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Ovulation and post-ovulational losses in strains of mice selected from large and small litters

By NIGEL BATEMAN

A.R.C., Animal Breeding Research Organisation, Edinburgh 9, *Scotland*

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1. INTRODUCTION

While responses to selection are generally attributed to genes acting at many loci, little is known about the biological components through which these loci gain their effect. Litter size is a trait which embraces many identifiable components. The present work, using strains of mice originating from a common stock and then bred for twelve generations from their largest or smallest litters, seeks to find which components of litter size were drawn on for the response. The measure of litter size, on which the selection was practised, was the number of live, newly-born young found in first litters born to mature mice of 12–16 weeks of age.

Litter size is biologically complicated. It is wholly female in some aspects; and part female, part male and part filial in others: it is the product of ovulation, of fertilization (which involves the timing of mating, semen quality, sperm transport, capacitation, penetration and conjugation), and of survival (i.e. ability of embryos to meet conditions provided by the female during early development, implantation, foetal development and birth). All of these components were open to selection; the question was: which components actually responded?

The work follows a similar investigation by Falconer (1960, 1963) who, in selecting within groups of litters from matings of full sisters to the same male, had selected neither on the male side nor on maternal effects. Falconer's responses were explained entirely by the female's ovulation rate and uterine influences on post-ovulational survival. It will be of particular interest to compare results as my own stocks were derived from Dr Falconer's and differed only in the manner of selection.

2. MATERIAL

I was happy to start my selections with mice that were broadly representative of early offshoots of Dr Falconer's high, low and control stocks. Dr R. C. Roberts had taken ten lines from each of Falconer's stocks and, having successfully inbred twenty-six lines to 50% inbreeding, crossed them (Roberts, 1960). Dr Roberts gave me ninety hybrids, and from their progeny I bred a homogeneous group of 124 litters from which to draw my own selected lines. The genes available to my

selections must have been similar to those with which Falconer started, although some embryonic lethals and semi-steriles were possibly lost during Roberts' period of inbreeding. Three strains with similar ancestries were drawn from the 124 litters and were then bred separately through twelve generations selected from their largest (SH and H strains) or smallest (L strain) litters. The SH and H strains differed only in the number of new-born young that they were permitted to rear, and this seems not to have affected their responses. Litters of the H and L strains were left at their natural size, while in the SH strain they were reduced to six young at birth. No unselected control was maintained, nor was it possible to reconstitute the foundation stock. All three strains were outbred. After the termination of selection the differences in nursing were removed, and all new-born litters were adjusted to the same number of young. Under these conditions, immediately before the present investigations, litters of these average sizes were born:

SH	$11{\cdot}2 \pm 0{\cdot}25$
H	$11{\cdot}1 \pm 0{\cdot}21$
L	$5{\cdot}5 \pm 0{\cdot}35$
Difference H – L	$5{\cdot}6 \pm 0{\cdot}41$

Body size and fertility are often associated in mice, but these strains were similar in weight, and when their females were mated at approximately 11 weeks they weighed 30·9, 29·1 and 27·5 g., respectively. Litters of the lightest strain might have had one less young on this account. We shall be concerned principally to account for the difference of 5·6 live young between the H and L strains. The SH strain, being equally unrelated to the H and L lines, provided suitably fertile mates for measuring the male's and female's contributions to litter size, and also provided hybrid offspring for measuring the contribution of offspring vitality.

The material for these investigations normally consisted of first litters conceived when the females were 9–13 weeks old, but the results of an exceptional investigation made on second litters of older mice have been included. All of the litters belonged to the strains' 17th–21st generations. Males were not present at their litters' birth, and were not responsible for any cannibalism of the new-born.

3. METHOD OF DETERMINING POST-OVULATIONAL LOSSES

The number of eggs shed and the number of young born alive from them cannot be counted in the same animal, but dissections of pregnant and of parturient females can cover the whole of development between ovulation and birth in two overlapping stages. The pregnant females showed what proportion of the eggs shed survived as foetuses, and the parturient females showed what proportion of their own foetuses survived birth. Accordingly, half of the females were dissected in late pregnancy to give counts of corpora lutea, implantation sites and live foetuses; the other half were dissected immediately after parturition to give counts of implantations, live foetuses and new-born young.

(i) *Pregnant females*

Dissections of ninety-eight females were made when they showed outward signs of imminent birth, usually about their 16th–19th day of gestation. Although Fekete (1950) has described one strain of mice where every ovary contained polyovular follicles, Falconer & Roberts (1960) and Falconer, Edwards, Fowler & Roberts (1961) (or see Falconer, 1963), who examined several strains, including those related to the present stock, found that the number of corpora lutea counted in late pregnancy always agreed closely with the number of eggs recovered from other females immediately after ovulation. Accordingly, as eggs cannot be counted without disturbing the process of pregnancy, counts of corpora lutea in late pregnancy have been used here in their place. These were made under binocular magnification with minimal dissection of the excised ovary, and usually with no uncertainty about the count. Foetuses were counted from the number of implantation sites together with their associated placentae or placental remnants. In the group of females bearing their second litters there were also some exceptionally small implantation sites isolated from any placenta or remnant. These sites were regarded as relics from the first pregnancy and were not included in the number of foetuses. In nine females one or two supernumerary foetuses were seen. These were attributed to errors of counting corpora lutea, rather than to polyovular follicles (Fekete, 1950), or identical twinning (Grüneberg, 1952). The supernumerary foetuses were roughly balanced between the H and L strains and were unlikely to bias the conclusions. In five other females supernumerary foetuses on one side were offset by deficiencies in the other uterine horn; these were treated as instances of foetal migration (McLaren & Michie, 1954). In seventy-one of the ninety-eight females there were between one and eleven fewer foetuses than corpora lutea. The deficiencies were attributed to eggs lost before implantation, perhaps because they were unfertilized. Dead foetuses were associated with implantation sites that looked yellow and were poorly vascularized. This was so over the entire range from fully grown foetuses to minute brown gelatinous remnants. Sites supporting live foetuses were red with prominent vascularization.

(ii) *Parturient females*

A search was made each morning for new births, and dissections of females and examination of litters proceeded throughout the day. Uteri were dissected and the yellow and red implantation sites were counted separately. Yellow sites were used as counts of dead foetuses which made little or no contribution to the litter found at birth. Thus, not one of forty-eight females with yellow sites had more young than red sites, and no fewer of their litters were deficient in young (twenty-four out of forty-eight litters) than were the litters from entirely red-sited females (twenty-one out of forty-eight). Placentae were normally eaten by the females; it seems that if unresorbed dead foetuses were born, they also were eaten. Accordingly, the expected size of the litter was taken from the counts of red sites, corresponding with the number of foetuses alive at the end of pregnancy. The number of

young found (including the obvious dead and fragments identified as additional dead) was compared with this expectation, and missing young ascribed to newborn young that were wholly cannibalized. Fifty females had the expected number of young; in forty-five females the young were outnumbered by red sites; and one female had a supernumerary young.

4. STATISTICAL METHODS

The significance of differences between experimental groups for single criteria like litter size were based on means and standard errors obtained from the relevant untransformed observation on each litter. Differences in proportions (as in the proportion of eggs that implanted) were first screened by chi-square analysis on each group's totals, applying Yates's adjustment where apposite (Snedecor, 1946). Where the differences proved insignificant this conclusion was regarded as valid; but if it appeared that the differences might be real, the χ^2 test was replaced. Natural proportions were transformed to angles (Fisher & Yates, 1949) and their variance analysed to assess differences between groups against heterogeneity of their own litters. In this analysis, variation between groups always appeared less significant than the χ^2 test had indicated.

5. RESULTS

(i) *Male fertility*

The fertilities of H and L males were first compared in terms of the size of litter they sired in matings to SH females. Twenty-one pairs of SH sisters were used, one sister of each pair being mated to an H male, the other to an L male. Every one bred.

Table 1. *Implantation in SH females mated to H and L males*

Males' strain	Corpora lutea (No.)	Implantation sites		Pre-implantational losses*	
		No.	(% of corpora lutea)	No.	(% of corpora lutea)
H	129	120	(93)†	9	(7)
L	148	133	(90)†	15	(10)

Heterogeneity $\chi^2_{(1)}$ adj $= 0{\cdot}52$; $P = 0{\cdot}50$.

* Excess of corpora lutea over implantation sites.

† Fertilizational capacity of the males equals this figure if all fertilized eggs implant, and could be higher.

Their litters averaged 11·9 and 11·5 young in favour of H males. But the difference of $0{\cdot}4 \pm 0{\cdot}62$ young ($P = 0{\cdot}50$) was small, so no important difference in male fertility had been revealed by this comparison. It was possible, however, that a real fertilizational difference had been obscured by counterbalancing fertilizational and

embryonic losses. Accordingly, the next step was to look at implantation rates. Ten SH females were mated to H males, and another ten were mated to L males. The females were dissected in late pregnancy when their corpora lutea and implantation sites were counted (Table 1). Eggs shed in matings with H males had the slightly superior implantation rate of 93%, in comparison with the others' 90%, but the difference was quite insignificant ($\chi^2 = 0{\cdot}52$, $P = 0{\cdot}50$) and excluded any important distinction of fertilizational capacity between H and L males. It was concluded that male fertility had not responded to the selection for litter size.

(ii) *Subviable offspring*

Falconer (1960) has suggested that selection for small litters would favour parents that were heterozygous for fully lethal or partially lethal recessive genes acting on the embryos. Where parents were heterozygous for the same gene, litters could be reduced by one-quarter. The reduction could be more if some parents were survivors from among homozygotes for partially lethal recessives. Thus any recessive lethal present in the stock initially should become more frequent in a small litter strain and disappear in a large litter strain, like the SH strain. No homozygotes for lethals should be generated by crosses to this strain and, if the reduced fertility of the L strain was entirely due to recessive lethality, both sexes should be restored to full fertility in outcrosses. The fertility of L males crossed to the SH strain has already been demonstrated; it remained to look at the fertility of outcrossed L females. Accordingly, litters from fourteen L females mated to SH males were compared with those from another twelve L females mated to L males. One of the latter matings failed to breed. The average size of L × SH litters was 6·64 young, compared with 7·18 young for L × L litters. The difference in litter size was $0{\cdot}54 \pm 1{\cdot}22$ young in favour of the pure-bred litters—a result that does not support the lethal gene hypothesis. As the genotype of L × L young was not unfavourable to their survival and L males were capable of fully normal fertilization, litter sizes must have been determined by the female. Further studies were accordingly turned to ovulation rate, and to the female's ability to conduct her offspring safely through gestation and birth.

(iii) *Ovulation and gestational losses in females having their second litters*

A preliminary study of ovulation and gestational losses was made on the second litters of twenty H females and seventeen L females remated to SH males. The females were dissected in the latter half of pregnancy when counts were made of the numbers of corpora lutea, and of live and dead foetuses (Table 2). L females were deficient in three ways—they shed fewer eggs, lost more eggs before implantation, and had more dead foetuses. Pre-implantational losses were incurred by 88% of L females and 45% of H females, and were twice as common in the affected L females as in the comparable H females.

Table 2. *Preliminary evidence from second litters on the determination of litter size during pregnancy in H and L strains*

Strain	H	L	H − L difference ± standard error
Number of females	20	17	
Average number			
Eggs (corpora lutea)	14·7	13·7	1·0 ± 0·8
Pre-implantational losses*	1·2	4·4	− 3·2 ± 0·9
Foetuses	13·5	9·3	4·2 ± 0·9
Dead foetuses	0·8	1·4	− 0·6 ± 0·4
Live foetuses	12·7	7·9	4·8 ± 1·0
Percentage distribution of eggs			
Pre-implantational losses	7·8	31·8	− 24·0
Foetuses	92·2	68·2	24·0
Dead foetuses	5·8	10·7	− 4·9
Live foetuses	86·4	57·5	28·9
Percentage distribution of foetuses			
Dead foetuses	6·3	15·7	− 9·4
Live foetuses	93·7	84·3	9·4

* Excess of corpora lutea over foetuses.

(iv) *Ovulation and gestational losses in first litters*

Nine months later, twenty-nine H and thirty-two L females were dissected while gestating first litters by SH males. The results are set out in Table 3 and in the first part of Fig. 1 which contains results from parturient females also. L females

Table 3. *Determination of litter size during first pregnancy in H and L strains*

Strain	H	L	H − L difference ± standard error
Number of females	29	32	
Average number			
Eggs (corpora lutea)	12·7	10·1	2·6 ± 0·6
Pre-implantational losses*	0·4	1·8	− 1·4 ± 0·4
Foetuses	12·3	8·3	4·0 ± 0·6
Dead foetuses	1·3	2·1	− 0·7 ± 0·4
Live foetuses	11·0	6·2	4·7 ± 0·7
Percentage distribution of eggs			
Pre-implantational losses	3·5	18·0	− 14·5
Foetuses	96·5	82·0	14·5
Dead foetuses	10·6	20·4	− 9·8
Live foetuses	85·9	61·6	24·3
Percentage distribution of foetuses			
Dead foetuses	11·0	24·9	− 13·9
Live foetuses	89·0	75·1	13·9

* Excess of corpora lutea over foetuses.

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were again inferior in every way, with the differences in eggs shed and pre-implantational losses being clearly significant. The number of dead foetuses in L females was 60% above the figure for H females but was not significantly greater. Yet there were more dead foetuses in L females although they had the fewer foetuses initially and, whereas 25% of their foetuses died, only 11% died in H females ($P < 0{\cdot}01$).

There were wide fluctuations in ovulation rate, pre-implantational losses and foetal deaths between the females with first and second litters. However, for both litters, L females shed fewer eggs than H females, lost four times as many eggs or embryos before implantation, had twice as many dead foetuses in proportion to their original number of foetuses, and finished up with 4·7 fewer foetuses alive.

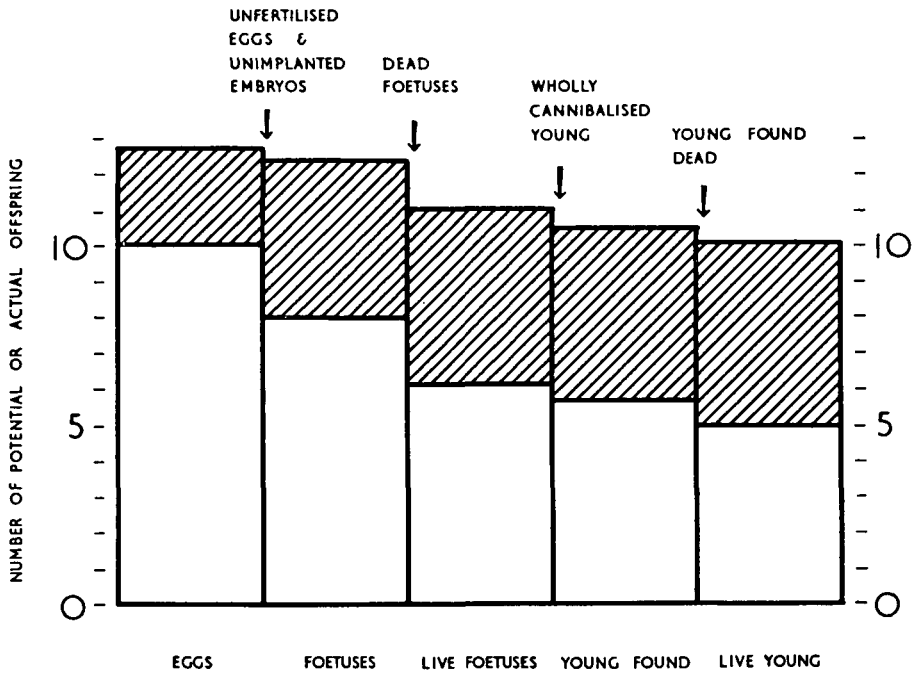

Fig. 1. Successive steps from ovulation through birth determining litter sizes in two strains of mice. Upper line, fertile strain (H); lower line, infertile strain (L); shaded blocks, strain differences. Figures for foetuses (live, dead and total) are averages from both pregnant and parturient females.

(v) *Post-implantational losses: preliminary statement*

Although most of the differential in litter sizes was already accounted for in ovulation rate and prenatal losses, it remained to ascertain the extent of deaths at birth. Parturient females used for this purpose supplied further evidence on foetal deaths. The preliminary examination included six L females and a mixed group of nineteen SH and H females (Table 4). The SH and H females had implanted 14·2 foetuses, against 8·3 for L females. Both groups lost 18% of their implanted foetuses in later gestation or parturition, half being cannibalized.

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Table 4. *Preliminary evidence on determination of litter size from implantation to birth*

Strains	SH & H	L	(SH & H) − L difference ± standard error
Number of females	19	6	
Average number			
Foetuses (red and yellow sites)	14·2	8·3	5·9 ± 1·1
Dead foetuses (yellow sites)	0·9	1·0	−0·1 ± 0·4
Live foetuses (red sites)	13·3	7·3	6·0 ± 1·1
Dead young: cannibalized*	1·5	0·5	1·0 ± 0·6
found	0·2	0·0	0·2 ± 0·1
total	1·7	0·5	1·2 ± 0·6
Live young (= 'litter size')	11·6	6·8	4·8 ± 0·9
Percentage distribution of foetuses			
Dead foetuses	6·7	12·0	−5·3
Live foetuses	93·3	88·0	5·3
Dead young	11·5	6·0	5·5
Live young	81·8	82·0	−0·2
Percentage distribution of live foetuses			
Dead young	12·3	6·8	5·5
Live young	87·7	93·2	−5·5

* Excess of red sites over live and dead young found at birth.

The number of yellow implantation sites in these parturient females (Table 4) was smaller than the number of dead foetuses found in pregnant females of Table 3, so later foetal deaths were not in evidence. Deaths at birth accounted for one-eighth of the live foetuses in SH and H females, against one-fifteenth in L females, i.e. for 1·7 and 0·5 young respectively. However, no statistical significance was attached to this distinction ($P = 0{\cdot}43$). Finally, the numbers of dead foetuses, cannibalized young and young found dead (18:28:3 for SH and H litters, and 6:3:0 for L litters) revealed no distinct modes of mortality ($P = 0{\cdot}4$).

(vi) *Post-implantational losses in purebreds and hybrids*

Four generations later, dissections were extended to purebred SH and to hybrid (SH × H) females and between fifteen and twenty-one females of each strain were dissected after parturition. The observations are set out in Table 5 and in the latter part of Fig. 1. Hybrid and SH females both had 13·0 foetuses on average, H females 12·7 and L females 7·7. Live young represented 90% of the foetuses in both hybrid and SH females, 80% in H females and only 65% in L females. Their statistical significance was evaluated after angular transformation. L females were twice as variable as all the others together and, compared with the H females alone, differed insignificantly from them (15·0 ± 8·9 degrees; $P = 0{\cdot}13$). However, an apparently real difference emerged (21·6 ± 7·9 degrees; $P = 0{\cdot}017$), on comparing L females with all of the others, so foetuses in L females produced the least live offspring of all.

These post-implantational deaths were equally divided between foetuses and the newly born. Two aspects of the foetal deaths stand out. First, their incidence, except in H females, was again no higher than that already apparent in pregnant females (Tables 2 and 3). This confirms the preliminary finding that late deaths were infrequent. Second, the female's hybrid vigour did not reduce the frequency of foetal deaths, which was the same in (SH × H) hybrids as the average in the pure SH and H females.

Table 5. *Determination of litter size from implantation to birth in hybrid and purebred females*

Strain	Hybrid SH × H	SH	H	L	H − L difference ± standard error
Number of females	18	21	17	15	
Average number					
Foetuses (red and yellow sites)	13·0	13·0	12·7	7·7	5·0 ± 1·1
Dead foetuses (yellow sites)	1·0	0·5	1·4	1·4	0·0 ± 0·6
Live foetuses (red sites)	12·0	12·5	11·3	6·3	5·0 ± 1·2
Dead young: cannibalized*	0·3	0·6	0·9	0·7	0·2 ± 0·3
found	0·1	0·2	0·4	0·7	−0·3 ± 0·5
total	0·4	0·8	1·2	1·3	−0·1 ± 0·6
Live young (= 'litter size')	11·7	11·7	10·1	5·0	5·1 ± 1·2
Percentage distribution of foetuses					
Dead foetuses	7·3	3·6	10·7	18·1	−7·4
Live foetuses	92·7	96·4	89·3	81·9	7·4
Dead young	3·0	6·6	9·7	17·2	−7·5
Live young	89·7	89·8	79·6	64·7	14·9
Percentage distribution of live foetuses					
Dead young	3·2	6·8	10·9	21·1	−10·2
Live young	96·8	93·2	89·1	78·9	10·2

* Excess of red sites over live and dead young found at birth.

About half the litters in every group were depleted by deaths at birth. Of these, two-thirds were wholly cannibalized, although few of the one-third that were found dead were mauled. These deaths at birth reduced litter sizes by the order of 10%. The death rate among the young born from live foetuses was 3·2% for (SH × H) hybrid females, 6·8% for SH females, 10·9% for H females and 21·1% for L females. Angular transformation of the death rate for each litter gave these means and standard errors:

Hybrid	6·4 ± 2·0 degrees
SH	8·4 ± 3·1 ,,
H	16·7 ± 3·3 ,,
L	25·4 ± 9·2 ,,

The four groups comprised a heterogeneous population ($P = 0{\cdot}025$) with a not unexpected trend in death rate, but no single comparison had much significance attached to it. On the face of it, the chance that a newly born young would survive was higher if it was born to a hybrid female than to an average H or SH female ($P = 0{\cdot}06$) and inbreeding seems to have contributed to the purebred females' somewhat poorer performance. For an unexplained reason, the chance of survival for young from H females was less than from SH females ($P = 0{\cdot}07$). The lowest chance of survival was for young born to L females, whose inferiority to H females, however, was far from proven ($P = 0{\cdot}4$). The high death rate and exceptional variance in litters born to L females were mostly due to three outstanding litters which were slightly below the L average in number of live foetuses but had no surviving young at birth. Nevertheless there were hardly any more dead and cannibalized young in the litters born to L females than in the litters born to H females and they added very little indeed to the prenatal differential in litter size.

(vii) *Timing of losses*

It has been seen that L females were prone to lose members of their litters at all stages—before implantation, during foetal development, and at birth. Table 6 details their prenatal losses in comparison with H females. Table 7 details their post-implantational losses in comparison with H, SH and (SH × H) hybrid females.

Table 6. *Contribution of pre-implantational and foetal losses to the total prenatal loss in L and H females. (Percentage contributions are given in brackets)*

Females' strain	Pre-implantational losses	Dead foetuses	Total prenatal losses
L	58 (47)	66 (53)	124
H	13 (25)	39 (75)	52

Heterogeneity $\chi^2_{(1)}$ adj $= 6{\cdot}34$; $P = 0{\cdot}013$.

Table 7. *Numbers of the three kinds of post-implantational loss in L, H, SH and (SH × H) hybrid females*

Females' strain	Dead foetuses	Cannibalized young	Young found dead	Total post-implantational losses
L	21	10	10	41
H	23	15	6	44
SH	10	13	5	28
(SH × H) hybrid	17	6	1	24

Heterogeneity $\chi^2_{(6)} = 10{\cdot}4$; $P = 0{\cdot}10$.

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Apparently the L females kept their dead foetuses, dead young and cannibalism in proportion, and only their pre-implantational losses were exceptional.

(viii) *Connexion between early and late losses*

A final question concerned the relation between earlier and later losses in females from the same strain. For example, if a female incurred heavy early losses were her later losses more or fewer than average, or was there no connexion? The answer was found in two correlations obtained from depleted litters in the material of sections (iv) and (vi). One compared the number of unimplanted eggs with the number of dead foetuses; the other compared the number of dead foetuses (yellow implantation sites) with the number of dead and cannibalized young. A positive correlation would be expected if the losses in the two periods had a sustained physiological cause; a negative correlation would be expected if the reduction in litter size at the early stage increased the probability of survival thereafter. The calculations were made within lines of females and were pooled into two average correlations estimated with 50 and 45 degrees of freedom respectively. Both were weak, being $-0{\cdot}16$ and $-0{\cdot}15$, and were insignificant ($P > 0{\cdot}10$). It seemed that the losses were to all intents and purposes uncorrelated, without physiological connexion, and had changed independently under selection for litter size.

6. DISCUSSION

It was reasonable to have presumed that a laboratory population of heterogeneous origin would have responded in any character or component to which selection was applied, and the result that neither the male nor the young had responded to the selection was therefore unexpected. It is not clear that there was no genetic variation in these components. Falconer's own evidence on unselected controls encouraged belief in variation in male fertility, but was somewhat equivocal (Falconer, 1960). No comparable information on the present strains is possible because, owing to the system of mating during their development, male and female influences within strains could not be disentangled. But there is plenty of more remote evidence of variation in male fertility. Finn's (1964) analysis of litter size in a long-established random-bred strain of mice showed that the male affected litter size far more strongly than the young females to which a male was successively mated, and in a way that persisted throughout his reproductive life. Finn did not himself refer to the female's influence on litter size, but what he called 'male × period interaction' was clearly the variation among a male's mates corrected for the average effects of the period over which they mated. Hancock (1962), in his review of fertilization in farm animals, mentions several sources of fertilizational failure in the male; and even embryonic mortality has been influenced by bulls through infectious agents in their semen (Foote & Bratton, 1952). However, there was no sign that such effects were important in differentiating my strains of mice, and of course they may not be heritable in these other species.

As for the young's contribution, Roberts (1960) found that litter size in the population ancestral to my own mice was sensitive to the inbreeding of the young, and it might have been anticipated that the same recessive lethals would have responded to my selection. Apparently they did not.

A remarkable response of the females contravened the usual government of pre-implantational losses, so that most of these cocurred in the strain with fewest eggs. Usually, the females which shed most eggs have the highest rate of loss. This is true of unselected mice (Bowman & Roberts, 1958), of rats (Harper, 1964) and of Falconer's selected mice, too (Falconer, 1963).

That was one of two ways in which the present females failed to repeat corresponding elements of Falconer's responses. The other concerned losses of the newly born. These occurred in both of the present lines, but not in Falconer's (Falconer, 1963). It seems, from tests carried out some 9–12 months apart, that the results of the present investigation were repeatable over a period of time. If so, the different results thrown up by this, Falconer's and Roberts' experiments represented real variation between experiments that started with essentially similar material. It is suggested that the paths along which any one population responds to selection are limited and are decided early by the chance selection of particular genes.

SUMMARY

This paper describes the aspects of fertility that had been affected by selection on litter size. For twelve generations previously the mice used as parents were chosen because they had been born in large or small litters. At the end of this time, litters in the fertile strain averaged 11·1 young born alive, while the less fertile strain averaged 5·5.

It was found that male fertility and inherent viability of the young had nothing to do with the response although neither was excluded by the method of selection. Several contributions, however, were made by the females, who were affected not only in ovulation rate, but also in their control of pre-implantational losses, foetal mortality and mortality of the newly born.

Females from the less fertile strain were particularly prone to pre-implantational loss of eggs. It remains to be shown whether these were due to fertilizational or implantational failure.

The incidence of earlier and later embroyonic losses in females of the same strain were uncorrelated—litters that were depleted early were neither more nor less inclined to be depleted later.

These results are compared with those of an earlier investigation by Dr D. S. Falconer. Their differences are discussed in relation to the availability of genetic variation.

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