PRENATAL AND POSTNATAL MATERNAL INFLUENCES ON GROWTH IN MICE SELECTED FOR BODY WEIGHT[1]

R. W. MOORE,[2] E. J. EISEN AND L. C. ULBERG

Animal Science Department, North Carolina State University, Raleigh, N. C.

Received June 25, 1969

ONE method of studying the inheritance of body size in mammals involves the divergent selection of lines for large and small size. A difficulty encountered in this type of experiment is that the differences obtained in body weight or in traits genetically correlated with body size may not be due solely to the genotype for growth rate *per se*, but may include prenatal and postnatal maternal differences between the two lines which have arisen as a correlated response to selection. Correlated changes in postnatal (lactational) maternal effects have been observed in mice, even when selection is made on a within-litter basis (BRUMBY 1960; WHITE, LEGATES and EISEN 1968). BRUMBY (1960) transferred embryos and cross-fostered whole litters between two lines of mice selected by FALCONER (1955) for high and low six-week body weight, and found marked correlated changes in prenatal (uterine) maternal effects on birth weight and subsequent growth rate. EL OKSH, SUTHERLAND and WILLIAMS (1967) isolated genetic prenatal maternal and postnatal maternal effects on birth weight and growth rate within a line of mice by superimposing sire groups on a cross-fostering scheme similar to that of COX, LEGATES and COCKERHAM (1959) and YOUNG, LEGATES and FARTHING (1965) and by sib analysis. The results from the two techniques were in good agreement and showed that the uterine effect on body weight was large at birth and then decreased rapidly to the age of six weeks.

The objective of the present study was to characterize the changes in prenatal maternal effects (as they environmentally influence the growth rate of the progeny from the blastocyst stage to 10 weeks of age) in two genetically different strains of mice developed by long-term selection for either increased or decreased six-week body weight. A previous cross-fostering study had clearly demonstrated a sizeable line difference in postnatal maternal influences on growth rate of these mice (WHITE *et al.* 1968). Data on embryo mortality will be given in a subsequent paper.

MATERIALS AND METHODS

Nulliparous mice used in this study were obtained from random matings within two lines selected for high and low body weight at six weeks of age, hereafter referred to as H_6 and L_6,

[1] Paper No. 2907 of the Journal series of the North Carolina State University Agricultural Experiment Station, Raleigh, North Carolina. This research was supported in part by Public Health Service Research Grants No. HD02923 and GM11546. Computing services were supported by NIH Grant No. FR-00011.

[2] Present address: Laboratory of Reproductive Physiology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, Pa.

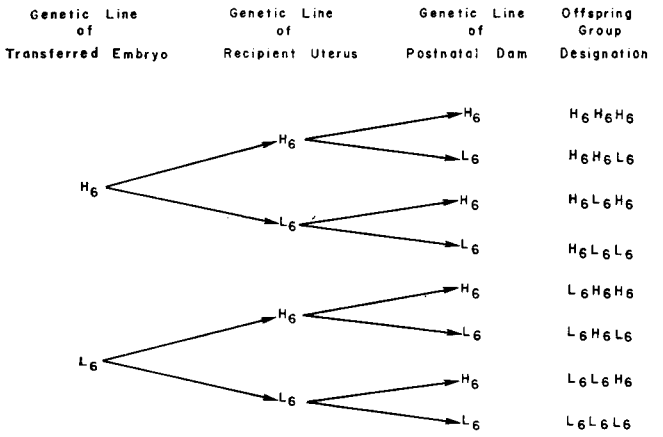

FIGURE 1.—Procedure used to form offspring groups, indicating the genotype of the embryo, the genotype of the uterus in which it developed and the genotype of its postnatal dam. H_6 is the line selected for large six-week weight and L_6 is the line selected for small six-week weight.

respectively. These lines have been previously described by ELLIOTT, LEGATES and ULBERG (1968) and by WHITE *et al.* (1968). Selection was carried out on a within-litter basis in order to minimize maternal and inbreeding effects.

Experimental procedures: The two lines of embryos (donors) were transferred to the two lines of uteri (recipients). Thus, four types of embryo-uterine relationships existed: (1) H_6 embryos into H_6 uteri, (2) H_6 embryos into L_6 uteri, (3) L_6 embryos into H_6 uteri and (4) L_6 embryos into L_6 uteri. Approximately one-half of the litters within each type of relationship were cross-fostered at birth. This procedure resulted in a 2^3 factorial experiment, i.e. eight offspring groups (Figure 1), temporally replicated once.

Donors were injected once with 10–15 internatl. units of pregnant mares' serum gonadotrophin (PMSG) at about 5:00 PM. Forty-eight hours later they were injected with 10 i.u. of human chorionic gonadotrophin (HCG) and pair-mated with a male of the same line. On the following morning, females were examined for the presence of a copulatory plug to determine if mating had occurred. At about 3:00 PM on Day-3 of pregnancy (the day of detection of the plug being defined as Day-0), females which had mated were sacrificed and their uteri were flushed. Most of the embryos were in the early blastocyst stage at this time, and only this type of embryo was transferred into the uterus of the recipient. The medium used for flushing and transfer of embryos was described by BRINSTER (1965).

Recipient females were caged continuously with vasectomized males and were examined each morning for the presence of copulatory plugs. They were used as recipients on Day-3 of pseudopregnancy, as defined above.

The embryos were counted into a finely drawn glass pipette containing a minimal amount of the transfer medium. The recipient was anesthetized with metofane (Methoxyflurane, Pitman-Moore), and a single median dorsal incision was made through the skin. This incision was pulled to one side until the ovary was observed through the body wall. A small incision was made through the muscle and peritoneum and the ovary and uterine horn were removed from the body cavity by means of forceps attached to the fat pad. The uterine horn was then held firmly by another pair of forceps so that it could be pricked by a 30 gauge needle to form a small opening into the uterine lumen. The end of the pipette was then inserted through this opening and the medium containing the embryos was ejected from the pipette into the lumen of the uterus. The tip of the pipette was moved gently back and forth to make certain it was in the lumen of the uterus. The above procedure was repeated by moving the skin incision to the opposite side of the

mouse. Two wound clips closed the skin incision and the recipient female was immediately isolated in a clean polypropylene cage.

In the first replicate, a total of 611 embryos was transferred into 61 recipients; the mean number transferred per recipient and the standard error was 10.02 ± 0.29. In the second replicate, the totals were 1570 embryos into 105 recipients; the mean number was 14.95 ± 0.46.

Recipient females were examined for litters at 9:00 AM and 6:00 PM daily. The numbers born, alive and dead, were recorded at the time of littering. At that time, where cross-fostering was carried out, whole litters were exchanged between dams that had littered within a 9-hr period.

Dams and their litters were maintained in polypropylene cages under husbandry conditions similar to those described by EISEN (1966). Individuals alive within each litter were weighed at birth and subsequently at 1, 2, 3 and 4 weeks of age to the nearest tenth of a gram. Litters were weaned at four weeks of age and placed, six to a cage, according to four different classes: H_6 males, H_6 females, L_6 males, and L_6 females. After four weeks, the weekly weighing was continued but was not always on the day of the week that the individual was born. These data were converted to equal weekly intervals after birth by assuming that the growth rate within a particular weekly interval was linear. All mice were weighed until they reached 10 weeks of age.

Statistical Analyses: The data were analyzed by the method of least squares for unequal subclass numbers as described by HARVEY (1960).

Birth weights of mice recorded as born dead were not included in the prenatal growth analysis. The remaining data on birth weight were divided into two viability classes: (1) alive at one week of age or (2) dead before one week. No difference between males and females was detected for birth weight so that a sex effect was not included in the model. There were 415 live birth weights recorded and analyzed according to the following model:

$Y_{ijklm} = \mu + r_i + g_j + u_k + v_l + (gu)_{jk} + (gv)_{jl} + (uv)_{kl} + \beta X_{ijklm} + \varepsilon_{ijklm}$, where Y_{ijklm} represents the birth weight of the m^{th} individual in the $ijkl^{th}$ subclass. The r_i, g_j, u_k and v_l are effects of the i^{th} replicate, j^{th} line of embryo, k^{th} line of prenatal dam and l^{th} viability classification ($i, j, k, l = 1, 2$), respectively. The $(gu)_{jk}$, $(gv)_{jl}$ and $(uv)_{kl}$ are the accompanying interaction effects while ε_{ijklm} represents experimental error. The term X_{ijklm} is the total number of mice born (alive plus dead) in the individual's litter and β equals the linear regression of birth weight on total number born. All main effects in the model were regarded as fixed effects. The interactions of the effect of replication with the other main effects were not statistically significant and were pooled with the error term, as were all second and higher order interactions.

Analyses of body weights from one to ten weeks were carried out on 217 mice for which there were complete postnatal growth records to 10 weeks of age. The following statistical model was used to describe a single observation of body weight at a particular age:

$$Y_{ijklmn} = \mu + r_i + g_j + u_k + p_l + s_m + (gu)_{jk} + (gp)_{jl} + (gs)_{jm} + (up)_{kl} + (us)_{km} + (ps)_{lm} + \beta X_{ijklmn} + \varepsilon_{ijklmn},$$

where Y_{ijklmn} represents an observation on the n^{th} individual in the $ijklm^{th}$ subclass. The additional main effects in the second model are p_l and s_m which are the effects of the l^{th} line of postnatal dam and the m^{th} sex, respectively ($l,m = 1,2$). The $(gp)_{jl}$, $(gs)_{jm}$, $(up)_{kl}$ and $(ps)_{ln}$ are the added interaction effects which clearly were not present for birth weight. The term X_{ijklmn} is either the number of mice in an individual's litter at the age of measurement (1 to 4 weeks) or at weaning (5 to 10 weeks) and β is the regression of body weight at the specified age on X_{ijklmn}. The added main effects in the second model, p_l and s_m, are also assumed to be fixed effects. As in the case of the prenatal growth data, the interactions of replicate effects with the other main effects were not statistically significant and were pooled with the error term, together with the second and higher order interactions.

The terms of particular biological significance in the present study are g_j, u_k, p_l, $(gu)_{jk}$, $(gp)_{jl}$ and $(up)_{kl}$. The g_j effect represents the genetic differences between the H_6 and L_6 lines for growth rate in the young. The u_k effect contains any prenatal maternal differences between the lines due to the uterine influence of the dams. In a previous cross-fostering study (WHITE *et al.* 1968), involving the same selected lines as those used in the present experiment, it was not possible to separate the total prenatal effect into its component parts, $g_j + u_k + (gu)_{jk}$. The

TABLE 1

Least-squares estimates of replicate, genotype, uterine, viability classification, and interaction effects on birth weight (g) adjusted for number born

Source of variation	Differences as percent of mean	Least-squares estimate
Overall mean	. .	1.467
Replicate (r)†	3.7	0.027**
Genotype of offspring (g)‡	11.0	0.081**
Uterine environment (u)‡	3.9	0.029**
Viability to one week of age (v)§	6.2	0.045**
g × u	. .	—0.018*
g × v	. .	0.009
u × v	. .	—0.001
Linear regression	. .	—0.047**

* $P < 0.05$. ** $P < 0.01$.
† A positive value means that the first replicate was greater than the second replicate.
‡ A positive value means that H_6 was greater than L_6.
§ A positive value means viability classification 1 was greater than viability classification 2.

term $(gu)_{jk}$ represents the interaction between genetic growth factors and prenatal maternal factors.

Postnatal maternal differences between the two lines, p_l, generally have been attributed to lactational performance although behavioral factors cannot be discounted. The remaining terms, $(gp)_{jl}$ and $(up)_{kl}$, are the interactions of the genotype of the embryo with postnatal maternal factors and prenatal maternal by postnatal maternal effects, respectively.

RESULTS AND DISCUSSION

Effect of genotype of the offspring and the prenatal maternal environment on prenatal growth: Table 1 shows that all main effects were significant for birth weight. Their relative magnitudes are assessed by the differences expressed as a percentage of the overall mean.

This indicates that the H_6 young grew at a more rapid rate during prenatal development than did the L_6 young ($P < 0.01$). The uterine environment provided by the H_6 dams was superior to that of the L_6 dams ($P < 0.01$). However, the genetic effect on prenatal growth was more than twice that of the uterine effect. The mice that were able to survive to one week of age (viability classification) had larger birth weights than nonsurvivors ($P < 0.01$). The absence of any significant genotype-by-viability class or uterus-by-viability class interactions suggests that the birth weights of survivors to one week of age were greater than nonsurvivors by approximately the same amount in both genetic lines.

The genotype-by-uterus interaction for birth weight was statistically significant ($P < 0.05$), although it was small in magnitude relative to uterine and genetic effects. The adjusted least-squares means (Table 2) show that the L_6 embryos grew at a faster rate in the uterus of H_6 dams than in the L_6 uterus. In contrast, the H_6 embryos grew at only a slightly lower rate in the uterus of L_6 dams compared with the H_6 uterus.

One possible explanation for this interaction is that selection has lessened the

TABLE 2

Birth weights (g) with replicates pooled: unadjusted means, least-squares means, and number of observations in the eight subgroups

Subgroup†	Number of observations	Unadjusted means	Least-squares means‡
	Survived to one week of age		
H_6H_6	49	1.67	1.61
H_6L_6	79	1.57	1.59
L_6H_6	75	1.43	1.47
L_6L_6	88	1.34	1.38
	Dead before one week of age		
H_6H_6	13	1.63	1.50
H_6L_6	27	1.46	1.48
L_6H_6	35	1.36	1.40
L_6L_6	49	1.31	1.30

† The first symbol designates the genotype of the embryo and the second symbol designates the genotype of recipient uterus.
‡ Adjusted for number born.

ability of the L_6 uterus to supply nutrients to the fetus. However, the L_6 uterus still functions at its maximum when it contains embryos having a greater demand for nutrients. BRUMBY (1960) postulates that the uterus of the genetically small mouse has been decreased in size and the uteri of both the large and small mouse have been decreased in efficiency. If this is correct then the above reasoning suggests that the decrease of efficiency in the L_6 uterus is also the result of a decrease in the demand by the embryo. In previous studies with mice (BRUMBY 1960) and rabbits (VENGE 1950) the genetic and uterine effects were similar in size and were additive. HUNTER (1956) and DICKINSON *et al.* (1962) also found a genotype-by-uterus interaction in birth weight when they performed embryo transfer experiments between large and small breeds of sheep. However, this interaction was due to a genetically small single lamb reaching its full genetic size in its normal uterus.

Genotype of the offspring effects and prenatal and postnatal maternal effects on postnatal growth rate: The least-squares means of male and female body weights from one to ten weeks of age for the eight different offspring groups are shown in Figure 2. The corresponding least-squares estimates of the main effects are summarized in Tables 3, 4 and 5. The regression coefficients of body weight on litter size were negative throughout the growth period, indicating that there was a tendency for growth to decrease as litter size increased.

The average body weight of the H_6 progeny was significantly larger than L_6 progeny at all ages. The absolute difference in growth rate of H_6 *vs.* L_6 mice increased continuously from one to ten weeks. However, the maximum difference between the lines, expressed as a percentage of the mean, was reached at five weeks of age and remained relatively stable thereafter. These results confirm previous studies which have demonstrated differences in growth rate from birth to maturity between the H_6 and L_6 populations as a correlated response to selec-

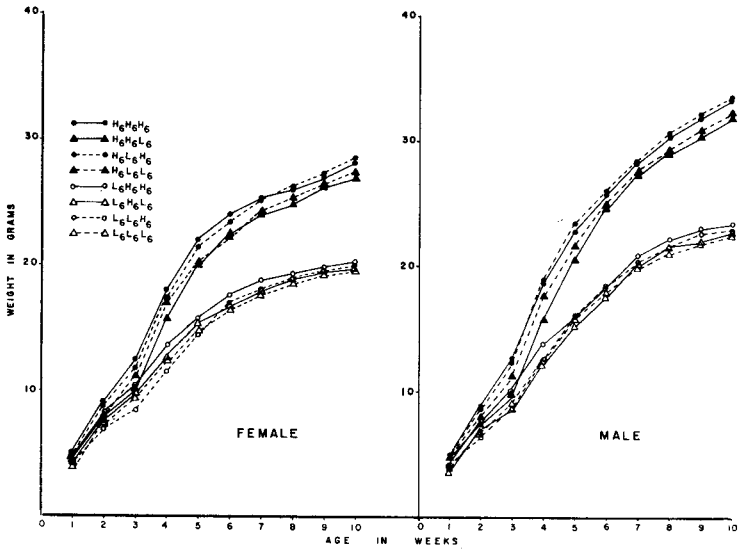

FIGURE 2.—The least-squares means of male and female body weight from one to ten weeks of age for the eight different offspring groups. Genotype sequence is that of the embryo, the uterus and the postnatal dam.

TABLE 3

Least-squares estimates of replicate, genotype, uterine, postnatal, sex and interaction effects on body weights (g) from 1 to 4 weeks adjusted for number alive

Source of variation	1 Week		2 Weeks		3 Weeks		4 Weeks	
	Differences as percent of mean	Least-squares estimate	Differences as percent of mean	Least-squares estimate	Differences as percent of mean	Least-squares estimate	Differences as percent of mean	Least-squares estimate
Overall mean	..	4.347	..	7.823	..	10.370	..	15.022
Replicate(r)†	1.5	0.033	6.5	0.253**	9.7	0.505**	11.2	0.843**
Genotype(g)‡	18.3	0.399**	13.4	0.522**	21.0	1.091**	21.9	2.395**
Uterine(u)‡	0.4	0.008	4.5	0.177*	2.0	0.105	0.5	0.036
Postnatal(p)‡	7.1	0.155**	6.9	0.270**	9.5	0.494**	7.4	0.558**
Sex(s)§	—1.6	—0.036	—4.9	—0.191*	—0.9	—0.047	3.3	0.248
g × u	..	—0.029	..	—0.230**	..	—0.285*	..	—0.385*
g × p	..	0.009	..	0.238**	..	0.365**	..	0.335
g × s	..	0.025	..	0.099	..	0.119	..	0.157
u × p	..	0.101*	..	0.219**	..	0.414**	..	0.451**
u × s	..	—0.077	..	—0.037	..	—0.137	..	—0.160
p × s	..	0.020	..	0.020	..	0.121	..	0.156
Linear regression	..	—0.087**	..	—0.425**	..	—0.605**	..	—0.537**

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

† A positive value means replicate 1 greater than replicate 2.

‡ A positive value means H_6 greater than L_6.

§ A positive value means that males were heavier than females.

tion for six-week body weight (WHITE *et al.* 1968). The present design, however, has provided an estimate of the average genetic effect on the growth curve due to directional selection for six-week weight which is unencumbered by either prenatal or postnatal maternal influences.

The postnatal maternal effect on growth rate was significant for all ages, reaching a maximum at the third week with a continual decrease in size for the remainder of the period. The genetic effects were twice as large as the postnatal effects from one to three weeks and four times as large at four weeks. This large decrease in the relative postnatal influence on growth during the period between three and four weeks is not surprising because most of the young mice were probably receiving little milk from their postnatal dams by three weeks post partum, even though they were not weaned until four weeks of age. The postnatal effects were a tenth of the genetic effects by ten weeks of age, though the former influences were still significant. These results are in close agreement with those reported by WHITE *et al.* (1968) for the H_6 and L_6 lines.

It is apparent from the present results that selection for decreased six-week body weight has led to a decrease in lactational performance, whereas selection for increased six-week body weight has resulted in a probable increase. However, it should be pointed out that inbreeding depression for postnatal maternal performance has probably nullified the positive correlated response in postnatal maternal performance in the H_6 line while magnifying the negative correlated response in the L_6 line (WHITE *et al.* 1968).

The most interesting feature of the postnatal growth data is the relatively

TABLE 4

Least-squares estimates of replicate, genotype, uterine, postnatal, sex and interaction effects on body weights (g) from 5 to 8 weeks adjusted for number alive at weaning

Source of variation	5 Weeks		6 Weeks		7 Weeks		8 Weeks	
	Differences as percent of mean	Least-squares estimate	Differences as percent of mean	Least-squares estimate	Differences as percent of mean	Least-squares estimate	Differences as percent of mean	Least-squares estimate
Overall mean	..	18.486	..	20.910	..	22.821	..	24.081
Replicate(r)†	3.4	0.318	2.5	0.260	4.4	0.503**	4.7	0.566**
Genotype(g)‡	33.3	3.077**	32.3	3.378**	31.6	3.601**	31.2	3.759**
Uterine(u)‡	0.1	0.012	0.6	0.065	0.3	0.035	0.1	0.010
Postnatal(p)‡	5.7	0.530**	4.9	0.510**	3.6	0.415**	3.6	0.433**
Sex(s)§	5.5	0.511**	8.4	0.882**	12.0	1.368**	14.4	1.736**
g × u	..	—0.166	..	—0.001	..	—0.142	..	—0.240
g × p	..	0.392*	..	0.156	..	0.095	..	0.182
g × s	..	0.143	..	0.331*	..	0.282	..	0.353*
u × p	..	0.162	..	0.047	..	0.109	..	—0.014
u × s	..	—0.273	..	—0.156	..	—0.040	..	0.044
p × s	..	0.089	..	—0.065	..	—0.015	..	0.037
Linear regression	..	—0.467**	..	—0.416**	..	—0.383**	..	—0.304**

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

† A positive value means replicate 1 greater than replicate 2.

‡ A positive value means H_6 greater than L_6.

§ A positive value means male greater than female.

TABLE 5

Least-squares estimates of replicate, genotype, uterine, postnatal, sex and interaction effects on body weights (g) from 9 to 10 weeks adjusted for number alive at weaning

Source of variation	9 Weeks		10 Weeks	
	Differences as percent of mean	Least-squares estimate	Differences as percent of mean	Least-squares estimate
Overall mean	..	25.067	..	25.911
Replicate(r)†	5.4	0.676**	4.3	0.555**
Genotype(g)‡	32.3	4.048**	34.5	4.464**
Uterine(u)‡	—0.3	—0.038	—0.1	—0.013
Postnatal(p)‡	3.4	0.421**	3.5	0.449**
Sex(s)§	14.9	1.873**	15.3	1.989**
g × u	..	—0.194	..	—0.178
g × p	..	0.121	..	0.193
g × s	..	0.425*	..	0.492*
u × p	..	0.039	..	0.029
u × s	..	—0.015	..	0.028
p × s	..	0.108	..	0.028
Linear regression	..	—0.278**	..	—0.312**

* $P < 0.05$. ** $P < 0.01$.
† A positive value means replicate 1 greater than replicate 2.
‡ A positive value means H_6 greater than L_6.
§ A positive value means male greater than female.

minor influence of uterine effects on this characteristic. Although the uterine effect was significant at birth, only in the second week postnatally did it again reach significance. This throws some doubt on the statement by BRUMBY (1960) that "a major portion of the maternal influence of the female on the growth of her young occurs during the prenatal period." He based this statement on two results in his work. First, that two groups of young mice which differed only in the effect of the uterus deviated in growth at six weeks of age. This deviation at six weeks could be an anomaly; if uterine effects on growth are real, it is difficult to see any reason why they should suddenly appear at six weeks. His other reason was that the growth rate of small-strain young reared by large-strain females proved no better than that of small-strain young reared by small-strain females. He concluded from this that the postnatal environment of the large strain was no better; and as he had already observed a difference in the total maternal performance of the two strains, he concluded that the difference between the maternal performance of the strains lies in the prenatal stage. This is a questionable conclusion, particularly since the large-strain mice reared by small-strain mice were smaller at weaning than those reared by large-strain mice. A more likely interpretation is that the small mice consumed less milk. Consequently, stimulus for milk production decreased in the larger dams.

The sex effect showed an unusual phenomenon at two weeks of age since females were significantly heavier than males. However, males became significantly larger than females by five weeks of age, and this difference continued to increase in magnitude to ten weeks of age. There was no significant interaction

of sex with either prenatal or postnatal maternal influences. The genotype-by-sex interaction was significant in the later weeks of postweaning growth, as the sex difference was greater in the H_6 than the L_6 line. That this interaction persists to mature body size has been suggested by the presence of a significant genotype-by-sex interaction in these lines for the estimated asymptotic body weights obtained by fitting the logistic function to individual growth curves (EISEN, LANG and LEGATES 1969).

The genotype-by-uterus interaction was negative throughout and was significant for the second, third and fourth week. The L_6 individuals that were grown in an H_6 uterus had a tendency to grow more rapidly than the L_6 individuals grown in an L_6 uterus. This result might be explained, in part, by the fact that L_6 individuals from the H_6 uterus had a larger birth weight. The genotype-by-postnatal maternal interaction was positive throughout and significant for the second, third and fifth week. This result was due to a slight tendency for H_6 and L_6 individuals to grow relatively better in their own postnatal maternal environment, probably due to some behavioral compatibility. The prenatal-by-postnatal maternal interaction was positive and significant for the first four weeks, probably indicating a cross-fostering effect.

The results in the present study agree with those of BUTLER and METRAKOS (1950) and of WHITE *et al.* (1968) that there are postnatal maternal effects on postnatal growth in lines of mice selected for adult body weight. They do not agree with MACARTHUR (1949) who found that postweaning weights were not affected by preweaning milk source. The results also agree with BRUMBY (1960) who found an interaction between the strain of postnatal mother and the strain of offspring being reared. This interaction was not observed by BUTLER and METRAKOS (1950) or by WHITE *et al.* (1968). The H_6 and L_6 strains of mice used by WHITE *et al.* (1968) were the same as those used in this study. Therefore, the absence of the above interaction in their data has to be reconciled with the present study. One reason for the discrepancy could be due to a difference in the technique of cross-fostering employed. WHITE *et al.* used standardized litters made up of two mice of each of the three strains (a control line was also included) while in this study whole litters were transferred and were not standardized. Another possible explanation may lie in the fact that prenatal effects in the study of WHITE *et al.* include genetic and uterine effects. Therefore, the prenatal-by-postnatal interaction in their study must be a combination of the genotype-by-postnatal maternal and prenatal maternal-by-postnatal maternal interactions assuming that the second order interaction, prenatal maternal-by-postnatal maternal-by-genetic effects, is zero.

It is a pleasure to acknowledge the expert technical assistance of MRS. CHRISTINA ROWLAND.

SUMMARY

The relative importance of genetic effects, uterine effects, and postnatal maternal effects in causing differences in growth was examined in two lines of mice selected for high (H_6) and low (L_6) body weight by means of embryo transfer

and cross-fostering at birth. The genetic effects were almost three times larger than the uterine effects in causing differences in mean birth weight. There was a statistically significant genotype-by-uterus interaction because the H_6 embryos did not grow at a more rapid rate in the H_6 uterus than in the L_6 uterus when the data were corrected for number born. It was also found that mice that survived to one week of age had larger birth weights than those that died before this time.—Genetic effects and postnatal maternal effects caused significant differences in body weight of mice from one to ten weeks of age. Genetic effects were twice as large as postnatal effects at one week and had become 10 times as large at 10 weeks of age. Uterine effects were small throughout and only reached statistical significance when the offspring were two weeks of age. The interactions suggested that there was a deleterious cross-fostering effect from one to four weeks and a tendency for the young mice to be relatively larger on a postnatal mother of their own strain from two to three weeks of age. Also, there was a significant genotype-by-uterus interaction from two to four weeks which probably was a result of this interaction being significant for birth weight, the L_6 mice from the H_6 uterus being larger than those from the L_6 uterus.

LITERATURE CITED

BRINSTER, R. L., 1965 Studies on the development of mouse embryos *in vitro*. IV. Interaction of energy sources. J. Reprod. Fertil. **10:** 227–240.

BRUMBY, P. J., 1960 The influence of the maternal environment on growth in mice. Heredity **14:** 1–18.

BUTLER, L. and J. D. METRAKOS, 1950 A study of size inheritance in the house mouse. I. The effect of milk source. Can. J. Res. **D28:** 16–34.

COX, D. F., J. E. LEGATES and C. C. COCKERHAM, 1959 Maternal influence on body weight. J. Animal Sci. **18:** 519–527.

DICKINSON, A. G., J. L. HANCOCK, G. J. R. HOWELL, ST. C. S. TAYLOR and G. WIENER, 1962 The size of lambs at birth—a study involving egg transfer. Animal Prod. **4:** 64–69.

EISEN, E. J., 1966 Comparison of two cage rearing regimes on reproductive performance and body weight of the laboratory mouse. Laboratory Animal Care **16:** 447–453.

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. Theoret. Appl. Genetics **39:** 345–351.

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. Fertil. **17:** 9–18.

EL OKSH, H. A., P. M. SUTHERLAND and J. S. WILLIAMS, 1967 Prenatal and postnatal maternal influence on growth in mice. Genetics **57:** 79–94.

FALCONER, D. S., 1955 Patterns of response in selection experiments with mice. Cold Spring Harbor Symp. Quant. Biol. **20:** 178–196.

HARVEY, W. R., 1960 Least-squares analysis of data with unequal subclass numbers. U. S. Dept. Agric., Agr. Res. Serv. ARS 20–8, Washington, D.C.

HUNTER, G. L., 1956 The maternal influence on size in sheep. J. Agric. Sci. **48:** 36–60.

MACARTHUR, J. W., 1949 Selection for small and large body size in the house mouse. Genetics **34:** 194–209.

VENGE, O., 1950 Studies of the maternal influence on the birth weight in rabbits. Acta Zool. **31:** 1–148.

WHITE, J. M., J. E. LEGATES and E. J. EISEN, 1968 Maternal effects among lines of mice selected for body weight. Genetics **60:** 395–408.

YOUNG, C. W., J. E. LEGATES and B. R. FARTHING, 1965 Prenatal and postnatal influences on growth, prolificacy and maternal performance in mice. Genetics **52:** 553–561.