

The effects on litter size of crossing lines of mice inbred without selection

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1. INTRODUCTION

In the exploitation of heterosis in plant and animal improvement, inbreeding is frequently employed to produce genetic differentiation in the parent material, through random changes in gene frequencies. But if the resultant crosses are to represent genetic progress, random differentiation alone becomes insufficient, for genotypes of special merit cannot be provided without selection at some stage. The selection, which may be either natural or artificial, can apply or be applied at any of these stages:

1. Selection within lines on inbred performance.
2. Selection between lines on inbred performance.
3. Selection between lines on crossing performance (general combining ability).
4. Selection between crosses on cross performance (special combining ability).

Natural selection will act primarily through the first two ways, if the character is an aspect of natural fitness. Artificial selection can also be applied during inbreeding, though theoretically it is best reserved until the crossing programme.

Little, however, is known about the efficacy of selection in the context of inbreeding, and the experiment to be described here was designed to provide information relevant to this general problem. The character studied was litter size in the mouse. The results are therefore relevant to some problems in animal improvement, especially to such characters as the fertility of pigs.

The general plan was to inbreed a number of lines without any artificial selection, and with minimal natural selection. To this end, it was imperative to preserve all possible lines. This in turn precluded raising the inbreeding coefficient above 50% or so, for by previous experience the loss of lines then becomes inevitable. Thus the experiment was of necessity restricted to only partly inbred material, but the obvious theoretical disadvantage of this was somewhat mitigated by greater practical application. For the difficulty and cost of maintaining inbred lines becomes prohibitive in farm animals, even in pigs (see, for instance, Donald, 1955), so that the use of partly inbred material must be explored.

The lines were crossed to obtain the following information:

(a) To compare the performance of the crossbred population with that of the original outbred population from which the inbreds were derived. This comparison would indicate what improvement, if any, would accrue from natural selection which operated almost entirely within lines (1 above).

(b) To estimate the variances of general and special combining abilities. These estimates would assess the effect of artificial selection applied in the manner of 3 and 4 above.

The application of selection in the manner of 1 and 2 above was the subject of another experiment, on the same stock of mice, described by Bowman and Falconer (1960).

2. THE CHARACTER—LITTER SIZE

Litter size would appear to be a self-explanatory term—the number of young born in a litter. This definition is unfortunately complicated by the disposition of mice to eat many of their still-born young—and possibly some others as well. The number of young found is thus influenced by the interval between birth and the examination of the litter. In the experiment reported here, cages were examined once daily, the number of live young being recorded as the litter size.

All the work was done on first litters only. The collection of sufficient information on second litters to be of material assistance would inordinately prolong the generation interval, sufficiently so as to nullify the advantage of more accurate measurement. The character chosen for study was therefore ‘the number of live young found in the first litter’. While this may not reflect accurately the common concept of ‘litter size’, the term as defined has complete operational validity.

Litter size as a character is one of considerable complexity. It has three major factors, each of which determines the upper limit of the succeeding one:

1. The number of ova shed.
2. The number of ova fertilized.
3. The number of zygotes carried to term.

The first of these is of course wholly a character of the dam. The second may be influenced by either the sire or the dam. Though Falconer (1955) showed the effect of the sire on litter size in outbreds to be negligible, this may not be so in an inbred population. While it may be tempting to regard the third component as a function of the viability of the young, we cannot exclude the potential influence of the dam, quite apart from her contribution to the genotype of the litter. It can be seen, therefore, that when litter size as a character is submitted to any genetical analysis, its constituent factors are intricately confounded. This problem will be discussed at greater length when the actual results are examined.

The complexity of the character, however, does not end with its multiple determination. For the number of young born is subject to a strong maternal effect dependent upon the weight of the mother. A large mother tends to produce a large litter, in which individual weights are consequently depressed. This handicap is still reflected in weight at mating time. Hence the daughter of a large mother tends to be light, and produces a small litter when she in turn bears offspring. The net effect is thus a negative regression of litter size on the size of the litter in which the dam was born, unless there also exists the positive genetic pathway expected of a heritable character. These complicated interactions were studied by Falconer (1955), who calculated the path coefficients relating litter size to the body weight of

the dam and the size of the litter in which the dam was born. The path diagram is shown in Fig. 1. The mother's body weight is inversely correlated with the size of the litter in which she was born, and directly with the size of her own litter. The product of these two coefficients is -0.07 , which would give the regression coefficient of litter size on maternal litter size if no other pathway were operative. There is, however, a direct genetic pathway, which is measured as the partial regression of litter size on maternal litter size holding the mother's weight constant. This coefficient is $+0.07$, as shown. From this, we see that litter size is affected by maternal

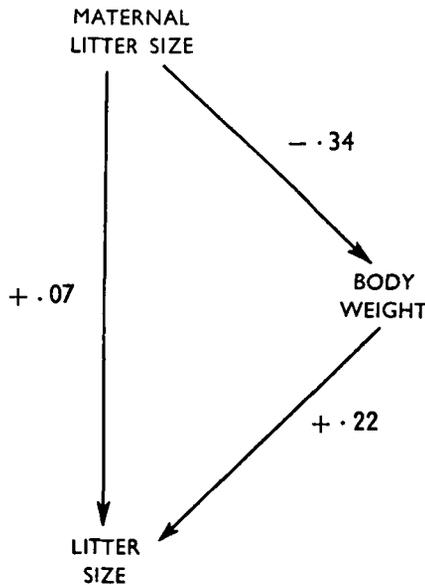


Fig. 1. Path diagram and standardized partial regression coefficients. After Falconer (1955).

litter size through two independent pathways of equal magnitude but opposite sign, explaining why the direct regression, when measured, comes out to be zero (Falconer, 1955).

The relevance of these maternal effects to the subject of this paper is apparent from the following considerations. Firstly, as litter size declines on inbreeding, a maternal effect will be initiated counteracting to some extent the direct effect of inbreeding. But body size itself, and other characters such as milk production, are also liable to be depressed by inbreeding. The possible interactions become so involved that the nett effect becomes obscure. At the present state of our knowledge, we can only approach the problem empirically, and this discussion of the complexity of the character has been presented to show that any attempts at a more sophisticated interpretation of the subject would only be of questionable validity.

3. MATERIALS AND METHODS

It was a premise of the experiment that no lines should be lost during inbreeding. Previous experience had shown that in practice it would be impossible to carry the

inbreeding coefficient beyond about 0.50 without introducing the likelihood of losing lines through low fertility or even complete sterility. It was clear from the start that the crossing would have to be done from partly inbred material.

The broad outline of the experiment was therefore as follows. The inbreeding stage was confined to three generations of brother-sister mating. The lines were then crossed at random giving crossbred litters. As litter size is largely a maternal character, these crossbreds had to be mated to test their fertility, for this was what the experiment was required to determine.

(i) *Inbreeding programme*

It was decided to start with thirty inbred lines, which were derived from mice surplus to the requirements of a selection experiment for litter size described by Falconer (1955). Ten inbred lines were derived from each of the high, low and control stocks of the selection experiment, which had then proceeded for ten generations. There was therefore some differentiation among the original material which had to be allowed for in the crossing programme. Ten litters were chosen from each stock; each litter came from one family and subsequently became the foundation of one inbred line. The largest and smallest litters in the 'high' and 'low' stocks respectively were of course required for the selection experiment. In choosing litters for the present work, this bias was counteracted by rejecting also the other extreme. With this exception, and the avoidance of sib litters, the foundation litters were taken at random.

The inbred lines were propagated in the following manner. All the available females of a litter were divided between two of their sib males, as a precaution against male sterility or accidental loss. Each line thus normally gave birth to more than one litter, one of which was taken at random. The random choice was occasionally disturbed by a litter not containing the required two males and two females, which was usually excluded in the interest of safeguarding the line. But any selection thereby introduced against litters of extreme sex ratio and against some small litters was so slight (and probably ineffective) that it was considered to be of little consequence.

The mice were mated when the youngest reached 6 weeks of age, the oldest mice of that generation being approximately 8 weeks by that time.

In spite of all reasonable efforts to maintain them, four lines in fact failed to complete the inbreeding stage of the experiment, and of course are not represented in the crosses. Two lines were lost for reasons unconnected with fertility, but the loss of the other two must be ascribed at least in part to low fertility. Each gave birth to small litters, all of which died before weaning. There was therefore undoubtedly a little selection during inbreeding, but its magnitude must be considered insufficient to affect materially any conclusions that emerged from the work.

(ii) *Crossing programme*

Ideally, each line should be crossed to all the other lines to form an orthogonal set of diallel crosses, but this was prevented by the exigencies of space. Any system

whereby the crossing was done at random would meet the basic requirements of the experiment, and the principle of the scheme finally adopted is illustrated in Fig. 2. In order to use all available lines as both male and female parents, pair-matings were employed. The size of the litter of any one pair was an estimate of the value of that cross. A certain number of replicate crosses was therefore required to assess the error variance.

All crossing was done within each of the three major groups from which the inbreds were derived. The scheme depicted in Fig. 2 was therefore used for each

LINE AS FEMALE PARENT

	1	2	3	4	5	6	7	8	9	10
1		1	2						2	1
2	1		1	2						2
3	2	1		1	2					
4		2	1		1	2				
5			2	1		1	2			
6				2	1		1	2		
7					2	1		1	2	
8						2	1		1	2
9	2						2	1		1
10	1	2						2	1	

LINE AS MALE PARENT

Fig. 2. The principle of the scheme of crossing the inbred lines. The number in each cell represents the number of matings between those lines.

group in turn. There were insufficient mice available to make all the matings required by this general scheme, but when a particular mating could not be made no other was substituted. This would introduce the least bias into the crossing programme.

The crossing programme required two stages, one to obtain the crossbred animals and another to test their fertility. The first cross measures the effect on litter size of crossbreeding in the litter, but still from an inbred mother. The second cross measures the further effect on litter size brought about by using a crossbred mother. In the second cross, litter size is regarded as a maternal character, as the direct effect of the male on litter size in fertile outbreds was known to be negligible (Falconer,

1955). We are interested in the effect on litter size of the genotype of the mother, as determined by her inbred parents.

In the second cross, matings between crossbred mice with a common parental line was avoided. Apart from that, the mice were mated schematically as before. The scheme of crossing employed was in principle a repeat of the first cross, except that a certain number of triplicate matings were substituted for the duplicate ones of the first cross. This was done as the error variance in the first cross was rather large.

As the inbreeding of parents and offspring are out of step throughout the experiment, Table 1 shows the inbreeding coefficients of parents and of offspring for every generation. The foundation animals are designated generation O, the inbred generations I, and the crosses X.

Table 1

Generation	Inbreeding coefficient		Litter size	Body weight of dam at 6 weeks (g.)
	Parents	Offspring		
O	0	0	8.12	21.9
I ₁	0	0.25	6.73	21.2
I ₂	0.25	0.375	5.82	20.8
I ₃	0.375	0.50	5.69	20.1
X ₁	0.50	0	6.20	21.5
X ₂	0	0	8.47	21.3

4. RESULTS

The data that accrued from the experimental work will be presented in three sections in the following order:

- (a) The effects of inbreeding and crossing on mean litter size.
- (b) The differentiation between inbred lines in litter size.
- (c) The analysis of variance of litter size in crosses between inbred lines.

(a) *Mean litter size*

To a limited extent, it is possible to observe separately the effect on litter size of inbreeding in the dam and inbreeding in the litter. In the first inbred generation, any reduction in litter size is clearly attributable to inbreeding in the young, as the parents are still outbred. Likewise, any increase in the first cross will be due to crossbreeding in the litter, and any further increase in the four-line crosses can be ascribed to crossbreeding in the parents. But, for the intermediate generations of the experiment, the inbreeding of parents and young will proceed simultaneously but at different stages.

The generation means for litter size during the inbreeding and crossing phases of the experiment are shown in Table 1, and are illustrated graphically in Fig. 3. The general picture is the expected one of decline on inbreeding, with subsequent recovery on crossing the inbred lines. In the first generation of inbreeding, mean litter size fell by 1.39 as a result of increasing the inbreeding coefficient of the young from

0 to 0.25. Over the next two generations, there was a further fall of 1.04 in mean litter size; as indicated earlier, it cannot be determined to what extent this is due to further inbreeding in the young, and to what extent it is caused by inbreeding in the parents.

In the first crossbred generation, when the inbreeding coefficient of the young was changed from 0.50 to 0, litter size improved by 0.51. This, of course, is a minimal

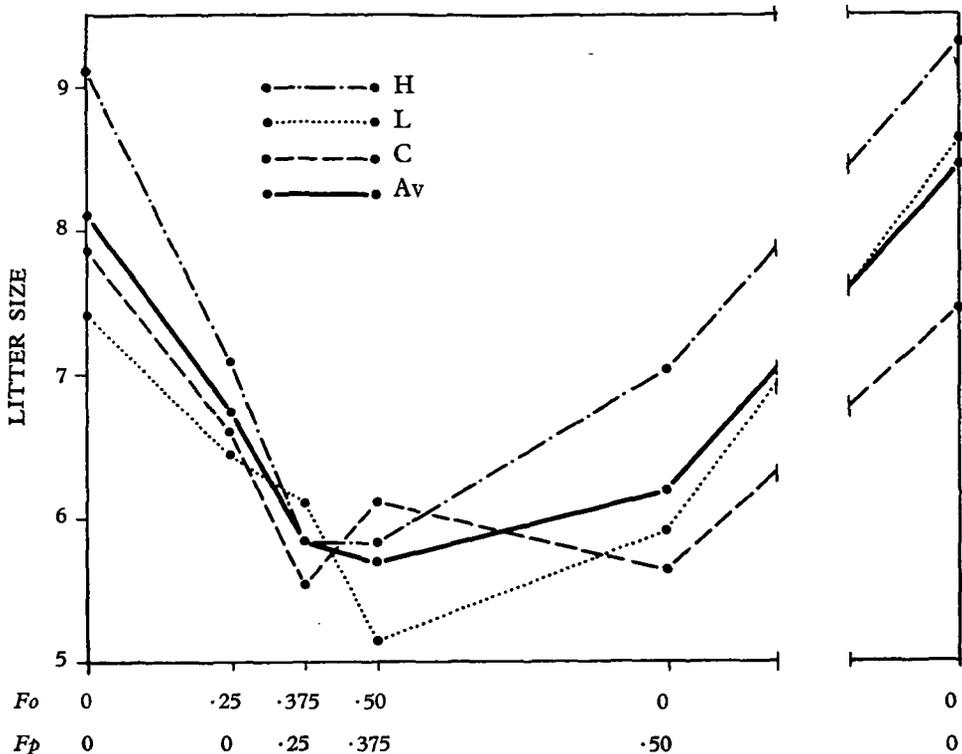


Fig. 3. Litter size plotted against inbreeding coefficient of the offspring (F_o). Inbreeding coefficient of parents (F_p) also shown. Group H—previously selected for high litter size; Group L—previously selected for low litter size; Group C—not previously selected; Av—average of all groups.

estimate of the initial effect of crossbreeding. Had the inbred parents borne inbred rather than crossbred young, their estimated litter size would be somewhere in the region of 5.0, assuming a linear decline. This would indicate that the real effect of crossbreeding in the litter was to increase litter size by rather more than one mouse. Nevertheless, this increase was considerably smaller than expected if we were to extrapolate from the results of the first inbred generation, where a bigger change in litter size occurred for only half the change in inbreeding coefficient. The anomaly does not end here. In the second inbred generation, the additional effect of inbreeding in the dam was barely perceptible over the expected effect of further inbreeding in the young. Yet, in generation X_2 , the effect of crossbreeding in the dam was to

increase litter size by 2.27 over the previous generation. The data suggest that inbreeding may impose a limit on the dam's potential fertility, and that no amount of heterozygosity in the young would increase litter size above a certain level. In outbred dams, on the other hand, any reduced viability through inbreeding in the unborn young would be fully revealed in the reduced litter size at birth.

The mean litter size of the crossbred mice in generation X_2 is 0.35 of a mouse higher than in the original outbreds, generation O. The comparison of these two means is of prime importance and represents one major interest of the experiment. The difference is not significant at the 5% level, despite the slight involuntary between-line selection during inbreeding, mentioned earlier. Over the period of the experiment, generation means of the outbred control varied between 7.00 and 8.17, which makes a difference of 0.35 appear unimportant. There is therefore no reason to suppose that natural selection operating within lines during inbreeding has had any effect on the mean performance of the derived crossbred population.

It is perhaps of some interest to consider separately the three groups of mice from which the inbred lines were derived. These groups, though initially of common origin, had become differentiated through selection for high and low litter size, the third group being an unselected control. It is conceivable therefore that the effect of inbreeding on litter size could well be different in the different groups. Considering first the two groups that had previously been selected, it seems that after three full-sib matings, litter size had declined in both by approximately the same proportionate amount to about two-thirds of the initial litter size. But the increase on crossing was relatively greater in the group erstwhile selected for small litters. However, the standard errors of all these estimates of group means were of the order of 0.4 of a mouse, and without any more elaborate statistical analysis it is clear that apparent differential trends of the magnitude observed would not be significant. In the group that had not previously been selected, litter size increased during the last generation of inbreeding and fell again when the lines were crossed. This does not accord with expectation nor with the behaviour of the other two groups. It seems probable that the estimate of the mean of the I_3 generation in this group is spuriously high either through sampling errors or through some short-term environmental influence which the other groups did not encounter.

Litter size, as mentioned earlier, is markedly affected by the weight of the dam, and the picture is therefore not complete without the examination of this correlated character for possible changes during the experiment. If weight were to decrease on inbreeding with a subsequent increase on crossing, this would have obvious repercussions on the interpretation of the observed effects on litter size. Because of this possibility, the weight of the females was recorded at 6 weeks, the approximate age at mating. The mean weight is shown in Table 1. The first conclusion is that 6-week weight did not change in any systematic manner with changes in heterozygosity. Secondly, such changes as were observed were so small that any correction of litter size for dam's weight would only have a trivial effect. Though body weight in standardized litters is known to decline on inbreeding, it seems that in this experiment the depression was more or less balanced by the advantage gained

through a simultaneous reduction in litter size. Likewise, when the lines were crossed, the potential increase in body weight was nullified by the increase in litter size.

(b) *Differentiation between inbred lines*

The classical theory of inbreeding indicates that inbred lines become differentiated, with a corresponding increase in uniformity within lines. The mathematical expressions for the variances between and within lines are $2F\sigma_A^2$ and $(1-F)\sigma_A^2$, respectively, where σ_A^2 is the additive genetic variance in the initial population and F is Wright's coefficient of inbreeding. At complete inbreeding the initial genetic variation is thereby doubled, and it all appears between lines. However, these expressions are true only if all the variance is additive; they will not hold where dominance and epistatic deviations exist, and in most instances the observed result on inbreeding will differ from expectation based on an additive model.

The theoretical treatment of the effect of inbreeding on variation in a non-additive situation has not been developed fully, but Robertson (1952) has examined the consequences on variation due to rare recessive genes. He showed that the within-line variance in such a case would increase on inbreeding until F is in the region of 0.5 and then decline. The between-line variance will also increase, but only slowly at first as the increase is proportional to F^3 . Robertson shows further that the same general conclusions will probably apply to genes showing over-dominance.

It appears therefore that, in an unknown genetic situation, changes in within-line and between-line variances are unpredictable, and for this reason every empirical observation is of some value. The results obtained from the present work are summarized in Table 2. The data from generation X_1 , where the offspring are crossbred, are not included as the variance observed cannot be partitioned in a simple manner into within-line and between-line components.

Table 2. *Variance components within and between inbred lines*

	Generation		
	I_1	I_2	I_3
Within-line component	5.19	6.70	3.16
Between-line component	1.49	0.08	2.81

With only three points available for examination, it is clearly impossible to establish any definite trend. Further, as the estimates of the within-line and between-line components are necessarily negatively correlated, it becomes difficult to deduce anything about their interrelationship. The values obtained for the I_2 generation must be spurious, for on no model would the differentiation between lines vanish so suddenly only to re-emerge in the subsequent generation. But if any reliance can be placed on the other estimates, it seems that the total variation is being repartitioned in the direction of increasing the differentiation between lines.

(c) Analysis of variance in crosses

The data have to be analysed in two distinct classifications. The first of these concerns crosses (irrespective of whether the cross is AB or BA), reciprocal members of the same cross, and error variance. In the second classification, the variance is partitioned between dam-lines, between sire-lines and the interaction between them. We shall consider the two classifications in this order.

The error variance is of course common to both. This was estimated from twenty-two duplicate crosses in the first cross, and forty triplicate matings in the second. In these replicate crosses, parents of the same sex were always taken from the same line. It proved to be immaterial whether replicates were taken from the same litter or from different litters from the same cross. Both analyses were made within the three major groups that constituted the experimental population. 'Group' refers to a set of lines of common origin. The results of the first analysis are shown in Table 3. There seems to be little evidence of variation between crosses in either generation. This indicates that no effective selection of good crosses from the array of possible ones could be made.

Table 3. *Analysis of variance in crosses*

	First cross			Second cross		
	d.f.	m.s.	<i>P</i>	d.f.	m.s.	<i>P</i>
Total	106	7.18		146	5.03	
Between groups	2	19.46	> 0.05 < 0.10	2	42.70	< 0.001
Within groups	104	6.94		144	4.51	
Between crosses	44	7.08	> 0.20	38	5.91	> 0.50
Within crosses	60	6.84		106	4.01	
Between reciprocals	38	5.93	> 0.20	26	6.54	< 0.01
Between replicates	22	8.41		80	3.18	

The influence of maternal effects on litter size is illustrated by the significant difference between reciprocals in the second cross. No such difference could be established in the first cross, probably because of the magnitude of the error mean square. The large error variance, especially in the first cross, is a disconcerting feature of the data. This suggests that no precise estimates of the components of variance involved could be obtained, without large-scale experimentation.

The second analysis attempted to partition the variance between lines, used both as male and female parents, and to measure the interaction between them. This should enable us to distinguish between the 'general combining ability' of a line, which can be defined as the average performance of crosses between that line and all other lines, and the 'special combining ability' of a cross, measured by the deviation of the performance of that cross from the expectation based on the general combining abilities of its parent lines. The variation in the general combining ability of lines will be represented by the sum of two components of variance, that

between dam-lines and the one between sire-lines. The variation in specific combining ability will be the interaction component of variance.

The method whereby the components were estimated was somewhat complicated, owing to the non-orthogonality of the system of crossing and also because a dam-line was crossed only to some of the sire-lines, and vice versa. The analysis is therefore not presented in any detail, but the principle involved is explained by Henderson (1953). The estimates obtained for the components in the two generations of crossing are shown in Table 4.

Table 4. *Components of variance of litter size in crosses*

Component	First cross	Second cross
Between sire-lines	0	1.08
Between dam-lines	0	0.36
Interaction	0	0.07
Error	8.41	3.18

In the first cross, all the components except error took a small negative value, giving zero as the best estimate in each case. In the second cross, the interaction component was very small indeed, indicating that, in this particular situation, specific combining ability is practically non-existent, and certainly very small compared with the general combining abilities of the lines. Because of their composition, the appropriate mean squares could not be adequately tested for significance level.

The order of magnitude of these components compared to the error variance again indicates that for accurate estimation the scale of the experiment is inadequate. But even after allowing for large error variance, there seems to be little evidence of any useful variation between crosses, indicating that selection between crosses would be ineffective.

5. DISCUSSION

The interpretation of the experimental data has been rendered somewhat imprecise by the complexity of the character of litter size. The difficulties involved can be attributed in no small measure to the dual genetic determination of the character, as the relative contributions of the dam and of the litter itself are seldom clearly distinguishable. In addition, we have strong maternal effects on litter size, and their interplay with inbreeding depression adds further intricacies. The examination of the underlying genetic situation will therefore be severely limited in its scope until such time as the constituent factors of litter size are more perfectly understood.

To some extent we have seen the genotype of the dam and the genotype of the litter acting on litter size separately. At the commencement of inbreeding, reduced viability of the unborn litter had a marked effect which was only partly recovered when the lines were crossed. By then, crossbreeding in the dam appeared to be of

predominating importance in increasing litter size, but the effect of inbreeding in the dam, when first introduced, had been barely perceptible. The explanation may be, in part at least, a maternal effect restricting litter size in inbred mothers irrespective of the heterozygosity of the young. The elimination of lethals with a heterozygote advantage cannot be invoked, for ultimately the mean litter size of the original outbred population was restored when the crossbred mice were used as parents. In the absence of selection, this is what theoretical considerations lead us to expect, for unselected inbred lines could then be regarded as a sample of the gametes of the original outbred population. A random cross would therefore represent one individual of the original outbreds.

It is only fair to admit that the apparent contradiction mentioned above could have arisen if the mean litter size for either the I_2 or X_1 generation had been spuriously low. Yet, this seems unlikely, for other workers report analogous findings. Eaton (1953) noted when he crossed inbred lines of mice that the effect on litter size of crossbreeding in the dam was much larger than the effect of crossbreeding in the litter, if inbreeding had proceeded for less than six generations. The assessment of the other point, namely the I_2 generation, is confirmed by Bowman and Falconer (1960), who with the same stock of mice in the same laboratory found a similar rate of decline on inbreeding. When all these complementary phenomena are considered together, the possibility of sampling error becomes reduced, and it would seem that the decline in litter size is not linearly related to inbreeding when its effect in the dam and in the litter are considered separately.

The effect on crossbred performance of any natural selection operating within lines during the inbreeding stage appears now to be unimportant. The improvement in fertility normally associated with crossing subsequent to inbreeding must therefore be ascribed to some other form of selection, as a result of which many of the poorer genotypes would not be represented in the crossbred population. Hybrids between a random array of inbred lines have no intrinsic merit except to the extent that the population was selected during inbreeding. For certain characters, inbreeding and crossing may well provide means of rapid selection, whether natural or artificial, that might not otherwise be possible. Apart from this possibility, the only advantage of the system would be the ability to replicate any desired cross at will.

The lack of variation between the means of the crosses was somewhat unexpected, for the inbred lines were clearly differentiated in the last generation of inbreeding. The probable explanation lies in the use of partly inbred material. It may be shown from a paper by Robertson (1952) that the expected variance between the means of line crosses is $F\sigma_A^2 + F^2\sigma_D^2$, where F is Wright's coefficient of inbreeding when the lines are crossed, σ_A^2 is the additive component of variance, and σ_D^2 is the variance due to dominance. Hence, in this particular experiment only half the additive and a quarter of the dominance variance was available. The additive genetic component of variance in this stock of mice is of the order of 1.5. No similar estimate can be made of the variance due to dominance, but only in special circumstances would it be much greater than the additive component (see, for instance, Mather, 1949). It

is apparent therefore that compared with the error variance observed, these estimates of the genetic sources of variation to be expected, when divided between two generations, become very small. This indicates that before any useful selection could be made between crosses, not only should the experiment be on a larger scale, but also the level of inbreeding should be advanced well beyond 50 per cent.

It can also be shown, from Robertson's paper, that the term $F\sigma_A^2$ represents the component of variation due to the general combining ability of the lines, while $F^2\sigma_D^2$ is a component ascribable to special combining ability of lines in particular crosses. It can therefore be seen that until the level of inbreeding is well advanced, special combining ability will always play a subsidiary role to the general combining ability of the lines, unless the dominance variance is exceptionally large compared to the additive genetic component. Such a situation might occur if overdominant loci, with genes at intermediate frequencies, were contributing largely to the total variance. Employing a somewhat subjective assessment and applying the law of parsimony, it seems that overdominance at a number of loci was not encountered in this study.

The application of these results will be limited to situations of similar genetic control, but in conclusion, inbreeding and crossing as a method of improving a character such as the one described in this paper will not prove useful unless lines at a fairly advanced level of inbreeding are maintained. Even then, many if not most crosses may not be successful in increasing litter size. In view of this, it is encouraging that the within-family selection experiment, carried out on the same stock in this laboratory, has by now produced a substantial difference in litter size between the high and low lines (Falconer, 1955 and unpublished). It has just been shown that there is no reason to suppose that the character is controlled by many overdominant loci, which would preclude the successful outcome of a selection programme. Only in such circumstances would inbreeding and crossing be a better method of improving the character.

SUMMARY

1. The experiment was designed to provide basic information relevant to the utilization of heterosis in animal improvement. The character studied was the size of the first litter in mice.

2. Thirty inbred lines were crossed at random when the inbreeding coefficient reached 0.50 (three full-sib matings). The lines had been inbred without selection except for natural selection operating with lines.

3. The mean litter size of the crossbred mice did not exceed that of the outbred population from which the inbred lines had been derived. This indicates that the increased litter size normally associated with crossbred mice must be ascribed to some form of selection other than within-line natural selection.

4. Estimates were obtained of the variance components associated with general and special combining abilities. As anticipated, these estimates were very small, especially those relating to special combining ability. Before selection between crosses becomes possible, high levels of inbreeding must be achieved.

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