LONG-TERM SELECTION RESPONSE FOR 12-DAY LITTER WEIGHT IN MICE¹

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ABSTRACT

Long-term selection for increased 12-day litter weight in two replicate lines (W_2 , W_3) of mice resulted in an apparent selection limit at about 17 generations. Quadratic polynomial and exponential models were fitted to the data in order to estimate the plateaued response and half-life of the selection process. Using the polynomial results, the half-life estimates were 4.5 and 8.6 generations for W_2 and W_3 , respectively. The plateaued responses were 5.1 and 5.8 g which, when expressed in phenotypic standard deviation units, became 1.1 and 1.3. The exponential model provides similar estimates. A negative association between 12-day litter weight and fitness was not considered to be an adequate explanation for the plateau since there was no decrease in fertility of the selected lines. Evidence that exhaustion of genetic variability was not the cause of the plateau came from the immediate response to reverse selection. It was proposed that the plateau may be due to a negative genetic correlation between direct and maternal genetic effects, which would be expected to occur after many generations of selection. There were positive correlated responses in both replicates for adult body weight, which was in agreement with the positive genetic correlation between preweaning and postweaning body weight. The expected positive correlated response for number born was realized in only one of the replicates.

LONG-TERM selection for rapid growth of young mammals during the suckling period has received little experimental consideration. The phenotype for early postnatal growth may be influenced strongly by the individual's own genotype and by the genotype of the mother (WILLHAM 1963). FALCONER (1947) suggested that 12-day weight of a standardized litter size would be a useful measure of the influence of maternal performance on early postnatal growth in mice. Subsequent studies indicated that mammary gland activity (MUNFORD 1963a,b) and milk yield (HANRAHAN and EISEN 1970) reached a maximum between days 11 and 13 postpartum. Cross-fostering studies showed that postnatal maternal influences accounted for a large proportion of the variability in 12-day litter weight, but that direct genetic effects were still important (COX, LEGATES and COCKERHAM 1959; YOUNG, LEGATES and FARTHING 1965; EL OKSH, SUTHERLAND and WILLIAMS 1967). EISEN, LEGATES and ROBISON (1970) found that a large percentage of this maternal variation was non-genetic.

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Several investigations (BATEMAN as reported by FALCONER 1955; LEGATES and FARTHING 1962; DALTON and BYWATER 1963) were unable to increase 12-day litter weight by selection. However, EISEN *et al.* (1970) were successful in selecting for increased 12-day litter weight in four replicated lines. The present study reports on the long-term response to selection for 12-day litter weight in two of these lines.

MATERIALS AND METHODS

Details of the experimental procedure through ten generations of within family selection were given by EISEN *et al.* (1970). Litter size was standardized to six mice at five days of age, using two males and four females where possible. The selection unit was the total 12-day litter weight of a family of six mice. First litters only were used. The mean number of males and females per line-generation subclass was 28.9 and 48.8 respectively, with an average of 3.3 full sisters scored per family. Due to space limitations only a random sample of two (W_2 and W_3) of the four selected lines and one (R_1) of the two control lines were continued through 22 generations. The means in the two selected lines were expressed as a deviation from the control line mean (R_1) each generation.

The selected line generation mean deviations were fitted by least squares to a quadratic polynomial regression model and an exponential model (JAMES 1965; FRAHM and KOJIMA 1966) for comparative purposes. The polynomial regression model was

$$w_i = \beta_0 + \beta_1 t_i + \beta_2 t_i^2 + \epsilon_i$$

where w_i = 12-day litter weight deviation for the i^{th} generation ($i = 0, 1, \dots, 22$), t_i = generation of selection, β_0 = fitted litter weight deviation at t_0 , β_1 and β_2 = partial regression coefficients due to linear and quadratic effects, respectively, and ϵ_i = experimental error. The exponential model, fitted by an iterative least squares procedure (MARQUARDT 1963), was of the form

$$w_i = A(1 - ce^{-kt_i} + \epsilon'_i$$

where A = asymptote, c = constant of integration, k = rate constant and ϵ'_i = experimental error. The error terms in both models are assumed to be normally, identically and independently distributed with mean zero and respective variances σ^2 and σ'^2 . The criterion used to determine which model provided the best statistical fit to the data was the coefficient of determination (R^2).

Two key parameters useful in the interpretation of long-term selection experiments are the total response at the selection limit and the half-life of the selection process (ROBERTSON 1960). An estimate of total response may be obtained directly as a parameter (A) of the exponential curve. Total response may also be estimated from the polynomial equation by finding the weight response at $\frac{dw}{dt} = 0$ which will yield a maximum of the regression equation. The half-life of the selection process may be estimated from the exponential curve as $t^* = \frac{1}{k} (\ln 2 + \ln c)$, and from the polynomial model by finding the appropriate root of the quadratic equation

$$\beta_2 t^2 + \beta_1 t + (\beta_0 - \frac{1}{2} w_{\max}) = 0$$

where $w_{\max}$ = estimated total response.

Correlated traits which were considered in the selection study were adult body weight at 6 and 8 weeks of age and number born. The correlated responses, taken as a deviation from control line means, were fitted to generations of selection by polynomial regression. Realized genetic regression coefficients (b_{GY-w}) were obtained from the regression of the unselected trait (γ) gen-

eration mean deviations on 12-day litter weight (w) mean deviations. The realized genetic correlation was then calculated from the formula.

$$r_G = b_{Gy \cdot w} \frac{h_w \sigma_{Pw}}{h_y \sigma_{Py}},$$

where h_w and σ_{Pw} are the square root of heritability and phenotypic standard deviation for 12-day litter weight and h_y and σ_{Py} are the corresponding parameters for the correlated trait. Parameter estimates were taken from the base population (YOUNG *et al.* 1965; EISEN *et al.* 1970). The realized genetic correlations were compared with the genetic correlation estimates from the base population.

Reciprocal F_1 crosses between W_2 and W_3 were made in generation 11. This newly formed population will be identified as W_{23} . Within family selection for increased 12-day litter weight was initiated in the F_3 from this cross and continued for four generations.

Reciprocal F_1 crosses between the control lines, R_1 and R_2 , also were carried out in generation 11. The crossbred population (R_{12}) was maintained as a control for W_{23} . In addition, a random sample of mice from the F_3 generation of the R_{12} line was used to initiate four generations of individual selection for 12-day litter weight.

After 17 generations of selection in W_2 and W_3 it appeared that the rate of selection response had decreased. In order to see if any useful genetic variance remained, reverse selection was initiated on a within full sib family basis in generation 17 from a subset of W_2 , designated W_{2b} .

RESULTS

Long-term response: Response to selection for 12-day litter weight is plotted against generation of selection in Figure 1. The means of W_2 and W_3 are given in Tables 8, 9, and 10 for generations 11–22. It is apparent that selection response continued beyond generation 10 in both lines. The means of the selected lines significantly ($P < 0.01$) exceeded that of the control line from generations 11–22. However, as stated earlier, there was some suggestion from the plot of the generation means that the selection response was greatly diminished by generation 17. The linear regression of response on generation number from generations 17 to 22 was not significantly different from zero within each line (Table 1), which tends to verify the earlier observation that the lines were approaching a plateau.

The results of fitting the polynomial and exponential models to the selection response data are presented in Table 2. Both models gave almost identical R^2 values, which suggests that either model would adequately describe the data. Only the polynomial curves are graphed in Figure 1 since plots of the fitted curves for each model were not distinguishable within the range of the observed data.

TABLE 1

Linear regression of selection response in 12-day litter weight (g) on generation number in the last six generations (17–22) of selection

Replicate lines	
W_2	W_3
$0.093 \pm .276$	$0.018 \pm .200$

TABLE 2

Results of fitting the polynomial regression and exponential models to the 12-day litter weight generation mean deviations

Polynomial regression model	Replicate lines	
	W ₂	W ₃
Intercept (β_0)	1.018 $\pm$.755	-1.198 $\pm$.637
Linear (β_1)	0.376 $\pm$.159**	0.579 $\pm$.134**
Quadratic (β_2)	-0.009 $\pm$.007	-0.012 $\pm$.006*
R ²	0.516**	0.811**
Exponential model	W ₂	W ₃
Asymptote (A)	6.27 $\pm$ 2.63**	8.19 $\pm$ 2.93**
Integration constant (c)	0.831 $\pm$.116**	1.144 $\pm$.126**
Rate constant (k)	0.076 $\pm$.079	0.066 $\pm$.039
R ²	0.509**	0.805**

* P < 0.05, ** P < 0.01.

Estimates of the parameters of the fitted functions are listed in Table 3. Heterogeneity between replicate lines in the selection limit is suggested by the higher plateaued response and longer half-life of W₃ compared with W₂. When pooled over replicate lines, the predicted 12-day litter weight responses at the selection limit were 5.43 and 7.23 g for the polynomial and exponential functions respectively. The corresponding half-life estimates were 6.56 and 9.58 generations. The polynomial estimates of litter weight at the selection limit may be more realistic,

FIGURE 1.—Response to selection for 12-day litter weight in two replicate lines.

TABLE 3

Estimated plateaued response and half-life for 12-day litter weight from each model

Parameter estimate	Model	Replicate lines		
		W_2	W_3	Mean
Plateaued response (g)	Polynomial	$5.06 \pm .66$	$5.79 \pm .84$	5.43
	Exponential	$6.27 \pm .26$	$8.19 \pm .29$	7.23
Half-life (t)	Polynomial	4.48	8.58	6.56
	Exponential	6.68	12.48	9.58
Response/ σ_p^a	Polynomial	1.09	1.25	1.17
	Exponential	1.35	1.76	1.55

$\sigma_p^a = 4.65 =$ Phenotypic Standard Deviation.

since they were closer to the 12-day litter weight responses averaged over the last six generations (17–22) of selection: 4.74 ± 1.04 and $5.48 \pm .75$ g for the W_2 and W_3 lines respectively. There is, however, an empirical distinction between the two functions which must be considered. The polynomial regression curve predicts a maximum weight after which time the weight declines, whereas the exponential curve projects a plateaued weight. The latter is presumably more descriptive of the underlying biological model (JAMES 1965).

The total response may best be expressed in standard deviation units (FALCONER 1955; ROBERTS 1966a) when comparison with other traits is desired. The response per phenotypic standard deviation unit was approximately between 1.0 and 1.5 (Table 3). The tabulated values would be only slightly lower when converted from a litter to an individual basis. The standardized response was not expressed per additive genetic standard deviation unit due to the complication of maternal genetic effects.

The first derivative of the response function with respect to time provides the predicted rate of genetic gain at time t_i . Table 4 gives predicted responses at five generation intervals. The predicted responses for the two models are in excellent agreement from generations 0 to 15, but subsequently the exponential model gives a higher predicted response. The initial predicted response may be given as Sh^2 , where S = selection differential and h^2 = heritability of the selection criterion. The first ten generations of selection yielded an S of 2.0 g per generation

TABLE 4

Predicted response at several generations based on the polynomial and exponential models

Generation	Polynomial		Exponential	
	W_2	W_3	W_2	W_3
0	0.38	0.58	0.40	0.62
5	0.33	0.46	0.27	0.44
10	0.20	0.34	0.19	0.32
15	0.12	0.22	0.13	0.23
20	0.03	0.10	0.09	0.16

FIGURE 2.—Correlated responses to selection: female 6- and 8-week body weights and number born. Eight-week body weight was not recorded in generation 22.

and the h^2 predicted was 0.2 (EISEN *et al.* 1970). Thus, the initial (t_0) predicted response of 0.4 g is in agreement with W_2 , whereas the predicted response in W_3 is somewhat higher. The first 10 generations of selection for 12-day litter weight had given observed responses of 0.20 and 0.41 g per generation in W_2 and W_3 , respectively. These are in reasonably good agreement with the predicted responses in generation 10.

TABLE 5

Analyses of correlated responses to selection: 6- and 8-week body weight and number born regressed on generation number

	Replicate lines	
	W_2	W_3
6-week body weight		
Intercept	0.279 $\pm$.410	-0.825 $\pm$.306*
Linear	-0.089 $\pm$.165	0.242 $\pm$.065**
Quadratic	0.033 $\pm$.018	-0.005 $\pm$.003
Cubic	-0.0012 $\pm$.0005*	NS
R ²	0.713**	0.746**
8-week body weight		
Intercept	0.771 $\pm$.468	0.383 $\pm$.340
Linear	-0.284 $\pm$.207	-0.253 $\pm$.151
Quadratic	0.048 $\pm$.024*	0.044 $\pm$.018*
Cubic	-0.0016 $\pm$.0008*	0.0015 $\pm$.0006*
R ²	0.519**	0.591**
Number born		
Intercept	0.938 $\pm$.135**	-0.588 $\pm$.273*
Linear	0.102 $\pm$.020**	0.132 $\pm$.057*
Quadratic	NS	-0.005 $\pm$.002*
R ²	0.545**	0.209

* $P < 0.05$ ** $P < 0.01$ NS = Not significant.

Long-term correlated responses: Correlated responses in 6- and 8-week body weight of females and number born are plotted as a deviation from control against generation number in Figure 2 and the corresponding regression coefficients are given in Table 5. The results for adult body weight of males have been omitted since they were similar to the female data. The trend in 8-week body weight tends to be cubic in both replicates. There is an early positive response followed by a decline for five generations. The response in 8-week weight then increases exponentially and appears to plateau at about 1.5 g by generation 14. The result is similar for 6-week body weight, except that W_3 does not show the initial positive response. In general the replicate lines responded similarly for adult body weight.

There was significant heterogeneity between replicate lines for the correlated response in number born. The W_2 line showed a significant ($P < 0.01$) linear response. In contrast, W_3 showed no significant linear response but a significant quadratic response after adjustment for linear effects even though the overall quadratic fit was not significant.

The realized genetic regressions are presented in Table 6. There were no significant deviations from linearity for any of these relationships. The genetic regressions for adult body weight on 12-day litter weight did not differ between replicates. However, the genetic regression of number born on litter weight for the W_2 line was significantly ($P < 0.05$) different from that of W_3 . The realized

TABLE 6

Analyses of correlated responses to selection: realized genetic regression of unselected traits on 12-day litter weight

Unselected trait	Replicate lines	
	W ₂	W ₃
6-week body weight	0.368 ± .090**	0.363 ± .044**
8-week body weight	0.255 ± .087**	0.173 ± .049**
Number born	0.277 ± .096**	0.081 ± .042*

* P < 0.05 ** P < 0.01.

and predicted genetic correlations (Table 7) are in agreement for 8-week body weight, but the predicted genetic correlations for 6-week body weight and number born apparently underestimated the realized genetic correlations.

Control populations: Table 8 gives 12-day litter weights for the cross of the unselected lines (R₁₂). Although the F₁ did not differ significantly from the midparent value, the F₂ was significantly larger than the midparent value. The F₂ mean is expected to exceed the F₁ mean if there is any heterosis for maternal effects. However, no quantitative value for maternal heterosis can be given since F₁ and F₂ means are not contemporaneous. However, from the F₃ through F₇ generations R₁ and R₁₂ were of the same order of magnitude (Table 9). The R₁ control population was very stable for the trait under selection over the duration of the experiment since the linear regression of 12-day litter weight on generation number was only $-0.013 \pm .050$ with a coefficient of variation of 4.5% for the generation means. Hence, the non-significant negative trend in 12-day litter weight observed in the early generations of selection (EISEN *et al.* 1970) was probably not of biological importance.

The R₁ control population did evidence some decline in fitness traits over the course of the experiment. The linear regressions of number born per litter and percent fertile matings on generation number were $-0.036 \pm .013$ (P < 0.01) and $-0.423 \pm .174$ (P < 0.05), respectively. Viewed in terms of total decline in fertility, the least squares estimates of the differences between final and initial generation means were -0.79 mice born per litter, -9.31% fertile matings and -1.49 mice born per mating.

TABLE 7

Predicted and realized genetic correlations (r_G) between 12-day litter weight and the unselected traits

Unselected trait	Predicted ^a	Realized
6-week body weight	0.49	0.81
8-week body weight	0.44	0.46
Number born	0.19	0.40

^a EISEN, LEGATES and ROBISON (1970).

TABLE 8

12-day litter weight means (g) and linear contrasts in generations 11 and 12 of selection

Generation ^a	Line means (sample size)						Error variance	Degrees of freedom
	R ₁	R ₂	R ₁₂ ^b	W ₂	W ₃	W ₂₃ ^b		
F ₁ (11)	41.0(29)	42.5(27)	41.6(50)	43.9(28)	45.8(28)	44.6(58)	24.4	214
F ₂ (12)	37.1(46)	37.3(35)	40.3(68)	44.0(44)	43.1(43)	43.9(68)	19.5	298
Linear contrasts								
Generation	R ₁₂ —½(R ₁ +R ₂)		W ₂₃ —½(W ₂ +W ₃)		½(W ₂ +W ₃ —R ₁ —R ₂)		W ₂₃ —R ₁₂	
F ₁ (11)	—0.2		—0.3		3.1**		3.0**	
F ₂ (12)	3.1**		0.4		6.4**		3.6**	

** P < 0.01.

^a F₁ refers to the generation following the crossing of R₁ with R₂ and W₁ with W₂, respectively, while the value in parentheses refers to the generation of selection in W₂ and W₃.^b Reciprocal F₁ means were not significantly different and were pooled.

Selection response in the cross of selected lines: The F₁ and F₂ crosses of the selected lines (W₂₃) did not differ significantly from the midparent value (Table 8). The response to within-family selection for increased 12-day litter weight in the W₂₃ line is given by the difference, W₂₃ — R₁₂, in Table 9. Although W₂₃ was significantly larger than R₁₂ from the F₃ to F₇ generations, the W₂₃ line actually declined. The regression of the difference, W₂₃ — R₁₂, for 12-day litter weight on generation number was $-0.430 \pm .234$.

TABLE 9

12-day litter weight means (g) and linear contrasts in generations 13–17 of selection

Generation ^a	Line means (sample size)						Error variance	Degrees of freedom
	R ₁	R ₁₂	W ₂	W ₃	W ₂₃ ^b	W _m ^c		
F ₃ (13)	40.7(43)	40.6(67)	44.8(56)	43.6(44)	46.3(65)	—	23.0	270
F ₄ (14)	40.9(40)	40.5(57)	45.3(46)	44.6(52)	47.4(56)	42.4(53)	21.5	298
F ₅ (15)	37.9(42)	38.6(47)	41.7(55)	43.0(50)	43.8(50)	41.8(60)	22.7	298
F ₆ (16)	38.0(49)	38.1(51)	45.9(54)	43.3(54)	42.7(46)	39.3(51)	20.7	299
F ₇ (17)	36.8(45)	35.4(57)	40.1(47)	41.7(42)	40.1(37)	36.9(43)	27.3	265
Linear contrasts								
Generation	R ₁₂ —R ₁		W ₂₃ —½(W ₂ +W ₃)		½(W ₂ +W ₃)—R ₁		W ₂₃ —R ₁₂	
F ₃ (13)	—0.1		2.1**		3.5**		5.7**	
F ₄ (14)	—0.4		2.5**		4.0**		6.9**	
F ₅ (15)	0.7		1.4		4.4**		5.2**	
F ₆ (16)	0.1		—1.9*		6.6**		4.6**	
F ₇ (17)	—1.4		—0.8		4.1**		4.7**	

* P < 0.05 ** P < 0.01.

^a See footnote "a" in Table 8.^b Within full sib family selection initiated in F₃ of W₂₃.^c Mass selection initiated in F₃ of R₁₂ to form W_m.

TABLE 10

12-day litter weight means (g) and linear contrasts in generations 18–22 of selection

Generation	Line means (sample size)				Error variance	Degrees of freedom
	R ₁	W ₂	W ₃	W _{2b} ^a		
18	37.8 (42)	43.9 (42)	43.7 (42)	39.1 (39)	27.4	161
19	40.0 (50)	45.5 (58)	46.4 (67)	39.9 (28)	24.3	199
20	40.7 (47)	45.0 (52)	45.2 (59)	42.2 (55)	26.3	209
21	36.8 (53)	40.9 (61)	43.1 (60)	36.9 (53)	28.3	223
22	36.4 (57)	41.8 (57)	41.6 (57)	34.5 (49)	24.6	215

Generation	Linear contrasts		
	$\frac{1}{2}(W_2+W_3)-R_1$	W _{2b} -W ₂	W _{2b} -R ₁
18	6.0**	-4.8**	1.3
19	5.9**	-5.6**	-0.1
20	4.4**	-2.8**	1.5
21	5.2**	-4.0**	0.1
22	5.3**	-7.3**	-1.9*

* P < .05 ** P < .01.

^a Reverse selection initiated in generation 17 of W₂ to form W_{2b}.

Response to individual selection: The response to individual selection for 12-day litter weight is given by the difference, $W_m - R_{12}$, in Table 9. The first two generations of response were quite high, but this was followed by a cessation of response for two generations. The linear regression of response on generation number was $0.330 \pm .379$. This response was slightly higher than that observed per generation from the first 10 generations of within-family selection (EISEN *et al.* 1970). However, the advantage in increased response would be offset by a more rapid rate of inbreeding.

Reverse selection: The response to reverse selection for 12-day litter weight was immediate in the W_{2b} line. Mean litter weight was 4.8 g less in W_{2b} compared with W₂ after one generation of selection (Table 10). After five generations of reverse selection the difference had increased to 7.3 g and the W_{2b} line was significantly ($P < 0.05$) below the control line. The linear regression of 12-day litter weight as a deviation from control ($W_{2b} - R_1$) on generation of selection was $0.800 \pm .248$ ($P < 0.05$).

DISCUSSION

Twenty-two generations of selection for increased 12-day litter weight demonstrated many of the classical features of long-term selection experiments reviewed by FALCONER (1960). The initial selection response was linear (EISEN *et al.* 1970), which was followed by a gradual decline in the rate of response until an apparent selection limit was reached. The standardized selection limit for 12-day litter weight was smaller than comparable values for adult body weight selection with mice (ROBERTS 1966a; WILSON *et al.* 1971). The number of generations required to reach the selection limit is difficult to assess precisely. However, no

increase in selection response appeared to occur beyond generation 17, which is in reasonable agreement with results from selection for 6-week body weight (ROBERTS 1966a). WILSON *et al.* (1971) reported continued selection response to generation 35 for 60-day body weight in mice.

The half-life of selection response is more amenable to quantitative estimation than is the number of generations to the selection limit. Even then the method of estimation may be arbitrary (ROBERTS 1966a) or, as in the present study, different models may lead to slightly different half-life estimates. The replicate lines had different half-life values, a shorter half-life being associated with a lower selection limit. The most reasonable estimates of half-life were taken to be five and nine generations for the W_2 and W_3 lines, respectively. Thus, one-half of the total selection response was attained by generation seven on the average. These estimates of half-life are in the range of those reported by ROBERTS (1966a) for 6-week body weight. JAMES (1965) reported half-life estimates of 2.6 and 2.7 for shank length and egg production in poultry and 5.5 for abdominal bristle number in *Drosophila melanogaster*. Collectively, these results from a wide range of species suggest that the half-life of selection response occurs extremely early in the selection process.

ROBERTSON (1960) formulated a theory of selection limits which predicts that for an additive model half of the total genetic gain should be achieved in approximately $1.4 N_e$ generations, where N_e is the effective population number. The effective number in the present study was about 70 (EISEN *et al.* 1970). Using the observed half-life of seven generations and $N_e = 70$, the formula yields a half-life of $0.1 N_e$ generations. The coefficient of 0.1 is clearly below that predicted from an additive model. These results, together with the apparent small standardized selection response, suggest that the nature of the selection limit may not have been due to an exhaustion of genetic variability.

Reduction in genetic variance would be expected to lead to a reduction in phenotypic variability. However, Figure 3 shows that the phenotypic coefficient

FIGURE 3.—Response of coefficients of variation in 12-day litter weight.

of variation in 12-day litter weight did not change with selection. FALCONER (1955) reported a similar result when selecting for large 6-week body weight in mice. The lack of change in phenotypic variability in the present study could have resulted from either no decrease in genetic variability or from an increase in environmental variance as the genetic variance declined (FALCONER 1960).

Conclusive evidence that additive genetic variability was present in the selected lines near the selection limit comes from the immediate response to reverse selection for 12-day litter weight in the W_2 line. Thus, the nature of the selection limit for large 12-day weight is different from that observed by ROBERTS (1966b) for large adult size, where additive genetic variance was indeed exhausted. The disparity in results is not entirely clear but several possibilities are likely. Since the genetic correlation between early postnatal and adult body weight is approximately .5, different genetic factors are likely to be operating to influence body weight at the two ages. Maternal factors also are known to be more important during the early postweaning phase of growth (YOUNG *et al.* 1965).

One cause of cessation of selection response in the presence of genetic variability is a negative relationship between fitness values and the trait under selection. To investigate this possibility, percent fertile matings in the last six generations were examined (Table 11). The W_2 and W_3 lines exhibited no decrease in fertility relative to the control line. In point of fact percent fertile matings, taken as a deviation from control, increased over the course of the experiment. The reverse selection line exhibited no increase in percent fertile matings. The conclusion is clear that decreased fertility, an important component of fitness, is not the reason why the selected lines have ceased to respond.

If selection favored heterozygotes at some loci, an equilibrium would be reached wherein only non-additive genetic variance would be present. Since reverse selection would not result in an immediate response under this genetic mechanism, it may be eliminated from consideration as a cause of the selection plateau.

Another way in which a selection limit may be reached in the presence of genetic variability is heterozygote superiority due to the combined effects of artificial and natural selection (FALCONER 1960). Although this hypothesis may

TABLE 11

Percent fertile matings in generations 17-22 of the control (R_1) and selected lines (W_2, W_3) and the five generations of the reverse selection line (W_{2b})

Generation	Lines			
	R_1	W_2	W_3	W_{2b}
17	80.9	86.9	85.9	—
18	84.2	90.0	94.1	93.5
19	89.9	92.7	94.6	74.5
20	84.1	83.4	95.5	93.5
21	83.3	95.8	94.4	94.0
22	86.4	88.6	89.5	91.7
Mean	85.0	89.6	92.4	91.2

be a plausible explanation of the selection limit reached for 12-day weight, its proof would require information, which is not available, on specific gene loci influencing the quantitative trait and fitness.

A genetic model which may adequately explain the selection limit is related to the fact that neonatal growth is influenced by both additive direct and additive maternal genetic effects. EISEN *et al.* (1970) reported an initial positive genetic correlation between these two factors. Just as with the case of two quantitative traits selected simultaneously, the genetic correlation between direct and maternal effects for one trait would become negative after continued selection. After selection had resulted in an increase in the frequency of pleiotropic loci that act favorably by both increasing neonatal growth directly and through an improved maternal environment, these loci would contribute little to the genetic correlation. The remaining pleiotropic loci would then tend to have a negative relationship between direct and maternal effects. The result would be a cessation of response even though additive genetic variability was still present. This might also explain the lack of response in the W_{23} line.

A physiological basis for the proposed genetic model may be associated with the limitation in the amount of nutrient energy consumed by the dam which could limit the quantity of nutrients available to the neonate. This would result in the absence of further selection response for increased 12-day weight, whereas reverse selection would not be hindered. EISEN and HANRAHAN (1970) found that the difference in 12-day weight between the lines selected for increased 12-day litter weight and the control lines was greater on a high energy diet than on the diet used throughout the selection experiment (5.4 versus 4.1 g). Although this result was not statistically significant, it is in the direction expected under the above hypothesis.

The correlated responses to selection for 12-day litter weight were, for the most part, in agreement with that predicted from parameter estimates in the base population. The increase in adult body size was anticipated since the genetic correlation between preweaning and postweaning weights was positive. The genetic correlation between weights at different time periods tends to decrease as the period between weights increases. Thus the realized genetic correlation between 12-day and 8-week weight was less than that between 12-day and 6-week weight. The nonlinearity of the growth process and environmental variability may partially account for this result. The increase in number born in the W_2 line was expected because of the positive genetic correlation between adult body weight and litter size. FALCONER (1955) found that selection for adult size also increased litter size. The absence of a correlated response in number born for the W^3 line was unexpected. Genetic sampling may be a partial explanation for the replicate heterogeneity in the correlated response for number born. Recently, BRADFORD (1971) reported no correlated response in litter size after 23 generations of selection for postweaning weight gain.

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