Theor. Appl. Genetics* **39**: 251-260.
- EISEN, E. J., J. E. LEGATES and O. W. ROBISON, 1970 Selection for 12-day litter weight in mice. *Genetics* **64**: 511-532.
- ELLIOTT, D. S., J. E. LEGATES and L. C. ULBERG, 1968 Changes in the reproductive processes of mice selected for large and small body size. *J. Reprod. Fert.* **17**: 9-18.
- FALCONER, D. S., 1953 Selection for large and small size in mice. *J. Genet.* **51**: 470-501. —, 1955 Patterns of response in selection experiments with mice. *Cold Spr. Harb. Symp. Quant. Biol.* **20**: 178-196. —, 1960 *Introduction to Quantitative Genetics*. Ronald Press, N.Y.
- FOWLER, R. E., 1958 The growth and carcass composition of strains of mice selected for large and small body size. *J. Agric. Sci.* **51**: 137-148.

- FOWLER, R. E. and R. G. EDWARDS, 1960 The fertility of mice selected for large or small body size. *Genet. Res.* **1**: 393-407.
- FRANKHAM, R., L. P. JONES and J. S. F. BARKER, 1968 The effects of population size and selection intensity in selection for a quantitative character in *Drosophila*. I. Short-term response to selection. *Genet. Res.* **12**: 237-248.
- HANRAHAN, J. P. and E. J. EISEN, 1973 Sexual dimorphism and direct and maternal genetic effects on body weight in mice. *Theor. Appl. Genetics* **43**: 39-45.
- HANRAHAN, J. P., E. J. EISEN and J. E. LEGATES, 1973 Effects of population size and selection intensity on short-term response to selection for postweaning gain in mice. *Genetics* **73**: 513-530.
- JAMES, J. W., 1962 Conflict between directional and centripetal selection. *Heredity* **17**: 487-499.
- KERR, W. E. and S. WRIGHT, 1954 Experimental studies of the distribution of gene frequencies in very small populations of *Drosophila melanogaster*. I. Forked. *Evolution* **8**: 172-177.
- LANG, B. J. and J. E. LEGATES, 1969 Rate, composition and efficiency of growth in mice selected for large and small body weight. *Theor. Appl. Genetics* **39**: 306-314.
- LATTER, B. D. H., 1960 Natural selection for an intermediate optimum. *Aust. J. Biol. Sci.* **13**: 30-35.
- LEGATES, J. E., 1969 Direct and correlated responses to selection in mice. pp. 149-165. *Genetics Lectures*. Volume 1. Edited by R. BOGART.
- LENER, I. M., 1954 *Genetic Homeostasis*, Oliver and Boyd, London.
- MACARTHUR, J. W., 1944 Genetics of body size and related characters. II. Satellite characters associated with body size in mice. *Amer. Nat.* **78**: 224-237. —, 1949 Selection for small and large body size in the house mouse. *Genetics* **34**: 194-209.
- RAHNEFELD, G. W., W. J. BOYLAN, R. E. COMSTOCK and M. SINGH, 1963 Mass selection for postweaning growth in mice. *Genetics* **48**: 1567-1583.
- RAHNEFELD, G. W., R. E. COMSTOCK, M. SINGH and S. R. NAPUCKET, 1966 Genetic correlation between growth rate and litter size in mice. *Genetics* **54**: 1423-1429.
- RICHARDSON, R. H., K. KOJIMA and H. L. LUCAS, 1968 An analysis of short-term selection experiments. *Heredity* **23**: 493-506.
- ROBERTS, R. C., 1966 The limits to artificial selection for body weight in the mouse. II. The genetic nature of the limits. *Genet. Res.* **8**: 361-375.
- ROBERTSON, A., 1956 The effect of selection against extreme deviants based on deviations or on homozygosity. *J. Genet.* **57**: 236-248. —, 1960 A theory of limits in artificial selection. *Proc. Roy Soc. London, B* **153**: 234-249. —, 1961 Inbreeding in artificial selection programs. *Genet. Res.* **2**: 189-194.
- ROBINSON, D. W. and G. E. BRADFORD, 1969 Cellular response to selection for rapid growth in mice. *Growth* **33**: 221-229.
- RUMBALL, W. and A. L. RAE, 1968 The effect of selection intensity on selection response in *Tribolium*. *N. Z. J. Agric. Res.* **11**: 745-756.
- TANTAWY, A. O., 1956 Selection for long and short wing length in *Drosophila melanogaster* with different systems of mating. *Genetics* **28**: 231-262.
- TIMON, V. M., E. J. EISEN and J. M. LEATHERWOOD, 1970 Comparisons of *ad libitum* and restricted feeding of mice selected and unselected for postweaning gain. II. Carcass composition and feed efficiency. *Genetics* **64**: 41-57.
- VERGHESE, M. W. and A. W. NORDSKOG, 1968 Correlated responses in reproductive fitness to selection in chickens. *Genet. Res.* **11**: 221-238.