

MATERNAL EFFECTS AMONG LINES OF MICE SELECTED FOR BODY WEIGHT¹

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A number of reports have been cited (ROBERTS 1966) which verify that directional selection can produce changes in the body weight of mice. However, the favorable response to selection for body weight may be nullified in part if maternal effects are negatively correlated genetically with body weight. Apparent increases in 12-day litter weight of mice selected for large six-week weight for nine generations were reported by FALCONER (1953, 1955) and LEGATES, FARTHING and COCKERHAM (1958). Small positive genetic correlations between postnatal maternal performance, as measured by the 12-day weight of a standardized litter, and preweaning and early postweaning gains, also were suggested by the results of YOUNG and LEGATES (1965).

The relative importance of maternal influences on growth changes with the stage of development of the offspring. BUTLER and METRAKOS (1950) concluded that the postnatal maternal influence of the dam was important throughout the period from birth to 140 days of age. COX, LEGATES and COCKERHAM (1959) and YOUNG, LEGATES and FARTHING (1965) have shown that postnatal maternal influences on body weight are responsible for 65% of the variance at 21 days, while only 16% of the variance is attributable to these influences at 56 days. BRUMBY (1960) utilized embryo transfer techniques to study changes in both prenatal and postnatal maternal influences on growth among lines of mice selected for body weight by FALCONER (1955). He found that prenatal maternal effects had a much more important influence than has been reported by other workers with different strains.

The objective of this investigation was to characterize the magnitude and nature of the changes in the postnatal maternal influences of mice that had been subjected to long term selection for increased and decreased six-week body weight. Concomitantly, an assessment was to be made of the feasibility of using reciprocal cross-fostering among selected lines to evaluate maternal and genetic effects.

MATERIALS AND METHODS

The mice studied in this investigation were from two lines that had been selected on a within-family basis for increased and decreased body weight at six weeks of age for 40 generations,

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hereafter referred to as H_6 and L_6 , respectively. A third line (C_2) included in the study consisted of an unselected control maintained for 11 generations contemporaneously with the selected lines. All three lines originally were derived by reciprocally crossing two F_1 stocks (CAF_1 , $AKD2 F_1$) from The Jackson Laboratory, Bar Harbor, Maine.

Laboratory procedures: The reciprocal cross-fostering technique utilized in this experiment was similar in design to that followed by BATEMAN (1954), COX *et al.* (1959) and YOUNG *et al.* (1965), for cross-fostering within random bred strains. Only first litters were used. Three dams, (one each from H_6 , L_6 , C_2 mated with males of the same line) that littered within a 12-hour interval were assigned to each cross-fostering group. Each dam then nursed two of her own young and two from each of the other two females in her group. The remainder of the young were discarded. New-born mice were sexed, standardized to six mice, and uniquely identified for genetic line by toe clipping. The offspring were weighed individually, then randomly assigned to the postnatal dams in their particular cross-foster group. In two successive experiments, repeated over time, 132 cross-foster groups were formed from 396 litters.

At 12 days of age, litter weights and individual body weights were recorded, and the young were permanently identified by toe clipping. Mice were weaned at 21 days and weighed individually. At weaning, mice of the same genetic line were placed in postweaning cages with four mice per cage. Individual body weights were recorded at 42 and 56 days of age. All weights were recorded to the nearest tenth of a gram.

Shortly after the cross-fostered females were 56 days of age, they were randomly mated to unrelated males of the same genetic line. The total number born, number born alive, number in the litter at five days, and the 12-day weight of the standardized litter were subsequently recorded. In this part of the study, litters were standardized to three males and three females at five days. Litters of at least three mice were augmented to six with surplus mice from other litters of the same genetic line born on the same day. Litters of less than three mice at five days were discarded.

Statistical techniques: The experimental design utilized was a randomized complete block repeated over time with prenatal and postnatal dams arranged factorially in each block (cross-foster group). Of the 132 groups originally formed, 82 had at least one observation for each prenatal by postnatal cell at 56 days; and these groups were used in the analysis for growth traits. Forty-seven of the 82 groups were complete, but in 35 groups, one or at most two offspring had died at some time after the groups were formed. In each case when an individual was missing, the weights and gains for that particular individual were estimated by duplicating the weight of its surviving full-sib in the same prenatal by postnatal cell. The analysis was then completed as though all values were present, with one degree of freedom being subtracted from "Within cells" for each individual weight estimated (Table 1). The analysis of the prolificacy and 12-day litter weight for cross-fostered females included all females that littered with at least three offspring.

TABLE 1

Analysis of variance table for testing means

Source	df	Expected mean squares
Experiments (S)	1	$\sigma_e^2 + 18 \sigma_{g/s}^2 + 738 \theta s$
Groups in experiment (G/S)	80	$\sigma_e^2 + 18 \sigma_{g/s}^2$
Prenatal (A)	2	$\sigma_e^2 + 2 \sigma_d^2 + 492 \theta a$
Postnatal (P)	2	$\sigma_e^2 + 2 \sigma_d^2 + 492 \theta p$
Prenatal \times postnatal (A \times P)	4	$\sigma_e^2 + 2 \sigma_d^2 + 164 \theta ap$
Experiment \times prenatal (S \times A)	2	$\sigma_e^2 + 2 \sigma_d^2 + 246 \theta sa$
Experiment \times postnatal (S \times P)	2	$\sigma_e^2 + 2 \sigma_d^2 + 246 \theta sp$
Experiment \times pre- \times postnatal (S \times A \times P)	4	$\sigma_e^2 + 2 \sigma_d^2 + 82 \theta sap$
Experimental error	640	$\sigma_e^2 + 2 \sigma_d^2$
Within cells	738	σ_e^2

The form of analysis used in this experiment is presented in Table 1 and is based upon the model:

$Y_{ijklm} = \mu + s_i + g_{ij} + a_k + p_l + (sa)_{ik} + (sp)_{il} + (ap)_{kl} + (sap)_{ikl} + d_{ijkl} + e_{ijklm}$, where Y_{ijklm} represents an observation on the m th mouse of the l th postnatal and k th prenatal litter in the j th group of the i th experiment. The s_i , g_{ij} , a_k , and p_l are effects of the i th experiment, j th group within the i th experiment, k th line of prenatal dam and l th line of postnatal dam, respectively, where $i = 1, 2$; $j = 1, 2, \dots, 41$; $k, l = 1, 2, 3$; and $m = 1, 2$. The $(sa)_{ik}$, $(sp)_{il}$, $(ap)_{kl}$, and $(sap)_{ikl}$ are the accompanying interaction terms; while d_{ijkl} represents the experimental error and the e_{ijklm} include differences among full-sibs reared alike. In this model, g_{ij} , d_{ijkl} , and e_{ijklm} were assumed to be independent random variables with zero means and variances $\sigma^2_{g/s}$, σ^2_d and σ^2_e , respectively. The remaining effects were assumed to be fixed.

The form of analysis for the prolificacy and lactational traits was the same as that shown in Table 1 with the exception that groups within experiment (G/S), experimental error, and within cells sums of squares were pooled to provide the error term for tests of significance. This was necessitated by inequality in the subclasses which required the use of least squares procedures for non-orthogonal data (HARVEY 1960). Thus, the size of the matrix to be manipulated for the analysis shown in Table 1 would have been prohibitive.

The effects of particular biological importance in this study are a_k , p_l , and $(ap)_{kl}$. The a_k represent differences due to prenatal factors which include genetic line differences among the young and prenatal maternal differences due to uterine influences of the dam. The p_l effects arise from postnatal influences of the genetic line of the dams upon the litter they suckle. The $(ap)_{kl}$ represent the interaction between prenatal and postnatal effects. This interaction term was subdivided, *a priori*, into orthogonal contrasts as shown in Table 2. The first contrast measures the effect of fostering *per se*, since the comparison is among offspring nursed by their own dams and those nursed by foster dams of another line. The second contrast compares reciprocal effects such as HC *vs.* CH, HL *vs.* LH, and CL *vs.* LC. The third and fourth contrasts which complete the set are complex and have little direct biological interpretation.

Preliminary analyses indicated the need to adjust 42- and 56-day weight for sex differences. A procedure derived by FALCONER and KING (1953) was used to adjust for these differences. With this method, male and female weights within each genetic line were multiplied by $(1 + 1/r)/2$ and $(1 + r)/2$, respectively, where r is the ratio of the average weight of males to females.

The only other adjustment of the data was applied to 12-day weights of litters born to and nursed by females that had been cross-fostered. The 12-day weights of litters, with at least three but less than six mice surviving at this age, were adjusted to a basis of six mice by multiplying the weight of the litter by $6/N$, where N is the number of mice in the litter at 12-days.

RESULTS AND DISCUSSION

Prenatal and postnatal effects upon preweaning traits: Means and standard

TABLE 2
Orthogonal coefficients appropriate for single degree of freedom contrasts in the prenatal by postnatal interaction

Contrasts	Treatment combination*								
	HH	HC	HL	CH	CC	CL	LH	LC	LL
1	-2	+1	+1	+1	-2	+1	+1	+1	-2
2	0	+1	-1	-1	0	+1	+1	-1	0
3	-1	+1	0	+1	0	-1	0	-1	+1
4	-1	-1	+2	-1	+2	-1	+2	-1	-1

* The first letter refers to the prenatal line and the second to line of postnatal dam.

TABLE 3

Means and standard deviation of individual weights at birth (X_1), 12 days (X_2), 21 days (X_3) and gain from birth to 12 days (X_4) and 12 to 21 days (X_5)*

Line	Birth X_1		12-day X_2		21-day X_3		0 to 12 X_4		12 to 21 X_5	
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Prenatal Line										
H ₆	1.58	0.15	6.97	1.12	10.59	2.02	5.38	1.09	3.62	1.15
C ₂	1.50	0.14	6.93	1.03	10.18	1.69	5.43	1.01	3.25	0.96
L ₆	1.26	0.10	5.55	1.01	7.73	1.60	4.28	0.98	2.18	0.85
Postnatal Line										
H ₆	1.45	0.19	6.77	1.20	10.19	2.00	5.32	1.11	3.43	1.05
C ₂	1.45	0.19	6.95	1.14	10.22	2.02	5.50	1.03	3.27	1.09
L ₆	1.45	0.19	5.73	1.01	8.88	1.79	4.27	0.91	2.36	1.06

* Each mean includes 492 observations.

deviations for birth, 12-, and 21-day weight and gains from birth to 12 days and 12 to 21 days are shown in Table 3. Corresponding analyses of variance are presented in Table 4. The prenatal dam means in Table 3 refer to the individual weights of offspring born to high (H₆), control (C₂), and low (L₆) line dams.

TABLE 4

Analyses of variance for individual preweaning weights and gains

Source	df	Mean squares				
		Birth X_1	12-day X_2	21-day X_3	0 to 12 X_4	12 to 21 X_5
Experiments (S)	1	0.44*	1.18	26.32	2.98	14.64*
Group/Experiment (G/S)	80	0.06	3.87	9.33	3.64	3.26
Prenatal (A)	2	13.90**	323.47**	1177.73**	206.20**	277.32**
H ₆ vs. C ₂	1	1.57**	0.39	42.00**	0.46	...
(H ₆ + C ₂) vs. L ₆	1	25.72**	642.88**	2309.21**	412.67**	...
Postnatal (P)	2	0.01	214.21**	738.94**	216.63**	165.03**
H ₆ vs. C ₂	1	...	8.27**	0.17	8.10**	...
(H ₆ + C ₂) vs. L ₆	1	...	422.54**	1479.00**	427.52**	...
A × P	4	0.02	0.50	5.37	0.55	2.41*
(1) ^a	1	...	0.82	4.11	1.32	0.93
(2)	1	...	0.54	8.88	0.39	4.37*
(3)	1	...	0.27	3.55	0.22	1.59
(4)	1	...	0.30	5.00	0.33	2.46
S × A	2	0.01	0.02	3.54	0.01	2.87*
S × P	2	0.01	4.45*	6.15	4.16*	0.13
S × A × P	4	0.01	0.45	2.24	0.38	1.01
Experimental Error	640	0.02	1.08	2.72	1.02	0.91
Within Cells	738 ^b	0.01	0.26	0.85	0.22	0.35

* Statistically significant ($P < 0.05$).

** Statistically significant ($P < 0.01$).

^a See Table 2 for contrasts involved in the individual degree of freedom.

^b 738 df for X_1 , 729 for X_2 and X_4 , and 720 for X_3 and X_5 .

Postnatal dam means refer to the average weights of young that had been nursed by H_6 , C_2 and L_6 dams.

Differences in prenatal dam means were statistically significant ($P < 0.01$) for all five preweaning traits. Orthogonal contrasts in Table 4 indicated that selection for body weight at six weeks, plus differences in intra-uterine environment, have significantly increased the birth weight of the H_6 line and decreased the birth weight of the L_6 line. This correlated response has been asymmetrical. Due to a slightly more rapid growth rate from birth to 12 days in the C_2 mice, the difference between the H_6 and C_2 lines was not statistically significant at 12 days. At 21 days, H_6 offspring were again significantly larger than the C_2 . The L_6 offspring were significantly smaller ($P < 0.01$) than the average of the H_6 and C_2 at all three preweaning weight periods.

Postnatal birth weights shown in Table 3 indicated that random placement of mice in postnatal litters resulted in means that were identical to two decimal places. Postnatal orthogonal contrasts in Table 4 indicated that young which had nursed C_2 dams were significantly larger ($P < 0.01$) at 12 days of age due to a significantly more rapid ($P < 0.01$) growth rate between birth and 12 days than those that had nursed H_6 dams. Young that had been suckled by L_6 mothers were over a gram smaller at 12 days than those that had nursed either H_6 or C_2 dams (Table 3). At 21 days, there was no significant difference between weights of mice that had nursed H_6 and C_2 dams. This lack of difference was due largely to the fact that mice that had been suckled by H_6 mothers gained more rapidly from 12 to 21 days than those that had nursed C_2 dams. This suggests a tendency for H_6 dams to be slightly more persistent lactators than controls. However, no critical test of this point could be made from the present data, and the presence of the significant prenatal by postnatal interaction prevents a definitive conclusion.

Weaning weights of young that nursed L_6 dams were 1.31 grams lighter than those that nursed H_6 or C_2 dams; a reduction of about 13%. These results are similar to those of BUTLER and METRAKOS (1950), who found significant reductions in weaning weight for individuals nursing small strain dams.

It may be observed from Table 4 that the experiment by postnatal interaction was significant ($P < 0.05$) for 12-day weight and gain from birth to 12 days. In addition, significant ($P < 0.05$) interactions between experiments and prenatal effects were observed for gain from 12 to 21 days. The graphs in Figure 1 show that the interactions in 12-day weight and gain from birth to 12 days occurred because the offspring of C_2 dams were heavier in Experiment II than in Experiment I; whereas, the reverse was true for H_6 and L_6 . In regard to 12 to 21 day gain, the results for Experiments I and II were more divergent for H_6 than for C_2 and L_6 . However, the ranking of the prenatal and postnatal lines did not change for the two experiments. Since the interaction effects were not of sufficient magnitude to change the ranking of the lines, inferences regarding the main effects should be affected very little by these interactions.

The only other interaction of any consequence was the prenatal by postnatal interaction for gain from 12 to 21 days. This interaction is characterized by the graphs presented in Figure 2. There was no change in rank in prenatal means

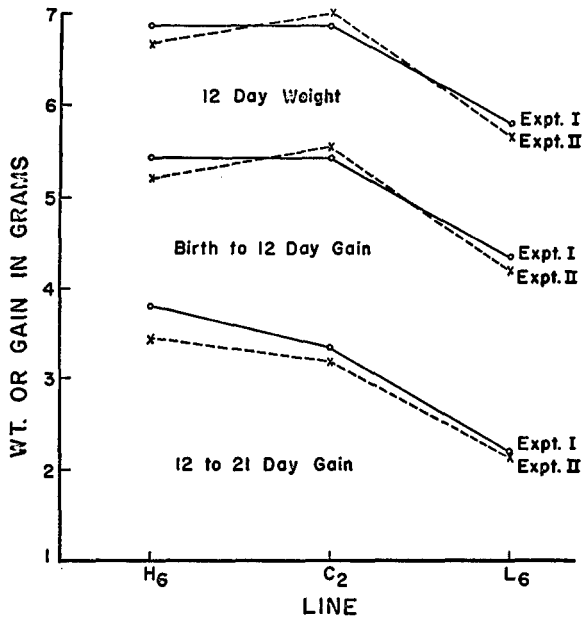


FIGURE 1.—Experiment by postnatal interaction for 12-day weight and birth to 12-day gain plus experiment by prenatal interaction for 12 to 21-day gain.

when considered over prenatal lines. Thirteen variables were analyzed and this particular $A \times P$ interaction was the only one that proved to be statistically significant. It might be presumed that the significance of this interaction was merely a chance occurrence. The single degree of freedom comparisons in Table

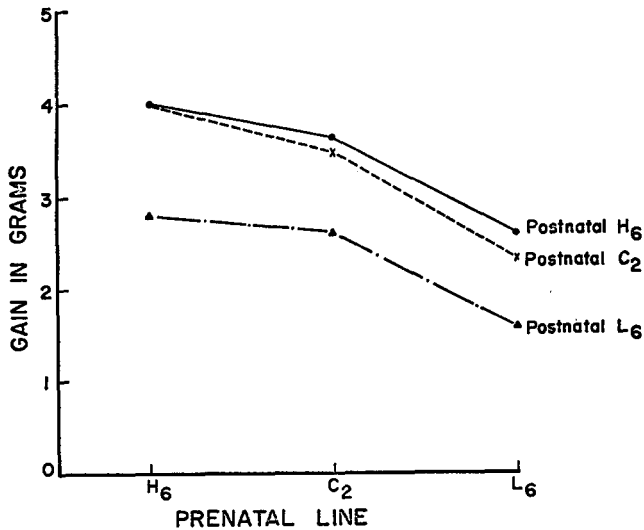


FIGURE 2.—Prenatal by postnatal interaction for gain from 12 to 21 days.

4 clearly show that the interaction did not arise from cross-fostering *per se* (comparison 1). Rather if this interaction is real, it most likely arose from differences between reciprocals (HC *vs.* CH, etc.).

None of the remaining $A \times P$ terms were important for preweaning traits. Apparently, dams of the three lines, when nursing a standardized litter of six young, of which two were her own and the other four were foster offspring, gave no preferential treatment to the young. Therefore, it may be concluded that this technique was useful in studying differences in maternal performance among these selected lines of mice. BATEMAN (1954), COX *et al.* (1959) and YOUNG *et al.* (1965) reported similar conclusions when fostering within a random line. BRUMBY (1960) found no effects due to fostering *per se* on preweaning weights when transferring entire litters among selected lines. However, he did report an apparent line of offspring by line of postnatal dam interaction in 21-day (weaning) weight.

Prenatal and postnatal effects upon postweaning traits: Postnatal maternal influences may be reflected in weights of the young taken after weaning. Postweaning gains may indicate another type of direct effect of the postnatal dam, in that compensatory growth may occur in those individuals that nursed poor mothers. Prenatal effects on postweaning weights and gains simply reflect line differences in growth rate and residual intra-uterine influences that may have not dissipated.

Means and standard deviations for postweaning weights and gains are presented in Table 5. It may be noted from the analyses of variance (Table 6) that experiment to experiment differences were apparent in postweaning growth. Experiment means in Table 4 for gain from 12 to 21 days were also significantly different. However, the same weight at 56 days was attained in both experiments.

It is apparent from the prenatal means in Table 5 that line differences existed

TABLE 5

*Mean and standard deviations for 42-day weight (X_6), 56-day weight (X_7), gain from 21 to 42 days (X_8) and gain from 42 to 56 days (X_9)**

Line	Trait							
	42-day X_6		56-day X_7		21 to 42 X_8		42 to 56 X_9	
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
	Prenatal Line							
H ₆	25.58	2.59	29.39	2.37	14.98	1.94	3.81	1.45
C ₂	23.12	2.43	26.21	2.22	12.92	1.84	3.10	1.44
L ₆	18.06	2.37	20.73	1.81	10.31	1.50	2.86	1.17
	Postnatal Line							
H ₆	22.83	3.69	25.85	4.08	12.62	2.45	3.03	1.31
C ₂	23.09	3.94	26.12	4.24	12.86	2.48	3.04	1.39
L ₆	20.84	3.94	24.35	3.97	12.73	2.85	3.52	1.54

* Each mean contains 492 observations.

TABLE 6

Analyses of variance for individual postweaning weights and gains

Source	df	Mean squares			
		42-day X_6	56-day X_7	21 to 42 X_8	42 to 56 X_9
Experiments (S)	1	204.57	2.06	381.38**	172.51**
Groups/Experiment (G/S)	80	12.86	11.06	8.12	4.33
Prenatal (A)	2	7234.73**	9438.02**	2703.49**	160.80**
H vs. C	1	1488.89**	2487.78**	1044.09**	124.01**
(H + C) vs. L	1	12977.19**	16394.67**	4345.96**	195.31**
Postnatal (P)	2	743.20**	451.04**	7.25	39.22**
H vs. C	1	16.62	18.38	14.17*	2.69
(H + C) vs. L	1	1474.19**	885.78**	0.03	78.21**
A × P	4	0.90	2.06	4.65	1.19
S × A	2	0.41	0.62	2.12	0.20
S × P	2	9.88	4.48	0.87	1.09
S × A × P	4	9.10	2.22	2.97	3.25
Experimental Error	640	6.49	4.99	3.46	2.07
Within Cells	701 ^a	2.87	2.52	1.78	1.10

* Statistically significant ($P < 0.05$).** Statistically significant ($P < 0.01$).^a 700 df for X_7 and X_9 .

for postweaning growth. The H_6 offspring were larger at both ages and grew more rapidly than the C_2 . As reported by LEGATES and FARTHING (1962), response to selection has been asymmetrical, since at six weeks of age the H_6 line was 2.46 g above and the L_6 line was 5.06 g below the C_2 .

Postnatal means in Table 5 reveal that there was practically no difference in six or eight-week weights between young that nursed H_6 dams and those that nursed C_2 dams. However, those offspring that nursed C_2 dams were consistently, though not significantly, larger than those that nursed H_6 dams. Large and statistically significant ($P < 0.01$) differences existed between the averages of mice nursed by H_6 and C_2 dams and the L_6 dams for both postweaning weights. The superior postnatal maternal performance of the H_6 and C_2 dams had a continuing influence on the postweaning growth of the young which they nursed without regard to the genotype of these young.

Compensatory growth did occur though it was delayed in its action, since all young gained at approximately the same rate from 21 to 42 days. From 42 to 56 days, compensatory growth was evident in those offspring that had nursed L_6 dams. However, this compensatory growth was not nearly enough to offset the weight advantage enjoyed by those individuals that had nursed either H_6 or C_2 dams. These results are in contrast to those reported by MACARTHUR (1949) who reported no differences at 30 or 60 days of age among offspring that had nursed large or small strain dams. The results are in partial agreement with those of BUTLER and METRAKOS (1950), who reported that the postnatal maternal effect of large line dams was permanent, in that individuals nursing large dams were

larger at all ages from two to 140 days. In contrast to the present study, they found that young nursing large strain females gained faster to weaning (16 days) than young nursing small strain mothers, but slower to about day 36, after which they grew at about the same rate.

None of the interactions for postweaning traits were statistically significant. Therefore, the orthogonal contrasts for $A \times P$ do not appear in Table 6. These results are not in agreement with previous cross-fostering experiments which were conducted within unselected lines (COX *et al.*, 1959; YOUNG *et al.*, 1965; and COX and WILLHAM, 1962) who reported sizeable $A \times P$ interactions in late postweaning gains in mice and pigs.

Prolificacy and maternal ability of cross-fostered females: Four maternal characters were measured on the cross-fostered females in an attempt to determine if a carry-over effect of the postnatal dam could be detected in the next generation. Data were recorded in the same manner as those for cross-fostering. That is, a cross-fostered female remained in the same prenatal by postnatal cell of the group, and the maternal characters were recorded as further measurements on the fostered females. Least squares means and standard errors for these traits are presented in Table 7, and least squares analyses of variance and non-orthogonal mean comparisons are given in Table 8. The complete model for each variable was fitted in the original analysis. However, since there were no significant interactions for any of the traits, the interaction sums of squares were pooled with the error term, and only mean squares for the main effects and error are shown in Table 8.

It is apparent from Table 7 that prenatal line differences were present in all variables. The mean comparisons among prenatal means in Table 8 give added credence to the conclusion that maternal performance in the C_2 line was superior to that in either the H_6 or L_6 line. Even though significantly larger ($P < 0.05$)

TABLE 7

Least squares means and standard errors of number born (X_{10}), number born alive (X_{11}), number in the litter at 5 days (X_{12}), and 12-day weights (X_{13}) of litters born to cross-fostered females

	Trait											
	Number born X_{10}			Number alive X_{11}			Number 5-days X_{12}			12-day weight X_{13}		
	Number of litters	Mean	S.E.	Number of litters	Mean	S.E.	Number of litters	Mean	S.E.	Number of litters	Mean	S.E.
Prenatal line												
H_6	387	9.42	0.13	387	8.34	0.13	347	8.05	0.14	303	36.98	0.31
C_2	385	9.04	0.13	385	8.89	0.13	368	8.55	0.13	354	38.13	0.30
L_6	298	6.97	0.15	298	6.80	0.15	283	6.64	0.15	247	28.15	0.36
Postnatal line												
H_6	364	8.54	0.13	364	8.10	0.13	338	7.74	0.14	297	34.28	0.33
C_2	362	8.57	0.13	362	8.05	0.13	337	7.91	0.14	312	35.13	0.32
L_6	344	8.33	0.14	344	7.88	0.14	323	7.60	0.14	295	33.85	0.32

TABLE 8

Least squares analyses of variance and non-orthogonal comparisons for maternal traits on cross-fostered females

Source	df	Mean squares			
		Number born \bar{X}_{10}	Number alive \bar{X}_{11}	No. 5 days \bar{X}_{12}	12-day weight \bar{X}_{13}
Experiments (S)	1	6.01	5.24	22.07	8171.25**
Prenatal (A)	2	564.87**	385.18**	302.45**	8060.40**
Postnatal (P)	2	6.24	5.04	8.17	128.12*
Error ^a	1064	6.35	8.24	6.51	31.57
Comparison		Mean differences			
Prenatal					
H vs. C		0.37*	-0.55**	-0.50**	-1.15**
H vs. L		2.45**	1.54**	1.41**	8.83**
C vs. L		2.08**	2.09**	1.91**	9.98**
Postnatal					
H vs. C		-0.03	0.05	-0.17	-0.85
H vs. L		0.02	0.22	0.14	0.43
C vs. L		0.24	0.17	0.31	1.28**

* Statistically significant ($P < 0.05$).

** Statistically significant ($P < 0.01$).

^a 992 df for number at five days, and 898 for 12-day litter weight.

litters were born to H_6 dams, C_2 litters were actually larger than H_6 litters in the number of mice born alive. Litter size for the C_2 was also significantly ($P < 0.01$) larger at five days and the litters were heavier at 12 days. It was observed that H_6 females appeared to be rather nervous at parturition, and many instances of still-birth and cannibalism immediately after birth were observed. These results partially agree with those of FALCONER (1953) who observed that total litter size increased with selection for large body size and decreased with selection for small body size. LEGATES *et al.* (1958) have reported similar correlated responses in the lines used in the present investigation. However, the advantage observed for C_2 over H_6 dams in 12-day litter weight is contrary to results reported by either FALCONER (1953) or LEGATES *et al.* (1958). Both reported positive correlated responses, in that 12-day weights of high line litters were larger than controls. Both earlier reports were concerned with data collected from the early generations of selection (9 generations in both cases) when little inbreeding depression would be expected.

No significant differences were observed between postnatal means presented in Table 7, except among the mean 12-day litter weights. However, the means show a tendency for those females that had been nursed by L_6 dams to have smaller litters than those that had been nursed by either H_6 or C_2 dams. YOUNG *et al.* (1965) reported no effect of postnatal mother on the number of offspring born when cross-fostering within a population from the same genetic base as the C_2 line.

The comparisons in Table 8 show that the significant postnatal difference in 12-day litter weight was primarily associated with differences in weights of litters born to those females that had been subjected to the poorest maternal environment, L_6 , and those that had been subjected to the superior maternal environment, C_2 . YOUNG *et al.* (1965) reported essentially no effect due to postnatal dam on 12-day litter weight of cross-fostered females within a randomly maintained line (C_1) arising from the same genetic foundation as the lines studied here. Due to the fact that fostering was done within a random line, differences in postnatal effects may not be expected to be as large as those in the present study.

GENERAL DISCUSSION

When a selection response is realized for body size, a change in the maternal environment provided for the next generation may result. The mice used in the present investigation had been selected within litters, a scheme which is designed to avoid direct selection for maternal environment. However, the existence of a possible genetic relationship between growth and maternal performance must be examined.

From the results presented in the preceding sections, it is apparent that both prenatal and postnatal maternal effects were important in determining preweaning growth in these three lines of mice. Maternal performance in the L_6 line had been drastically reduced. Since it was shown that the line of preweaning dam had a very definite effect on postweaning weights, it can be concluded that the asymmetrical response to selection for weight at six weeks in these lines observed by LEGATES and FARTHING (1962) could be explained at least in part by this reduction in maternal performance in the L_6 line. Large reductions in maternal performance of mice selected for low six-week weight also have been reported by FALCONER (1953, 1955) and FALCONER and KING (1953). However, the slight, but significant, reduction in maternal performance of the H_6 line has not been previously reported, and a discussion of possible mechanisms behind this phenomenon is in order.

YOUNG and LEGATES (1965) reported small and non-significant, but consistently positive, genetic correlations between postnatal maternal performance, as reflected by the 12-day litter weight, and preweaning and early postweaning gains. Negative genetic correlations between postnatal maternal performance and gains from six to eight weeks were found in mice similar to the control line used in the present investigation. They attributed these correlations to a positive genetic relationship between postnatal maternal performance and protein anabolism and a negative one between postnatal maternal performance and fat deposition, which they assumed took place largely after six weeks. Based strictly on the genetic correlation, at least a slight improvement in maternal performance in the high line should have been realized after 40 generations of selection for body weight.

A second possible explanation of the discrepancy is the inbreeding depression. Inbreeding depression has been postulated by FALCONER (1953), FALCONER and

KING (1953), and LEGATES *et al.* (1958) to be at least in part responsible for the asymmetry of response to selection for large and small body weight in mice. In early generations of selection when inbreeding was low, FALCONER (1953) and LEGATES *et al.* (1958) have reported correlated increases in 12-day weight. Since maternal ability probably is more closely related to fitness than six-week weight, inbreeding depression would more likely have a larger effect on 12-day weight. There was a rather wide divergence in the coefficient of inbreeding between the control line, which had been in existence for only 11 generations, and the selected lines which had been continued for 40 generations. The average inbreeding coefficients through generation 26 were 25 and 31% for the high and low lines, respectively. By projecting the rate of increase in inbreeding during generations 20 to 26, estimated inbreeding coefficients of 40 and 50% are obtained for the H₆ and L₆ lines, respectively, in generation 40. The inbreeding coefficient for generation 11 of the C₂ was 6%. Therefore, the selected lines were much more inbred than the control line, and should have exhibited more inbreeding depression.

When the cross-fostered females were mated, the 12-day litter weights of litters born to C₂ dams were significantly heavier than those born to H₆ dams. These weights reflect both the genotype for growth in the young and the maternal performance of the dam, and the two could not be separated. However, it had been shown earlier that even though the C₂ offspring grew slightly faster from birth to 12 days than contemporary H₆ young, this difference did not approach statistical significance. It simply counteracted the advantage of the H₆ offspring in birth weight. Since H₆ females were significantly poorer mothers than C₂, and they were more inbred, the difference in part might be attributed to inbreeding depression.

A third line of reasoning is based on LERNER's (1954) concept of genetic homeostasis as modified by FALCONER (1955). This argument is based upon the assumption that maternal performance has two components, one related to anatomical development and the other to physiological efficiency. The anatomical component, larger mice have larger mammary glands, should be directly related to body size and increase as size increases in the H₆ line and decrease in the same way in the L₆ line. The physiological component, however, should not be directly related to body size, but rather would be a component of fitness and hence, should exhibit overdominance as postulated by LERNER (1954). The physiological component would then decrease in both lines as a result of the increased homozygosity brought about by changes in gene frequency due to selection and inbreeding. In the H₆ line, these forces would tend to counter-balance each other; and in the L₆ line, both would cause a rather large net decrease.

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SUMMARY

A reciprocal cross-fostering study was conducted with three lines of mice, two of which had been subjected to long term selection for six-week weight (H₆ and

L₆) and the other an unselected control line (C₂). The objective of the study was to investigate the magnitude and nature of line differences in prenatal and postnatal maternal influences upon growth and maternal ability. A total of 132 cross-foster groups were formed. Eighty-two of the above groups that were relatively complete when the young reached eight weeks of age were included in the analysis of maternal effects on growth. Cross-fostered females from all groups were included in the analyses of carry-over effects on maternal traits. Both prenatal and postnatal maternal effects were important in determining preweaning and postweaning growth of the three lines. Maternal performance in the L₆ line was markedly reduced, and the measures of the maternal performance of the H₆ line also were below those for the C₂. Since previous results have not supported a strong negative genetic relationship between growth and maternal ability, the increased inbreeding in the selected lines presumably permitted inbreeding depression to reduce maternal performance in both lines. Part of this depression probably was counter-balanced in the H₆ line due to the increase in body weight accompanying selection. Prolificacy and ability to maintain the litter to five days of age were not affected by line of postnatal dam. These traits were affected by the line from which cross-fostered females received their genetic complement. The lactational performance of cross-fostered females was significantly affected by both the prenatal and the postnatal line. The relative absence of any prenatal by postnatal interaction indicated that reciprocal cross-fostering was a valid and useful technique for studying maternal effects among these lines of mice. Tests of significance for an effect due to fostering *per se* proved to be negligible for all weights and gains.

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