EVALUATION OF CONTINUAL CROSSBREEDING WITH INBRED LINES OF MICE

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Summary
A breeding plan utilising continual crossbreeding of three strains of stock (to capitalise on heterosis for fertility) and selection in the crossbred females for weight, was tested with three standard inbred lines of mice (57 black, BALB/c, and CBA). Crossbreeding increased fertility by raising the number of females that had a litter, and it raised the weight in sons of crossbred dams. But in neither trait did performance equal that of an outbred control population. Selection in crossbred females for weight was ineffective. Thus genetic situations exist (highly inbred lines) where continual crossbreeding and simultaneous selection do not produce the sort of improvement one might expect from such a breeding plan with more variable populations of livestock.

I. INTRODUCTION

Studies in meat producing domestic species indicate growth rate to have a medium heritability and fertility to have a low heritability, but to respond to heterosis. Therefore, one would expect growth rate to respond to selection and fertility to crossbreeding. One should be able to improve both traits simultaneously by a continual crossbreeding scheme in which crossbred females are selected for growth rate and mated to males of an unrelated breed or strain. With males from three breeds available, a farmer can start with females of one breed and mate these to males from a second breed. The crossbred daughters may be mated to males from the third breed. The crossbred daughters of this last mating may be mated to a male from the first breed, and so on. The farmer usually cannot exercise selection in the males he buys, but he can select the females he uses on their own growth rate. Heterosis should keep fertility high while the selection exercised should improve growth rate. A scheme such as this may be useful even to producers with small herd or flock sizes.

Roberts (1965a, 1965b) has reviewed the contributions of the laboratory mouse to animal breeding research. He states that mouse experiments are useful if they elucidate the genetic control of particular situations. Similarly, mice are

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suitable for confirming rapidly, in traits with similar genetic control (similar \( h^2 \)
and response to heterosis), whether breeding plans that appear theoretically
sound, do in fact produce the results expected.

This paper describes an experiment in which a continual crossbreeding plan
for improving fertility and liveweight at a certain age was evaluated using three
standard inbred lines of mice. Results of the first five generations of progeny are
reported.

II. MATERIALS AND METHODS

The experimental mice were obtained from the Department of Physiology,
University of Melbourne (C57 black, BALB/c) and the Walter and Eliza Hall
Institute of Medical Research (CBA). These inbred mouse stocks have been
maintained by brother-sister matings for many years. The original mating for the
present experiment (generation 0) comprised 20 C57 black females and 10
BALB/c males, with two females being mated to each male. The crossbred female
progeny (generation 1) were selected into two lines as follows: line 8a-10 heaviest
females, line 8b-10 lightest females. These females were mated to 10 CBA males,
with one 8a and one 8b female being mated to each male. The crossbred females
of generation 2 were again selected and mated in the same way to 10 C57 black
males. Selection and mating have continued in this way with males used being, for
females of

  generation 3: BALB/c
  "  4: CBA
  "  5: C57, respectively

Data from mice of generation 6 are not yet available.

An unselected control line of mice (line 1) has also been mated at the same
times as the experimental mice of lines 8a and 8b. Generations 7 to 12 of line 1
corresponded to generations 0 to 5 of lines 8a and 8b. Since generation 4, line 1
has been bred from 20 pairs of males and females, with each pair (family) contrib-
uting 1 son and 1 daughter to the next generation whenever this was possible.
At the same time, while daughters remained in the family of their parents the
sons were moved systematically to other families as follows,
in generation 5, males moved to the next family,
in generation 6, males moved 2 families,
in generation 7, males moved 4 families,
in generation 8, males moved 8 families,
in generation 9, males moved 16 families,
in generation 10, males moved to the next family,
and so on. In this way, if all families leave a son and a daughter, the possibility of
inbreeding is avoided for five generations. The effective size of this population is,
therefore, very large.

The ancestors of line 1 (generation 0) came from the Division of Animal
Health, C.S.I.R.O., Parkville, where a population of mice is propagated, without
conscious selection, by at least 40 males and 160 females per generation. This
population should not be inbred.
The following records have been collected from the experimental and control mice, on a routine basis.

Litter size (number of live young born)
Weight at 3 weeks (weaning weight)

" 6 "
" 9 "

Sex ratio in the litter
Matings, and hence, pedigrees.

Fig. 1. — Litter Size (all females included)
111. RESULTS

Figures 1 and 2 present average sizes of litters born to dams in generations 0 to 4 of lines 8a and 8b, and the corresponding generations 7 to 11 of line 1. Figure 1 shows the total number of live young produced divided by the total number of dams mated. The matings of crossbred dams to inbred sires in generations 1 to 4 of lines 8a and 8b were more fertile than the matings of inbred dams to inbred sires of generation 0. Thus, crossbreeding has resulted in an improvement. Figure 2 shows the total number of live young born divided by the number of dams that actually had a litter. There was no improvement in the crossbred generations above the litter size in generation 0 in lines 8a and 8b. Hence, the effect of crossbreeding was to cause a greater proportion of crossbred females to become pregnant, without altering the number of young produced per litter. The parameter graphed in Figure 1 (average number of young born per dam mated) is difficult to analyse statistically. However, the number of matings that were fertile were significantly less in generation 0 than in subsequent generations when tested by Chi Square.

Average litter size of lines 8a and 8b, regardless of how it was expressed, never equalled that in the non-inbred control, line 1.

Figure 3 shows the average weights at nine weeks of the mice born in generations 1 to 5 in lines 8a and 8b, and in equivalent generations in line 1. Crossbred male young from crossbred dams (generations 2 to 5) were significantly heavier.
than crossbred male young from inbred dams (generation 1). Female young did not show this variation. Selection upwards and downwards for weight has produced almost no response. Total selection differential applied in the upward (5.60 g) and downward (5.48 g) direction in females has been 11.10 g. No selection differential has been applied in males as in every case, the same male was mated to a female from each of the lines 8a and 8b. Hence, the average selection differential over both sexes of parents was 5.55 g. The cumulative response to selection in generation 5 (Figure 3) was 0.65 g in males and 0.18 g in females.
Average response was 0.41g which is only 0.07 of the total selection differential of 5.55g. The weight of animals in the experimental populations has remained much lower than that of the control population.

IV. DISCUSSION

The continual crossbreeding plan tested was successful in improving fertility through increasing the proportion of female mice that had litters. It also raised the weight at nine weeks of male progeny of crossbred dams. This latter effect was probably environmental, a result of improved maternal ability of crossbred dams.

Selection for bodyweight in female parents seems to have been ineffective. Also the improvement in fertility was nowhere near sufficient to make performance of the experimental populations equal to that of the outbred control population.

Roberts (1965b) points out that the standard inbred lines of mice each have peculiar genetic constitutions. They have a high level of homozygosity and surviving lines cannot be carrying any lethal or seriously deleterious genes. Hence, the heterosis expected from crossing them is not great. As well, all three lines used here must have had a number of loci fixed with similar deleterious alleles, leading to the result that lines 8a and 8b never equalled the outbred line 1 in either trait.

Because inbred lines have a high degree of homozygosity, it is unlikely that this crossbreeding plan makes more than three alleles available at any locus, for selection to act on. The same one, two or three alleles are continually being reintroduced through the sires at a frequency of 0.05 every three generations even if selection has tended to increase or reduce their frequencies in the generations in between. Theoretical models of such situations (Beilharz, unpublished data) show that with three alleles under selection at a locus, allele frequencies tend towards equilibrium values that recur every three generations. But the first two cycles show noticeable average changes in allele frequencies. It appears that the strains of mice used did not provide much variation at the loci controlling body-weight.

This experiment has shown that, although fertility was improved and weight may have been slightly altered by the combination of continual crossbreeding and selection, the results have been disappointing. This means that in genetic situations in which highly inbred lines are used, such a plan may be ineffective in practice relative to working with less, inbred populations.

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VI. REFERENCES