

## Maternal effects on body weight in mice selected for large and small size

BY W. K. AL-MURRANI\* AND R. C. ROBERTS†

*Institute of Animal Genetics, West Mains Road, Edinburgh EH9 3JN*

(Received 14 August 1978)

### SUMMARY

Fertilized eggs were transferred reciprocally between large and small mothers, to study maternal effects on body weight in mice selected for large and small size, respectively. Prenatal maternal effects were not important in our material, but postnatal maternal effects were detectable. The postnatal effects accrued mostly from the inadequacy of small mothers for large offspring; small offspring were largely unaffected by the type of mother. Genetic maternal effects were only of limited importance; maternal influences of environmental origin arose from variation in litter size.

### 1. INTRODUCTION

Maternal effects on body weight in the mouse have been reviewed by Legates (1972) and by Eisen (1974). Generally, while maternal effects influence juvenile weights, they fade in importance as the mouse approaches maturity. Two main kinds of maternal effects are recognized: prenatal, associated with uterine properties, and postnatal, stemming from lactational or mothering abilities. Some of these effects may be a direct consequence of body size, e.g. large mice may have large uteri and large mammary glands. But there may be genes affecting maternal properties that do not operate through body size. Maternal effects may be either environmental or genetic; some implications of this distinction for biometrical analysis were discussed by Willham (1963) and by Falconer (1964). In addition, there may be interactions between the strain of the mother and the strain of the young, noted particularly by Brumby (1960) and by Mason, Nicholson, Bogart & Krueger (1960).

This paper reports on maternal effects in lines of mice selected for high and low body weight. The question was: To what extent was the difference in body weight attributable to genes directly affecting the character and how far to maternal effects associated with large and small mothers? In the selected lines, the two causes are confounded. To separate them, fertilized eggs were transferred reciprocally between large and small mothers, and the resulting offspring were reared in the litters in which they were born. Thus, large and small mice were

\* Present address: College of Veterinary Medicine, University of Baghdad, Al-America, Iraq.

† Agricultural Research Council, Unit of Animal Genetics.

subjected to the totality of the maternal environment of the other, and their subsequent growth measured.

## 2. MATERIALS AND METHODS

The mice were taken from generations 33 to 35 of the replicated Q lines, selected for high and low 6-week weight as described by Falconer (1973). Two stocks, one large and one small, were constructed for this study, the stocks being labelled with a colour marker to facilitate the identification of transferred offspring. The large (L) stock was coloured, and comprised samples from four of Falconer's six high lines. The small (S) stock was albino, and comprised samples from three of Falconer's six low lines. The albino gene did not affect body weight, the weighted mean difference (albino minus coloured) in the small parental lines being  $-0.178 \pm 0.225$  g at 6 weeks of age. Each stock was based initially on about 20 matings. The mean 6-week body weights of the L and S stocks, in natural matings over the period of study, were around 30 and 15 g, respectively, in good agreement with the parental Q lines over the same period.

The design is summarized in Fig. 1. Fertilized eggs were taken from L and S females, mated to males of their own stock, and transferred to pseudopregnant females either of their own stock or of the other, reciprocally. The number of eggs transferred was either ten or five. In addition, mixtures of 5L and 5S eggs were

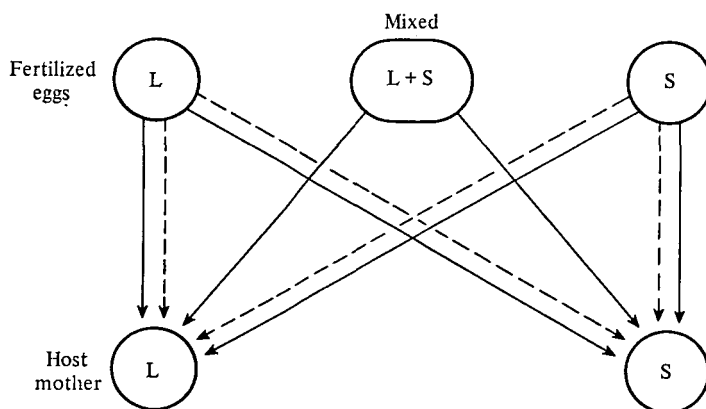


Fig. 1. Diagrammatic representation of the ten groups of transferred eggs. L and S represent large and small genotypes, respectively. Solid lines represent ten eggs transferred, and broken lines five eggs.

transferred into both L and S females. Transfers were conducted as described originally by McLaren & Michie (1956). Natural mating was used throughout, day 0 being when a vaginal plug was found. Most transfers were of  $3\frac{1}{2}$ -day eggs into  $2\frac{1}{2}$ -day mothers, with some synchronous transfers at  $3\frac{1}{2}$  days to avoid wastage (birth weights were the same in the two groups). Pseudopregnancy was induced by vasectomized males.

The ten groups of transferred eggs (Table 1) are designated by three letters: the

first, T(en) or F(ive), shows the number of eggs transferred, the second, L(arge), S(mall) or M(ixture) shows the genotype of the transferred eggs, and the third letters shows the genotype of the host mother. The number of transfer operations and recovery rates are also shown in Table 1. We hesitate to make any claims for the lower recovery rate from mixed transfers; it may mean nothing more than unavoidable delays during the transfer operations, as eggs had to be collected from different sources.

Table 1. *Number of successful transfer operations and mean number born in each group*

Designation	No. of transfers	Total no. of offspring born	Mean litter size at birth
FLL	12	37	3.08
FSL	9	29	3.22
TLL	11	83	7.55
TSL	7	57	8.14
FLS	28	82	2.93
FSS	15	50	3.33
TLS	8	60	7.50
TSS	12	91	7.58
TML	19	111	5.84
TMS	25	112	4.48
Totals	146	712	

### 3. RESULTS

As reported also by Brumby (1960), egg transfer *per se* had no effect on subsequent body weight, when comparative data were available. For instance, the TLL group had a mean litter size very close to the natural one of a stock (LAU) used by Al-Murrani & Roberts (1974), whose genetic history was similar; contemporaneous body weights in the two stocks were virtually identical at all ages.

#### (i) *Body weight differences in a standard maternal environment*

Table 2 shows the body weights of L and S genotypes in blocks where the maternal environment was the same for the two. The objective of a common maternal environment was most clearly achieved in the mixtures, in the same mothers, as this excludes accidental variation in litter size and sampling differences between dams. The difference between L and S within TML may be compared directly with (TLL-TSL), and similarly within TMS with (TLS-TSS). The agreement is generally good, and where any discrepancy is suggested, it falls well short of statistical significance. The difference in growth between L and S was magnified when only five eggs were transferred.

We conclude the following about the growth of L and S genotypes when maternal influences are removed. First, for similar litter sizes, birth weight is virtually unaffected by the genotype of the mother, and is overwhelmingly

a property of the offspring themselves, in these stocks. This excludes genetic prenatal maternal effects, leaving only environmental effects through variation in litter size. The comparisons set out in Table 3 support this with one exception (FLL-FLS); where only five L eggs were transferred, large mothers conferred some advantage. The superiority of L mothers is discussed further in the next section.

The second conclusion is that L genotypes exceed the weight of S genotypes by some 25% at birth, and this magnifies to about 80% at 6 weeks. This divergence, however, does not occur uniformly over time. The progeny from the mixed transfers

Table 2. *Body weights (g) at three ages in the different groups (unweighted mean of the two sexes),  $\pm 1$  S.E.*

Designation	Mean body weight at:		
	Birth	3 weeks	6 weeks
FLL	2.11 $\pm$ 0.05	12.69 $\pm$ 0.48	34.97 $\pm$ 0.96
FSL	1.47 $\pm$ 0.07	9.21 $\pm$ 0.25	16.63 $\pm$ 0.45
Difference	0.64 $\pm$ 0.09	3.48 $\pm$ 0.54	18.34 $\pm$ 1.06
TLL	1.75 $\pm$ 0.03	10.53 $\pm$ 0.57	30.62 $\pm$ 0.71
TSL	1.45 $\pm$ 0.04	8.12 $\pm$ 0.57	15.53 $\pm$ 0.29
Difference	0.30 $\pm$ 0.05	2.41 $\pm$ 0.81	15.09 $\pm$ 0.77
FLS	1.89 $\pm$ 0.04	11.42 $\pm$ 0.50	31.45 $\pm$ 0.79
FSS	1.55 $\pm$ 0.04	8.66 $\pm$ 0.41	16.78 $\pm$ 0.63
Difference	0.34 $\pm$ 0.06	2.76 $\pm$ 0.65	14.67 $\pm$ 1.01
TLS	1.62 $\pm$ 0.07	7.78 $\pm$ 1.16	26.97 $\pm$ 1.99
TSS	1.42 $\pm$ 0.04	6.91 $\pm$ 0.32	15.09 $\pm$ 0.49
Difference	0.20 $\pm$ 0.08	0.87 $\pm$ 1.20	11.88 $\pm$ 2.05
TML (L)*	1.86 $\pm$ 0.05	12.81 $\pm$ 0.60	33.03 $\pm$ 1.03
(S)	1.50 $\pm$ 0.05	9.54 $\pm$ 0.43	18.00 $\pm$ 0.44
Difference	0.36 $\pm$ 0.07	3.27 $\pm$ 0.74	15.03 $\pm$ 1.12
TMS (L)	1.86 $\pm$ 0.04	10.28 $\pm$ 0.58	30.54 $\pm$ 0.84
(S)	1.46 $\pm$ 0.04	8.21 $\pm$ 0.38	17.09 $\pm$ 0.59
Difference	0.40 $\pm$ 0.06	2.07 $\pm$ 0.69	13.45 $\pm$ 1.03

\* L offspring from TML, etc.

were weighed every 3 days, and the L/S ratio of weights is shown in Fig. 2, for L and S mothers separately. The ratio actually declines to 1.15 by 15 days, and only then do the genotypes diverge further. The L genotypes begin to express their superiority before weaning (21 days), possibly due to the earlier eruption of their molar teeth and their ability to eat solid food. Falconer (1973) had reported that most of the divergence between L and S genotypes occurred after weaning. These more detailed data suggest that differential growth starts earlier.

Falconer (1973) reported a L/S ratio of 2.3 at 6 weeks of age. The same ratio for various comparisons from Table 2 ranges from 1.8 to 2.1 when the maternal environment was standardized. Thus, maternal effects may have been responsible for some 10–20% of the divergence in body weight brought about by the original

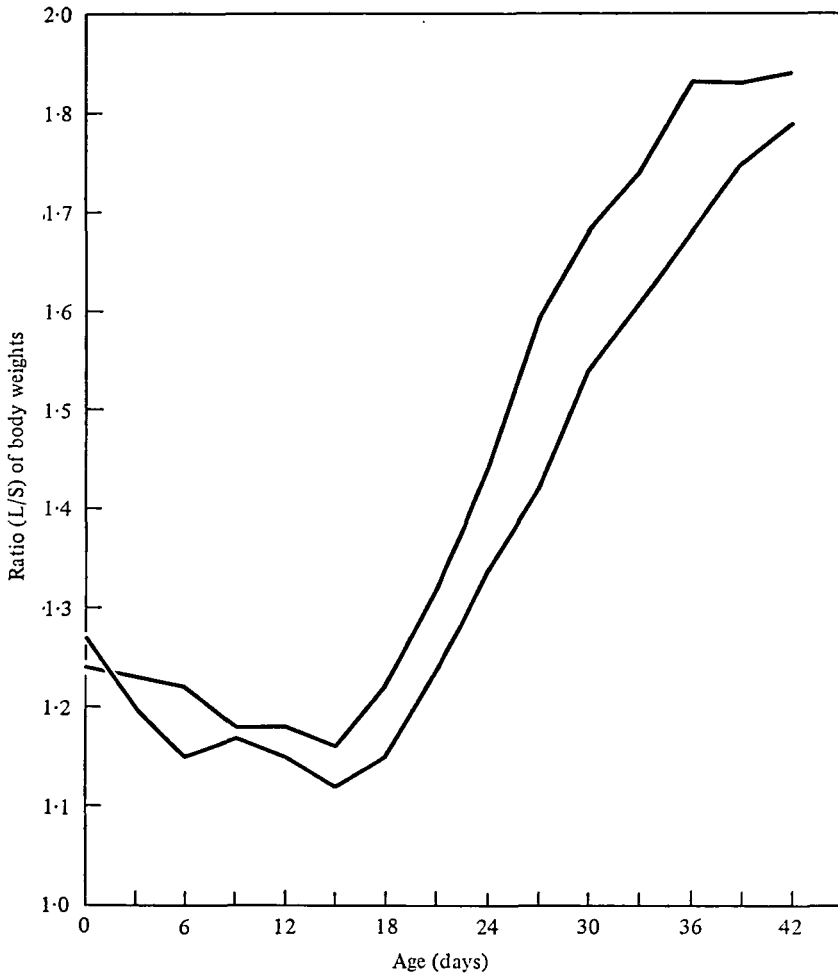


Fig. 2. Ratio (L/S) of body weights of L and S genotypes from mixed litters at different ages; upper line when gestation and suckling by large mothers, lower line by small mothers.

Table 3. Maternal effects on body weight at various ages. Groups with the same genotype and same number of transferred eggs compared in large and small mothers. Data from Table 2

Comparison	Difference in mean body weight (g) at:		
	Birth	3 weeks	6 weeks
FLL-FLS	0.22 ± 0.064	1.27 ± 0.69	3.52 ± 1.24
TLL-TLS	0.13 ± 0.076	2.75 ± 1.29	3.65 ± 2.11
FSL-FSS	-0.08 ± 0.081	0.55 ± 0.48	-0.15 ± 0.77
TSL-TSS	0.03 ± 0.057	1.21 ± 0.65	0.44 ± 0.57

selection. These maternal effects were almost wholly postnatal, reflecting lactational performance or some other aspect of maternal care.

(ii) *Maternal influences on growth*

As Table 2 shows, offspring weights were uniformly higher from L mothers, but this was mostly attributable to the depression in weight of L offspring in S mothers. The relevant comparisons are set out in Table 3. The last two rows show that by 6 weeks, S offspring were unaffected by the genotype of the mother, having derived only a small and transient advantage from L mothers at weaning time. L offspring, on the other hand, find S mothers relatively inadequate at all states (first two rows of Table 3). The postnatal maternal superiority of L mothers, shown in these comparisons, substantiates the conclusion reached earlier. But only L offspring are able to retain this advantage by 6 weeks; it disappears in S offspring.

Table 4. *Relative growth before and after weaning, at 3 weeks of age.  $W_0$ ,  $W_3$  and  $W_6$  are body weights at birth, 3 and 6 weeks, respectively. Unweighted means calculated by pooling values from Table 2*

Offspring	Parent	$\frac{W_3 - W_0}{W_3}$	$\frac{W_6 - W_3}{W_3}$
L	L	5.31	1.75
L	S	4.46	2.06
S	L	5.08	0.87
S	S	4.36	1.07

Table 5. *Regression coefficients of body weight at birth and at 3 weeks on number born alive, and at 6 weeks on number weaned. Data from either five or ten eggs transplanted into each group*

Source	No. of litters	Regression coefficients (g/mouse) of:		
		Birth wt./no. born	3 weeks wt./no. born	6 weeks wt./no. weaned
FLL + TLL	23	-0.069 ± 0.010	-0.27 ± 0.15	-0.53 ± 0.28
FLS + TLS	36	-0.066 ± 0.010	-0.64 ± 0.18	-0.33 ± 0.37
FSL + TSL	27	-0.010 ± 0.010	-0.29 ± 0.08	-0.27 ± 0.12
FSS + TSS	16	-0.023 ± 0.010	-0.39 ± 0.10	-0.41 ± 0.16

The L offspring retain maternal advantages into the postweaning period despite the counterbalancing effects of compensatory growth, whereby growth during any period is inversely related to the proportion of normal growth already achieved, as discussed by Monteiro & Falconer (1966). Table 4 shows the effects of compensatory growth in our material. Prewaning growth is somewhat depressed by S mothers, as noted earlier, but this leads to an increase in relative growth after weaning. The system thus behaves as if it has a built-in correction for maternal effects, though the correction is only a partial one in the case of L offspring.

Maternal effects clearly arise from variation in the litter size, as a result of either

five or ten eggs being transferred. The expected inverse relationship between body weight and litter size (Table 5) is almost uniformly significant for all groups at birth and at weaning time. The absolute difference is, on average, retained until 6 weeks of age, though its significance obviously declines as its relative importance diminishes.

#### 4. DISCUSSION

We conclude that maternal effects are of limited importance in our material. Before birth, they arise only from variation in litter size; during lactation, the same environmental source is detectable. But postnatally, L mothers are superior to S mothers in milk supply, or in some other aspect of maternal care. To the extent that this is a property of the mother's genotype (whether or not it is mediated through body weight), it may be termed a genetic maternal effect. Its contribution to the original selection response was at most 20%, and generally seemed to be somewhat less than this.

Cumulatively, however, maternal effects may be substantial. If we take our extreme comparison from Table 2 (FLL-TLS), the difference in 6-week weight is 8 g, almost 25% of the mean. But if we interpose an intermediate group (FLS or TLL), and split the difference accordingly, we see that litter size alone is responsible for fully half of the difference.

Several of the studies reviewed by Legates (1972) and by Eisen (1974) suggest that maternal effects have their maximum effect around 12–14 days *post partum*, which age coincides with the peak of lactation (Hanrahan & Eisen, 1970). But Monteiro & Falconer (1966) reported that maternal effects increased until 4 weeks of age, 1 week after weaning, and Brumby (1960) reported their persistence even to 12 weeks of age. In our material, some maternal effects were still detectable at 6 weeks of age, but this arose entirely because large offspring had been handicapped by small mothers. Small offspring, on the other hand, showed no residual maternal effects at 6 weeks, and even earlier, had failed to profit to any extent from the superiority of large mothers. These results could be described formally as an interaction between the strain of the mother and the strain of the offspring. Formal descriptions in such terms, however, are not very instructive.

Because of the ubiquity and magnitude of maternal effects, within-litter selection has frequently been favoured when selecting for body weight in the mouse. It avoids some of the complications, even though on other grounds its theoretical advantage is dubious. But even where within-litter selection has been used, as in our material, maternal effects nevertheless accrue. The divergence in body size had not detectably affected uterine performance, but lactational performance had been altered to correspond to the greater postnatal growth of the large lines. Even so, it is arguable whether the improvement in milk supply was adequate for the potential growth of the large lines, if we set as our standard the growth in the reduced litters following the transfer of five eggs only. Further, there was a rapid enhancement of the divergence between large and small mice just before weaning. This could be in part a reflexion of the suboptimal nutrition

of the large offspring up to that time, suppressing the expression of the full genetic difference in body weight and allowing the subsequent influence of compensatory growth.

W.K. A.-M. thanks the British Council and the Calouste Gulbenkian Foundation for financial support, and the University of Baghdad for leave of absence.

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