

## PRENATAL AND POSTNATAL MATERNAL INFLUENCE ON GROWTH IN MICE<sup>1</sup>

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**D**URING the last 50 years, many investigators have been concerned with the inheritance of body size in mammals (for review see VENGE 1950; DICKERSON 1954; HAFEZ 1963). The inheritance of body size has been examined by at least three main techniques (BRUMBY 1960): (1) selection of large and small size animals for several generations from a common base population; (2) the continued inbreeding, and crossbreeding of animals of different sizes; and (3) the resemblance between relatives used to partition the phenotypic variation into its genetic and environmental components. Each of these techniques has led to the conclusion that difference in growth is bound to be the cumulative result of divergent frequencies at many loci. But because of the confusing effects of environmental influences on growth, and in spite of the advances made in the quantitative theory, many complications remain in the interpretation of the observed experimental results. Several simplifying assumptions have had to be made in order that statistical methods could be derived to estimate the degree of determination by heredity or environment. Those commonly used include the absence of interaction between the genotype and environment, the stability of the environment from generation to generation, lack of correlation between the genotype and environment, the absence of cytoplasmic inheritance, and often the absence of maternal effects.

Maternal effects have been reported to influence the growth of chickens (HAZEL and LAMOREUX 1947), horses (WALTON and HAMMOND, 1938), rabbits (VENGE 1950, 1953), mice (BATEMAN 1954; COX, LEGATES and COCKERHAM 1959; YOUNG, LEGATES and FARTHING 1965), cattle (KOCH and CLARK 1955), sheep (HUNTER 1956), and man (ROBSON 1955). Maternal environment affects the growth of the offspring at two stages. Before birth, the fetus is entirely dependent upon its mother for nutrition, so that fetal growth is subject to her control; this is called the prenatal maternal effect. After birth, the young animal is entirely dependent upon maternal care at first and thereafter is largely dependent for a considerable period. A most important feature of the maternal care is the milk supply available; this is called the postnatal maternal effect.

Maternal effects introduce important complications to the study of body size

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inheritance in mammals since they can be a major source of resemblance between maternal relatives and their effects may be confused with resemblance resulting from genetic similarities between those relatives. Since the latter is the chief source upon which quantitative genetic theory is based, an understanding of the nature and magnitude of the maternal influence seems necessary.

Most previous studies on maternal influence have been concerned with crosses and reciprocal crosses of animals that are widely different in size. The present study was an attempted evaluation of the maternal effects on body weight from birth through six weeks of age in mice showing normal ranges of variation in hopes of shedding some light on the possible importance of maternal effects in other mammals, and particularly in domestic animals.

A part of this study was devoted to a cross-nursing experiment designed partially as suggested by Cox *et al.* (1959), in an attempt to separate experimentally prenatal and postnatal maternal effects and to assess their relative importance on growth from birth through six weeks of age. Also examined were the probable consequences of the maternal influence on conventional methods of estimating heritabilities.

## MATERIALS AND METHODS

### *Nature and Source of Data*

The stocks used in the present study came from an unselected control line of mice maintained in the laboratory. The control line originated from crossing four highly inbred strains of mice originally purchased from Jackson Laboratory, Bar Harbor, Maine, and was maintained each generation by mating 18 males to 36 females. Random mating was used in the control line, and in the early generations from which the mice were taken for the present experiment, inbreeding beyond that existing in the base generation (25% as a result of crossing four highly inbred lines) was essentially zero. Temperature was maintained at approximately 25°C, and the young mice were kept with their mothers or foster mothers at a standard litter size of six or eight depending upon the phase of the experiment, until weaning at 21 days of age. The feed was a standard commercially prepared pelleted ration of not less than 17% protein, and was available free-choice with water at all times.

The following weights were recorded in grams and decigrams: 1. Birth weight—Pregnant females were checked twice daily for new born litters so that young mice were weighed within a 12-hour period. 2. Seven day weight—This weight was thought to represent the beginning of a growing period largely characteristic of the dam's milk supply and without undue complication of any carry-over of prenatal factors. 3. Fourteen day weight—Young mice begin to consume solid food at this age as soon as their eyes open. At this time genetic factors influencing growth become more important. 4. Twenty-one day weight—Young mice were weaned at this age, marking the end of their dependency on their mothers and the beginning of complete dependence on their own inherited ability to grow. 5. Forty-two day weight—This was the final weighing, and is the age at which mice are commonly used for breeding.

From these body weights the amounts of gain made during the respective periods are obtained; namely, (a) gain from birth to seven days of age, (b) gain from 7 to 14 days of age, (c) gain from 14 to 21 days, and (d) gain from 21 days to six weeks of age.

*Description of matings: First matings.* Sixty females and 30 males were chosen at random and matings made among them. Each male was randomly mated to two females avoiding mating of full and half-sibs, and no two sisters or half sisters were mated to the same sire.

Progeny produced in these matings were identified by sex, and the litters were standardized to eight mice with the two sexes being equally represented whenever possible. Litters of less than

TABLE 1

*Average weights (grams) of males and females for mice produced from the first matings*

Age	Males		Females		Difference $\pm$ s.e.	Total	
	N	Mean	N	Mean		N	Mean
Birth	192	1.37	214	1.33	0.04 $\pm$ .013	406	1.35
7 days	185	4.45	203	4.51	-0.06 $\pm$ .058	388	4.48
14 days	185	7.31	203	7.51	-0.20 $\pm$ .094	388	7.41
21 days	183	9.88	202	9.88	0.00 $\pm$ .134	385	9.88
42 days	182	19.65	199	16.63	3.02 $\pm$ .201	381	18.10

*Matings to produce maternal half-sibs.* A group of 32 dams mated to 18 sires produced second litters in which the mice were maternal half-sibs to those in the first litter. Data obtained on maternal half-sibs in this way provide information on maternal influence which is a permanent characteristic of the dam, i.e., by comparison of the phenotypic resemblance among groups of maternal versus paternal half-sibs. The average weights are shown in Table 2.

eight, but not less than five, mice were also used; in this case, extra young mice were marked and added, but no data were taken on those. Birth weights were immediately recorded on individual mice as described, and the newborn animals were marked for identification and kept with their mothers.

Subsequent weighings were carried out as previously described. Table 1 shows the average weight of the mice produced from the first matings.

*Cross-nursing experiment.* From the first litter progeny a total of 48 male and 192 female mice were randomly chosen (i.e. by their number in the record books, without regard to any characteristic of any individual mouse) for use in the cross-nursing experiment. The procedure involved the fostering of young mice directly after birth in such a way as to allow the separation of the total maternal environment into its prenatal and postnatal components. It was hoped that at least three dams per sire would conceive and produce satisfactory litters of at least six mice each, and thus fit into the cross-nursing scheme.

Litters born in the same 12-hour period were arranged in cross-nursing groups of three litters each according to the following restrictions: (a) Each litter should consist of at least six mice and whenever possible male and female mice were equally represented. (b) No sire should be represented by more than one litter in a given cross-nursing group, and by no more than three litters in the whole experiment. (c) No two sisters or half-sisters should have their litters in the same cross-nursing group. This was believed to be important since a considerable amount of the differences in mothering ability between dams is suspected to be genetically determined.

One hundred and seventeen litters satisfied the above requirements and were arranged in 39 cross-nursing sets. Individual mice were weighed and marked for identification. Within a cross-nursing set, each dam received two of her own mice and two from each of the other two dams,

TABLE 2

*Average weights (grams) of males and females for mice produced from the second matings*

Age	Males		Females		Difference $\pm$ s.e.	Total	
	N	Mean	N	Mean		N	Mean
Birth	202	1.40	187	1.37	0.03 $\pm$ .014	389	1.39
7 days	198	4.37	181	4.48	-0.11 $\pm$ .061	379	4.43
14 days	199	6.86	185	6.93	-0.07 $\pm$ .084	384	6.89
21 days	197	8.35	181	8.27	0.08 $\pm$ .111	379	8.31
42 days	179	16.68	165	14.19	2.49 $\pm$ .201	344	15.49

assignment being made randomly, i.e. without regard to any characteristic of any mouse except sex; as far as possible the two mice were of opposite sex. No difficulty was encountered in getting the foster mother to accept the new litter. Birth weights were taken while sets were being established, within approximately 12 hours after the litters were born. It is, therefore, possible that birth weight may contain some initial postnatal influence resulting from suckling before measurements of the birth weight were recorded.

The mice were weighed at 7 and 14 days of age as previously explained. Weaning was again at 21 days of age, when the young mice were weighed, pedigreed, and separated by sex. Average weights and the numbers of mice represented are shown in Table 3.

#### Methods of Analysis

At the earlier ages virtually no difference existed between the weights of the two sexes. At six weeks of age, however, males were highly significantly heavier than females, so that correction procedures had to be adopted. Paternal and maternal half-sib data were analyzed on a within sex basis and then pooled within sex. In the cross-nursing analyses, individual weights for males and females were adjusted to the mean of both sexes. A multiplicative correction factor similar to that described by FALCONER (1953) was used; each female observation was adjusted to the overall mean by multiplying it by the ratio of the mean for both sexes to the mean of all females; similarly, each male observation was adjusted to the overall mean by multiplying it by the ratio of the mean of both sexes to the mean of all males.

*Sib analysis:* Maternal effects cannot be measured directly on the phenotype; the effects must be inferred from comparing the observed resemblance of varying degrees of paternal versus maternal relatives. The theoretical component parts which are expected to influence such resemblance have been worked out by DICKERSON (1947, 1960) and WILLHAM (1963).

*Paternal half-sib analysis:* The data used in this phase of the analysis came from a total of 406 mice produced in the first matings (Table 1) and from 389 mice from the repeated matings (Table 2). The method of analysis was that of analysis of variance for unequal subclass numbers as described by KING and HENDERSON (1954). The model used was  $Y_{ijk} = \mu + s_i + d_{ij} + e_{ijk}$  where  $Y_{ijk}$  is the observation measured on the  $k$ th individual born to the  $j$ th dam by the  $i$ th sire and  $\mu$  is the overall mean of all observations. Assuming random mating, the sire component of variance ( $V_s$ ) is expected to contain  $\frac{1}{4}$  of the additive genetic variance ( $V_a$ ) plus approximately  $\frac{1}{8}$  of the epistatic variance ( $V_I$ ). The dam component of variance ( $V_d$ ) is expected to estimate  $\frac{1}{4}$  of  $V_a$  plus  $\frac{1}{4}$  of the variance due to dominance ( $V_D$ ) plus  $\frac{1}{8}$  of  $V_I$ ; in addition, however, the dam component will contain all of the variance due to maternal effects and common cage environment plus the covariance of the genes for growth transmitted by the dam and her direct maternal environment ( $V_m + V_c + Cov_{mg}$ ). The remaining variation, contained in the offspring component ( $V_o$ ) measures the variance within full sib litter mates ( $\frac{1}{2} V_a + \frac{3}{4} V_D + \frac{3}{4} V_I + V_w$ ) where  $V_w$  is the random environmental variance due to the specific environmental differences among members of the same litter. Table 4 summarizes these constituents of the variance components.

TABLE 3

*Average weights (grams) of mice used in the cross-nursing study*

Age	Males		Females		Difference $\pm$ SE	Total	
	N	Mean	N	Mean		N	Mean
Birth	360	1.32	342	1.28	0.04 $\pm$ .008	702	1.30
7 days	354	4.26	340	4.24	0.02 $\pm$ .037	694	4.25
14 days	343	6.84	333	6.85	-0.01 $\pm$ .063	676	6.85
21 days	347	8.14	337	8.04	0.10 $\pm$ .068	684	8.09
42 days	309	16.12	299	13.89	2.23 $\pm$ .201	608	15.02

TABLE 4

*Biological constituents of the variance components in half-sib analysis*

Component of variance	Genetic			Maternal environment	Common environment	Remainder
	* $V_G$	$V_D$	$V_I$	$V_m$ $Cov_{mg}$	$V_c$	$V_w$
Sire ( $V_s$ )	1/4	0	1/16	0	0	0
Dam ( $V_d$ )	1/4	1/4	3/16	1	1	0
Offspring ( $V_o$ )	1/2	3/4	3/4	0	0	1
Total variance ( $V_T$ )	1	1	1	1	1	1

\* Definitions of symbols:  $V_G$ =additive genetic variance;  $V_D$ =dominance variance, i.e. due to intralocus interactions;  $V_I$ =epistatic variance, i.e. due to interlocus interactions;  $V_m$ =variance due to direct maternal effects;  $Cov_{mg}$ =covariance of genes for growth transmitted by the dam and her direct maternal environment;  $V_c$ =variance due to common environmental factors other than maternal environment, common to full-sib families;  $V_w$ =random environmental variance among members of the same litter.

These variance components allow estimates of the various correlations among relatives; the sire component of variance estimates the covariance among paternal half-sibs and constitutes the numerator of the correlation  $t_1$  as defined by ROBERTSON (1959).

$$t_1 = \frac{V_s}{V_T} = \frac{[(1/4)V_G + (1/8)V_I]}{(V_G + V_D + V_I + V_m + Cov_{mg} + V_c + V_w)}$$

The dam intraclass correlation is defined as

$$t_2 = \frac{V_d}{V_T} = \frac{[(1/4)V_G + (1/4)V_D + (3/8)V_I + V_m + Cov_{mg} + V_c]}{(V_G + V_D + V_I + V_m + Cov_{mg} + V_c + V_w)}$$

If the quantity  $(1/4 V_D + 1/8 V_I)$  is negligible, and no common environment exists (other than maternal environment), the difference  $(t_2 - t_1)$  estimates the proportion of the phenotypic variance which is determined by maternal effects, so that

$$(t_2 - t_1) = (l/V_T)(V_m + Cov_{mg}).$$

The correlation among full sibs is given by the expression

$$t_{FS} = \frac{Cov_{FS}}{V_T} = \frac{(V_s + V_d)}{V_T} = \frac{[(1/2)V_G + (1/4)V_D + (1/4)V_I + V_m + Cov_{mg} + V_c]}{(V_G + V_D + V_I + V_m + Cov_{mg} + V_c + V_w)}$$

and is, of course the sum of the sire and dam intraclass correlations.

*Maternal half-sib analysis:* Maternal half-sib correlations, besides containing a component due to the genetic likeness of half-sibs, are also expected to contain a component due to the maternal environment of a permanent nature provided by the dam. Factors of this sort would be in most part hereditarily determined. This phase of the analysis was carried out according to the model

$$Y_{ijk} = \mu + d_i + l_j + (dl)_{ij} + e_{ijk}$$

where  $Y_{ijk}$  is the individual observation recorded on the  $k$ th offspring, born in the  $j$ th litter (either first or second litter) out of the  $i$ th dam.  $\mu$  is the overall mean of all 422 mice, the number used in this phase of the experiment produced by 31 dams, each of which produced two litters.

The dam component of variance ( $V_d$ ), obtained from the analysis of variance, should contain in addition to the genetic likeness or half-sibs  $(1/4 V_G + 1/8 V_I)$ , an additional component of variance due to permanent environment factors  $(V_{m_1} + Cov_{mg_1})$ . A litter effect ( $L^2$ ) as measured from the overall difference between first and second litters should not contain any genetic differences since the same group of parents was used to produce first and second litters, provided that large numbers of matings are made and sampling variation of parental genes between first and second matings is negligible. The expected composition of the various components of variance is summarized in Table 5.

TABLE 5

*Biological constituents of the variance components in the maternal half-sib analysis*

Component of variance	Genetic			Maternal environment		Common environment	Remainder
	$V_G$	$V_D$	$V_I$	Perma- nent	Tem- porary		
				$v_{m_1}$ <i>coe</i> $mg_1$	$v_{m_2}$ <i>coe</i> $mg_2$	$V_c$	$V_w$
Dam ( $V_d$ )	1/4	0	1/16	1	0	0	0
Litter ( $L^2$ )	0	0	0	0	1	1	0
Interaction ( $V_{a_1}$ )	1/4	1/4	3/16	0	0	0	0
Offspring ( $V_o$ )	1/2	3/4	3/4	0	0	0	1
Total variance ( $V_T$ )	1	1	1	1	1	1	1

The various types of sib analysis described, plus some results from the following section on cross nursing thus provide six types of correlation with the expected composition listed in Table 6. The assumption is made that no correlation existed between the various causes which made up these correlations, so that they may be analyzed into their respective biological compositions. The prenatal maternal environmental variance was subdivided into two components,  $V_{m_1}$  and  $V_{m_2}$ , the variance due to permanent and temporary maternal effects respectively; similarly the variance due to postnatal maternal environment was subdivided into permanent and temporary fractions,  $V_{p_1}$  and  $V_{p_2}$ . Nonmaternal common environment is symbolized by  $V_c$ , and the remainder by  $V_w$ .

It should be emphasized that all of these correlations are not independent of each other, and the expected compositions do not form six independent equations. For example the correlation of full sibs litter mates is the sum of the paternal half-sib and the dam intraclass correlations. Thus the number of independent equations is much fewer than the number (9) of unknowns. Instead, variance due to combinations of causes was obtained.

The table does not include "full sibs not litter mates," owing to some problems encountered when making exact repeat matings.

*Cross-nursing experiment:* This phase was designed to allow experimental partitioning of the

TABLE 6

*Types of relationships and their expected composition used in the sib analysis*

Type of relationship	Expected composition								
	$V_G$	$V_D$	$V_I$	$v_{m_1}$	$v_{m_2}$	$v_{p_1}$	$v_{p_2}$	$V_c$	$V_w$
(1) Full sibs litter mates	1/2	1/4	1/4	1	1	1	1	1	0
(2) Full sibs cross-nursed	1/2	1/4	1/4	1	1	0	0	0	0
(3) Maternal half-sibs	1/4	0	1/16	1	0	1	0	0	0
(4) Paternal half-sibs	1/4	0	1/16	0	0	0	0	0	0
(5) Dam intraclass correlation*	1/4	1/4	3/16	1	1	1	1	1	0
(6) Dam intraclass correlation (cross-nursed)†	1/4	1/4	3/16	1	1	0	0	0	0
Complete determination	1	1	1	1	1	1	1	1	1

\* Dam intraclass correlation is defined as  $t_2 = V_d/V_T$  where  $V_d$  is the variance among groups of full sibs as born and reared.

† Dam intraclass correlation (cross-nursed) is defined as  $t_2 = V_d/V_T$  where  $V_d$  is the prenatal component, measuring the variance among groups of full sibs as born.



TABLE 8

*Observed phenotypic correlations for the various weights and weight gains used in the sib analysis*

Type of relationship	df	Birth weight	7-day weight	14-day weight	21-day weight	42-day weight
(1) Full sibs (litter mates)	616	0.592**	0.758**	0.748**	0.646**	0.457**
(2) Full sibs (cross-nursed)	656	0.625**	0.392**	0.364**	0.307**	0.262**
(3) Maternal half-sibs	364	0.301**	0.467**	0.326**	0.247**	0.116**
(4) Paternal half-sibs	1272	0.000	0.056†	0.068†	0.111*	0.054*
(5) Dam intraclass correlation	616	0.378**	0.631**	0.700**	0.523**	0.457**
(6) Dam intraclass correlation (cross-nursed)	656	0.625**	0.392**	0.319**	0.270**	0.188**

Type of relationship	df	Gain: Birth to 7 days	Gain: 7 to 14 days	Gain: 14 to 21 days	Gain: 21 to 42 days	
(1) Full sibs (litter mates)	616	0.802**	0.795**	0.407**	0.347*	....
(2) Full sibs (cross-nursed)	656	0.307**	0.380**	0.211**	0.243**	....
(3) Maternal half-sibs	364	0.447**	0.100*	0.065*	0.084*	....
(4) Paternal half-sibs	1272	0.032†	0.009†	0.058*	0.077*	....
(5) Dam intraclass correlation	616	0.741**	0.795**	0.406**	0.298**	....
(6) Dam intraclass correlation (cross-nursed)	656	0.307**	0.380**	0.194**	0.153**	....

\* Significant at (0.05) level.

\*\* Significant at (0.01) level.

† Nonsignificant.

## RESULTS

*Sib analysis:* The phenotypic correlations obtained in the various phases of the sib analysis are presented for the body weights and for the weight gains in Table 8. Virtually all, save the paternal half-sib, are highly significant.

From the expected compositions of these correlations, previously presented in Table 6, the variance due to the various causes is now obtained through a series of comparisons of the correlations. For example the genetic variance (actually  $V_A$  plus  $\frac{1}{4} V_I$ ) may be estimated by four times the paternal half-sib correlation, 4 in Table 8. Another estimate is afforded in this analysis from four times the cross nursed paternal half-sibs, given actually by the difference between "full sibs cross-nursed" (correlation 2, Table 8) and the "dam intraclass correlation cross-nursed" (6 in Table 8). These two estimates were both taken and averaged, and are presented in Table 9.

The total maternal environmental variance was estimated from the difference between the dam intraclass correlation and the paternal half-sib correlation (5 and 4 in Table 8), as explained previously. Separation of permanent and temporary effects was by comparison of the paternal versus maternal half-sib correlations (4 and 3 in Table 8) for the permanent, and by comparison of the dam intraclass with the maternal half-sib (5 and 3 in Table 8) for the temporary.

Separation of the total maternal influence into variance due to prenatal and postnatal effects involved more complex comparisons, in an effort to utilize the maximum amount of information. Postnatal effects are given by comparing



either full sibs (litter mates) with full sibs (cross-nursed), or by the dam intra-class correlation (cross nursed) with the dam intraclass correlation—both were in fact taken and averaged. The prenatal effects may be obtained either by comparing the dam intraclass correlation (cross nursed) with the paternal half-sib correlation (6 and 4 in Table 8), or by comparing the full sibs (cross nursed) with twice the paternal half-sib correlation (2 and 4 in Table 8). In fact, since the paternal half-sib correlation (4) has an expected composition equal to the difference between correlations 1 and 5 (full sib litter mate and dam intraclass) and since the values used in these were not completely dependent, (being obtained from slightly different analyses), this difference (1-5) was incorporated into the estimate of the prenatal maternal effect. The complete set of results is shown then in Table 9.

The genetic variance represented 0.00, 11.20, 22.60, 29.60, and 25.60% of the total variance in birth weight, 7-day weight; 14-day weight, 21-day weight and 42-day weight respectively. Gains were genetically determined by 6.4, 1.8, 15.0 and 33.4% of the total variance for the four-gain periods, respectively. These results were in general agreement with what might be expected, as the genotype for growth was expected to increase in importance as the mouse grew older.

The total maternal environment represented 37.8, 57.5, 63.2, 42.1 and 40.3% of the total variance in birth weight, 7-day weight, 14-day weight, 21-day weight and 42-day weight respectively. The maximum influence of the total maternal environment was thus at the age of 14 days, after which it followed a steady decrease. Maternal environment was responsible for 70.9, 78.6, 34.8 and 22.1% of the total variance for the four gain periods respectively, with the highest influence thus seen during the second growth period (gain from 7 to 14 days), after which it decreased steadily to account for only 22.10% of the variance in post-weaning gain. In both body weight and weight-gains the maternal environment

TABLE 9

*Sources of variation and the percent they represent of the total variance in body weights and weight gains obtained from the sib analysis*

	Genetic	Maternal environment				Total $v_{m_1} v_{m_2}$ $v_{p_1} v_{p_2}$	Remainder $V_e$
		Prenatal $v_{m_1} v_{m_2}$	Postnatal $v_{p_1} v_{p_2}$	Permanent $v_{m_1} v_{p_1}$	Temporary $v_{m_2} v_{p_2}$		
<b>A. Body weight</b>							
Birth weight	00.00	51.80	—14.00	30.10	7.70	37.80	62.20
7-day weight	11.20	27.25	30.25	41.10	16.40	57.50	31.30
14-day weight	22.60	24.95	38.25	25.80	37.40	63.20	14.20
21-day weight	29.60	11.60	29.60	13.60	27.60	41.20	29.20
42-day weight	25.60	17.10	23.20	6.20	34.10	40.30	34.10
<b>B. Weight gains</b>							
Birth to 7 days	6.40	24.45	46.45	41.50	29.40	70.90	22.70
7 to 14 days	1.80	37.10	41.50	9.10	69.50	78.60	19.60
14 to 21 days	15.00	14.40	20.40	0.70	34.10	34.80	50.20
21 to 42 days	33.40	9.65	12.45	0.70	21.40	22.10	44.50

decreased sharply just prior to weaning (21 days). This may reflect the fact that the young mice began to consume solid food at around 12 days of age and thus became less dependent on their mother's milk supply.

In general the total maternal environmental influence was always (with the exception of postweaning gain) larger than the genetic variance. This emphasized the importance of such influence on growth in mice and demands a considerable amount of consideration in breeding experiments dealing with body weight even at the age of 42 days (maturity).

The total maternal environment was broken down in two ways: Prenatal *vs.* postnatal, and permanent *vs.* temporary (Table 9).

All of the maternal environment at birth was prenatal (51.8% of the total variance); in fact, postnatal maternal environment represented a negative 14% of the total variance and was considered as equal to zero. Prenatal maternal environment showed a steady decrease (with the exception of 42-day weight) throughout, while postnatal maternal environment began to increase after birth with a maximum value of 38.25% at 14 days after which it began to decrease.

The results of body weight gains showed very much the same general trend for both prenatal and postnatal maternal influences (except prenatal environment during the second gain period). They both showed a general decrease in importance as the mouse grew older with postnatal maternal environment being all the way larger than prenatal environment.

The total maternal environment was again broken down to its permanent and temporary components (Table 9). Permanent maternal environment accounted for 30.1, 41.1, 25.8, 13.6 and 6.2% (a steady decrease) of the total variance in birth weight, 7-day weight, 14-day weight, 21-day weight and 42-day weight respectively. The temporary maternal environmental factors accounted for 7.70, 16.40, 37.40, 27.60 and 34.10% of the total variance for the same traits respectively. It seemed that most of the maternal environment at birth was permanent in nature (31.1% *vs.* 7.7%), the same at the age of 7 days (41.1% *vs.* 16.4%). This observation seemed to reverse itself beginning at the age of 14 days through 42 days of age (Table 9); that is temporary maternal environment became more important. Similarly, the results for weight-gains seemed to confirm the above observation (Table 9). Permanent maternal environment during the first week of growth was more important than temporary maternal environment (41.5% *vs.* 29.4%), while during the rest of the growth period this order was reversed (9.1%, 0.7% and 0.7% *vs.* 69.5%, 34.1% and 21.4%) for permanent and temporary maternal environment respectively.

The above results, if they represent a real trend, would tend to indicate that the early maternal environment (apparently the milk supply) is a permanent characteristic of the dam. On the other hand, the last part of the maternal influence tends to be more of a temporary than permanent characteristic of the dam. In other words, measuring the maternal ability of the dams during early growth of their offspring seems to be more accurate than if done later in growth; or early growth response of the young reflects more of the dam's maternal ability than its later growth.

TABLE 10  
*The components of variation and the percent they represent of the total variance in the complete analysis for the various weights*

Component of variance*	Birth Comp.	Birth weight Comp. %	7-day weight Comp.	7-day weight Comp. %	14-day weight Comp.	14-day weight Comp. %	21-day weight Comp.	21-day weight Comp. %	42-day weight Comp.	42-day weight Comp. %
Sire ( $V_s$ )	-0.00173	00.00	0.0010	00.26	0.05167	4.75	0.04780	4.00	0.55450	7.19
Dam ( $V_d$ )	0.01077	60.95	0.1077	27.47	0.16060	14.77	0.17380	14.51	1.00422	13.00
Postnatal ( $V_n$ )	-0.00028	00.00	0.1993	50.84	0.68946	63.41	0.62676	52.33	1.18836	15.39
Interaction ( $V_{dn}$ )	-0.00027	00.00	0.0052	1.31	-0.00285	00.00	0.01894	1.58	0.33995	4.40
Error ( $V_e$ )	0.00690	39.05	0.0789	20.12	0.18560	17.07	0.33030	27.58	4.63470	60.00
Total variance ( $V_T$ )	0.01767	100.00	0.3921	100.00	1.08733	100.00	1.19760	100.00	7.72173	100.00

\* Negative components were assumed = 0.

TABLE 11  
*The components of variation and the percent they represent of the total variance in the complete analysis for the various weight gains*

Component of variance*	Birth to 7 days Comp.	Birth to 7 days Comp. %	7 to 14 days Comp.	7 to 14 days Comp. %	14 to 21 days Comp.	14 to 21 days Comp. %	21 to 42 days Comp.	21 to 42 days Comp. %
Sire ( $V_s$ )	0.00062	0.18	-0.00008	00.00	0.00543	2.12	0.51258	9.08
Dam ( $V_d$ )	0.08400	24.14	0.09990	21.78	0.02070	8.05	0.62617	11.08
Postnatal ( $V_n$ )	0.20208	58.08	0.27361	59.66	0.11186	43.52	0.64998	11.50
Interaction ( $V_{dn}$ )	0.00480	1.39	-0.00545	00.00	0.01605	6.24	0.40460	7.16
Error ( $V_e$ )	0.05640	16.21	0.08510	18.56	0.10300	40.07	3.45700	61.18
Total variance ( $V_T$ )	0.34790	100.00	0.45861	100.00	0.25704	100.00	5.65033	100.00

\* Negative components were assumed = 0.

*Cross-nursing analysis:* The results from the cross-nursing phase of the experiment are presented in Tables 10 and 11, analyzed according to the model presented earlier. From these results, the genetic effects were extracted—these were taken as four times the sire component. The difference between the sire and dam components ( $V_a - V_s$ ) provided the prenatal maternal environment, while the postnatal effects were given directly by the component  $V_n$ . The “remainder” is actually the error component minus twice the sire component, presumably leaving only nongenetic variation plus any effect of sex that the correction failed to account for. These results are presented graphically in Figures 1 and 2.

*Body weights:* Sires had virtually no effect on either birth weight or 7-day weight, but by 14 days they accounted for some 5%; at 21 and 42 days sire influence accounted for 4% and 7% of the total variance, equal to heritability estimates of some 19% and 28% respectively. The influence of the dam was very strong; the pure prenatal effects (with genetic variance already removed) accounted for 61%, 27%, 10%, 10% and 6% of the total variance at the weights studied. Postnatal maternal effects, on the other hand, after exerting no influence at birth (as expected of course) increased to 51% by 7 days, up to 63% by 14 days, before declining somewhat to 52% by 21 days and sharply to 15% at 42 days. Interactions between prenatal and postnatal effects remained reassuringly low throughout.

The total effects of the dam, prenatal plus postnatal, thus decreased fairly

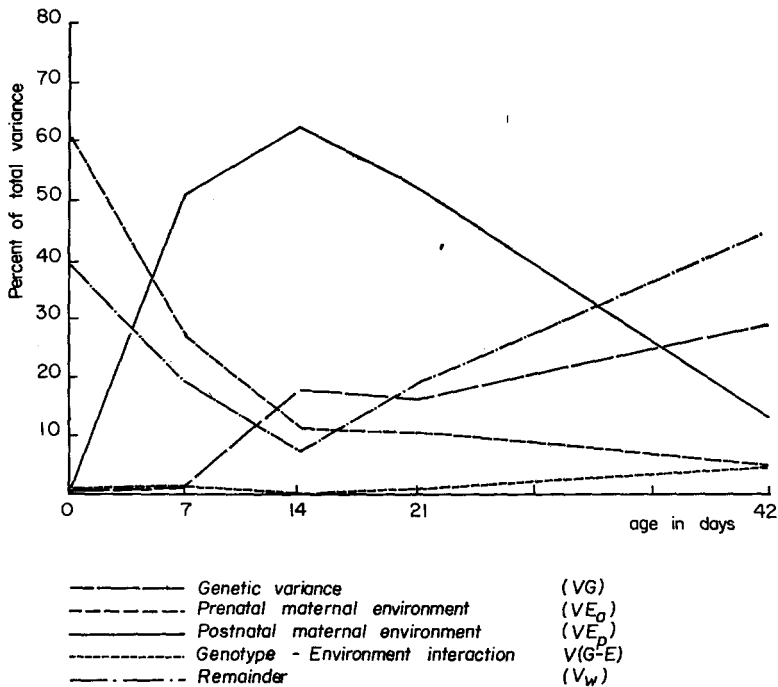


FIGURE 1.—Sources of variation and the percent they represent of the total variance in body weight.

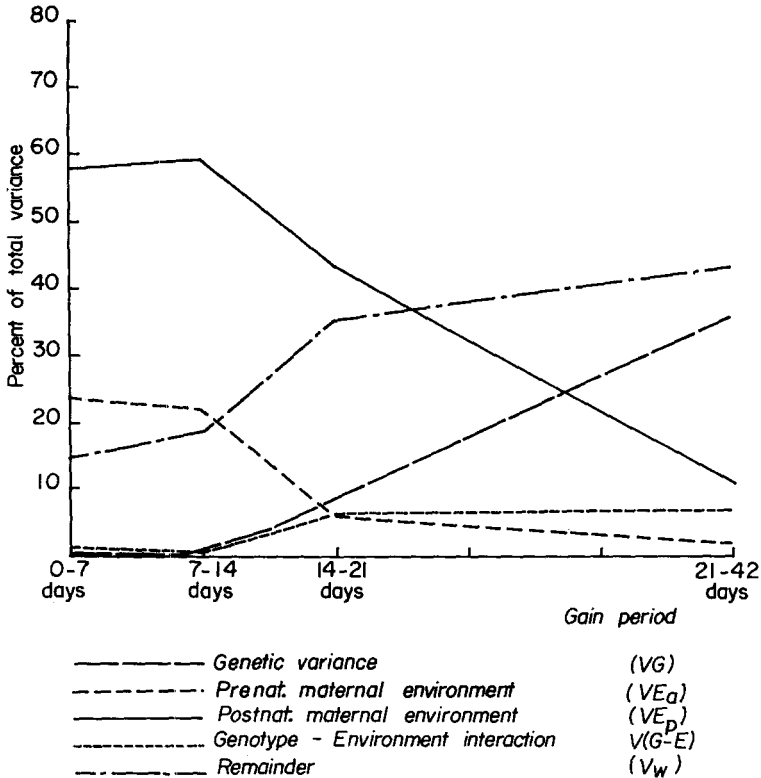


FIGURE 2.—Sources of variation and the percent they represent of the total variance in weight-gain.

markedly by sexual maturity (6 weeks) to account for some 28% of the total variance as opposed to 61% at birth and as high as 78% at both 7 and 14 days of age. But even at the age of 42 days the total influence of the dam was still some four times as strong as that of the sire (28% vs. 7%). If the above results hold true, one would expect that by using normal (nonfostered) data in the usual half-sib analysis, heritability of 42-day weight if estimated from the dam component will be four times as large as if estimated from the sire component of variance. On the other hand, by deleting the postnatal maternal influence through the use of the cross-nursing technique, heritability when estimated from the dam component would still be almost twice as large as (actually 1.8 times) the estimate from the sire component, owing to the presence of prenatal maternal environmental influence in the dam component of variance.

*Weight gains:* Genetic differences had no apparent influence on growth during the period from birth up to 14 days of age. Growth from 14 to 21 days of age (weaning) was 8.48% genetically determined, as estimated from a nonsignificant sire component which accounted for 2.12% of the total variance. Postweaning growth, on the other hand, was 36.32% genetically determined, as evidenced from a highly significant ( $P < 0.01$ ) sire influence which was responsible for

9.08% of the total variance. It was concluded, therefore, that by the time the young mice began to consume solid food, differences in genic values for growth began to exert an influence on the animal's growth response. This was particularly so during postweaning growth (see Figure 2).

The dam component of variance represented a highly significant ( $P < 0.01$ ) 24.14, 21.78, 8.05 and 11.08% of the total variance in gain during the period from birth to 7 days, 7 to 14 days, 14 to 21 days and 21 to 42 days respectively. It is obvious that during all the four growth periods, the dam had relatively more influence than the sire; the difference (equal to pure prenatal maternal environmental influence) was 24, 22, 6 and 2% of the total variance, showing as expected a pattern of steadily decreasing influence.

Postnatal maternal environmental factors on the other hand, accounted for 58.08% of the total variance in the first week's growth, then reached their maximum influence during the second week (59.66%), began a steady decline during the third week (43.52%) and finally were responsible for only 11.50% of the variance in gain from weaning to 42 days of age. Gain during the period from 7 to 14 days of age was the most influenced by the milk supply which led to the conclusion that gain during this period could be considered as a good criterion for measuring milk production of the dams. However, the absolute 14-day weight could be more sensitive to measure differences in milk production, since 63.41% of the total variance in 14-day weight was determined by postnatal factors (Table 10). Though no explanation was readily available as to why this was the case, the above results substantiated those reported by FALCONER (1947). In spite of the fact that he suggested the use of gain during the period from 5 to 12 days of age as a measure of milk production in mice, he found that 12-day weight was more sensitive in detecting postnatal maternal differences.

The total direct maternal environment influence was found to represent 82.04, 81.44, 49.45 and 13.50% of the total variance during the four gain periods respectively (Figure 2). The total influence of the dam on the growth of her offspring, through genes transmitted by her and the direct maternal environment, was found to account for 82.22, 81.44, 51.57 and 22.58% of the total variance during the four gain periods respectively. Comparable results for the sire influence were 0.18, 0.00, 2.12 and 9.08% respectively. This meant that in normal (nonfostering) experimental data, even in postweaning growth up to 42 days of age, the dam influence was almost 2.5 times as much as that of the sire. Consequently, heritability for postweaning gain if estimated from the dam component of variance in normal half-sib analysis would be seriously biased and would be expected to be some 2.5 times as large as if estimated from the sire component of variance.

Genotype-environment interaction was only significant ( $P < .05$ ) during the growth periods from 14 to 21 days and 21 to 42 days, accounting for 6.24 and 7.16% of the total variance respectively. The error component of variance, which also contains half of the genetic variance, represented 16.21, 18.56, 40.07 and 61.18% of the total variance during the four gain periods respectively.

*Comparison of result of sib analyses with cross nursing analysis:*—It is of

TABLE 12

*Summary of results from sib and cross-nursing analyses. Percentage of variance attributed to each cause*

	Genetic		Prenatal		Postnatal		Remainder	
	Sib	Cross-nursed	Sib	Cross-nursed	Sib	Cross-nursed	Sib	Cross-nursed
A. Weight								
Birth	0	0	51	61	-14	0	62	39
7 days	11	1	27	27	30	51	31	21
14 days	23	19	24	10	38	63	14	8
21 days	30	16	11	10	29	52	29	21
42 days	27	29	17	6	23	15	34	50
B. Weight gains								
Birth to 7 days	6	0	24	24	46	58	23	17
7 to 14 days	1	0	37	22	41	60	20	19
14 to 21 days	15	8	14	6	20	44	50	42
21 to 42 days	33	36	9	2	12	11	45	50

interest to compare the results obtained in the two entirely separate phases of the experiment; Table 12 summarizes the salient features of both for this comparison.

It is readily apparent that with a few exceptions, the results from the two phases are in remarkably good agreement. Furthermore, both phases show very good agreement with those found by YOUNG, LEGATES and FARTHING (1965).

## SUMMARY

Two major techniques were used to draw inferences concerning the maternal environmental influence on growth in mice—the comparison of various types of paternal versus maternal relatives (the sib analysis), and a cross nursing technique. Body weights were studied at birth, 7 days, 14 days, 21 days and 42 days, in addition to the weight gains between these ages. Except for the gain between 21 and 42 days, all traits were influenced much more strongly by the dam than by the sire (for example, from the sib analysis, 78% by the dam *vs.* 0.25% by the sire at 7 days of age). From the cross nursing analysis, prenatal maternal environment accounted for 61, 27, 10, 10 and 6% of the total variation in the respective body weights while postnatal maternal environment accounted for 0, 51, 63, 52 and 15% at the respective ages. The genotype of the mouse increased in importance with the age of the mouse, causing 0, 1, 19, 16 and 29% of the variance in the respective body weights.

## LITERATURE CITED

- BATEMAN, N., 1954 The measurements of milk production of mice through pre-weaning growth of suckling young. *Physiol. Zool.* **27**: 163-173.
- BRUMBY, P. J., 1960 The influence of the maternal environment on growth in mice. *Heredity* **14**: 1-18.
- COX, D. F., J. E. LEGATES, and C. C. COCKERHAM, 1959 Maternal influence on body weight. *J. Animal Sci.* **18**: 519-527.

- DICKERSON, G. E., 1947 Composition of hog carcasses as influenced by heritable differences in rate and economy of gain. *Iowa Agr. Exptl. Sta. Res. Bull.*, **354**: 489-524. — 1960 Techniques for research in quantitative animal genetics. pp. 56-105. *Techniques and Procedures in Animal Production Research*. American Society of Animal Science, Beltsville, Md. — 1954 Hereditary mechanisms in animal growth, pp. 241-276. *Dynamics of Growth Processes*. Edited by E. BOELL. Princeton University Press, Princeton, N. J.
- FALCONER, D. S., 1947 Milk production in mice. *J. Agr. Sci.* **37**: 224-235. — 1953 Selection for large and small size in mice. *J. Genet.* **51**: 470-501.
- HAFEZ, E. S. E., 1963 Symposium on growth; physio-genetics of prenatal and postnatal growth. *J. Animal Sci.* **22**: 779-791.
- HAZEL, L. N., and W. F. LAMOREUX, 1947 Heritability, maternal effects and nicking in relation to sexual maturity and body weight in White Leghorns. *Poultry Sci.* **26**: 508-514.
- HUNTER, G. L., 1956 The maternal influence on size in sheep. *J. Agr. Sci.* **48**: 36-60.
- KING, S. C., and C. R. HENDERSON, 1954 Variance components analysis in heritability studies. *Poultry Sci.* **33**: 147-154.
- KOCH, R. M., and R. T. CLARK, 1955a Genetic and environmental relationships among economic characters in beef cattle. I. Correlations among paternal and maternal half sibs. *J. Animal Sci.* **14**: 775-785. — 1955b Genetic and environmental relationships among economic characters in beef cattle. II. Correlations between offspring and dam and offspring and sire. *J. Animal Sci.* **14**: 786-796.
- ROBERTSON, A., 1959 Experimental design in the evaluation of genetic parameters. *Biometrics* **15**: 219-226.
- ROBSON, E. B., 1955 Birth weight in cousins. *Ann. Human Genet.* **19**: 262-268.
- VENGE, O., 1950 Studies of the maternal influence on the birth weight of rabbits. *Acta Zool.* **31**: 1-148. — 1953 Studies of the maternal influence on the growth in rabbits. *Acta Agr. Scand.* **3**: 243-291.
- WALTON, A., and J. HAMMOND, 1938 The maternal effects on growth and conformation in Shire horse-Shetland pony crosses. *Proc. Roy. Soc. Lond. B* **125**: 311-334.
- WILLHAM, R. L., 1963 The covariance between relatives for characters composed of components contributed by related individuals. *Biometrics* **19**: 18-27.
- 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.