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Effects of Selection for High Litter-Weight on Reproductive Performance in Mice[1]

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RINGKASAN

Prestasi pembiakan dari dua kumpulan tikus yang dipilih kerana berat litter ketika berumur sembilan minggu dan satu kumpulan kawalan telah dibandingkan hasil dari data yang diperolehi selepas 15 keturunan pembiakan. Dua puluh pasang baka dibiakkan bagi kumpulan kawalan dan sepuluh pasang untuk kumpulan-kumpulan yang dijalankan pemilihan. Pada setiap keturunan baka hanya dikahwinkan sekali. Dari kira-kira angkali pembiakan sedarah (inbreeding) menunjukkan kadar kenaikan angkali pembiakan sedarah yang tinggi di kalangan kumpulan yang dijalankan pemilihan.

Keputusan menunjukkan kurangnya kesan (response) yang dihasilkan dari pemilihan. Sebaliknya prestasi pembiakan telah merosot bersamaan dengan kenaikan angkali inbreeding di kalangan kumpulan yang dibuat pemilihan walaupun pertalian di antara kedua faktor ini tidak linear. Penambahan dari segi kenaikan berat badan dilihat pada peringkat awal. Akan tetapi apabila angkali inbreeding melebihi 40% sifat ini juga turut merosot.

SUMMARY

The reproductive performances of two lines of mice selected for high litter-weight at nine weeks of age and a control line were compared based on data obtained after 15 generations of breeding. Twenty pairs of parents were bred per generation in the control line and ten pairs in each of the selected lines. At each generation the parents were mated only once. Calculation of inbreeding coefficients from pedigrees indicated a rapid rise in inbreeding coefficient in the selected lines.

There was little response to selection for high litter-weight and in fact there was a general decline in reproductive performance associated with high levels of inbreeding in the selected lines although the relationship was not linear. Some initial response in bodyweight gain was observed but even this trait showed a decline in later generations when inbreeding coefficient exceeded 40%.

INTRODUCTION

Reproduction in a female mammal may be defined as its ability to produce offspring and raise them till they become independent of the parents. In mice reproduction is measured usually in terms of litter-size or total litter-weight. As in other traits, reproduction may be subjected to selection, both natural and artificial.

Natural selection is always acting to maximise fitness. It has been suggested that because the capability of animals to reproduce has been under natural selection throughout the evolutionary history of the species, little additive genetic variation is left and as a result we may expect it to be rather difficult to make marked genetic improvement (Robertson, 1963; Politiek, 1965; Karg, 1969). However, there is still genetic variation for reproductive traits as shown by successful selection experiments in Merino Sheep (Turner and Young, 1969).

This study is aimed at analysing the direct and indirect responses to selection for high total litter-weight at nine weeks of age in laboratory mice. Traits analysed in this study include litter-size at birth, total litter-weight at three weeks and at nine weeks of age, average body weight at three and nine weeks of age, and mortality of progeny between birth to three weeks and from three weeks to nine weeks of age.

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MATERIALS AND METHODS

The analysis was based on the records of performance at mating and subsequent growth of the litters produced by mice in the selected population (line 6A and line 6B) and the control population (line 1). The origin of the stock and the management practices have been documented by Beilharz (1970, 1972). The original mice stock came from the Division of Animal Health, C.S.I.R.O., Parkville, Melbourne, where a population of mice was propagated without conscious selection, by at least 40 males and 160 females per generation. This population should not have been inbred to any great extent. Of the 105 mice obtained from C.S.I.R.O., 20 males and 79 females were mated to found the mice colony at the School of Agriculture, University of Melbourne. These mice were designated as generation 0 and their progeny as generation 1.

The mice in generation 1 were divided to two populations at random, 37 litters into each of populations A and B. In both populations all litters were reduced to 6 at birth by random removal of the excess young. Population A was fully fed throughout. Mice from population B were fed a restricted amount (about 80% of the estimated full intake) between 3 and 9 weeks of age. At other times feeding in population B was *ad lib.* as for population A.

Fifty pairs of mice were mated in each population to produce generations 2 and 3. In generation 4, and in all subsequent generations, all mice were fed *ad lib.* A total of 582 mice were identified in generation 4 and they were all treated as one population. One control line (line 1) and 12 selected lines (including lines 6A and 6B) were separated from this population to produce generation 5.

Line 1 is an unselected population propagated by 20 pairs of mice each generation. Each pair was called a family (numbered from 1 to 20). One son and one daughter are chosen, at random from each family for breeding. If a family (say family n) fails to produce a son or daughter, a substitute is obtained from the family n+9 or n+11. While daughters remained in the family of their parents the sons were moved systematically to other families. In this way if all families leave a son and a daughter, the possibility of inbreeding is avoided for five generations

Lines 6A and 6B were selected lines where males and females were selected on high total weight of litter at 9 weeks of age. The only difference between lines 6A and 6B was that in line 6B mating of full sibs was avoided whenever possible. However, because of the family selection employed it was not always possible to avoid mating full sibs. Ten pairs of mice were mated at each generation. Variation in sex ratio was allowed for as follows: the sex difference (male-female) was calculated from the average weight of all male and female mice from line 1, line 6A and line 6B. This average difference was then added to the weight of each female.

The following records were collected from the selected and control lines on a routine basis: litter size (number of live young born), weight at 3 weeks (weaning weight), weight at 6 weeks, weight at 9 weeks, sex ratio in the litter, matings (and hence, pedigree), and mortality.

RESULTS

The coefficient of inbreeding for each individual at each generation was estimated using the path coefficient technique (Wright, 1922). Table 1 shows the mean changes in the coefficient of inbreeding over the generations.

In line 1, inbreeding started to increase at generation 8 and 9 but dropped at generation 10, increased steadily from generation 11 to 14 and showed a second drop in generation 15 before the next wave of increase from generation 16 to 18. In lines 6A and 6B, inbreeding coefficient increased rapidly from generation 6 onwards. The decrease in inbreeding coefficient observed in Line 6A from generation 6 to generation 7 was due to larger number of families selected to provide sufficient individuals to become parents for mice in generation 7 compared to that for generation 6.

Table 2 shows the percentage of successful mating in each generation. Mice in Line 1 continued to produce offsprings at each generation although a few families (maximum observed for any generation was 3 families) failed to produce any offsprings. In Line 6A, successful matings were maintained at 90 – 100% up to generation 8 after which there was a gradual decline and at generation 13 no offspring was produced and the line became extinct. In Line 6B, deterioration of fertility was observed at generation 14 when the percentage of successful mating dropped to 70%. Although there was a recovery at the next generation, the fertility continued to drop at generation 16 to 18 and at generation 19 no offspring was produced and the line became extinct.

Table 3 shows the intensity of selection *(i)* estimated as selection differential divided by standard deviation (Falconer, 1960) applied at

TABLE 1

Changes in coefficient of inbreeding

Generation	Average % of inbreeding within each line					
	Average for all litters			Average for selected mice		
	Line 1	Line 6A	Line 6B	Line 1	Line 6A	Line 6B
4	0	0	0	0	0	0
5	0	0	0	0	0	0
6	0	22.22	12.50	0	23.75	12.50
7	0	12.50	18.75	0	12.50	18.75
8	1.46	22.32	21.87	1.90	21.90	21.87
9	4.22	20.90	25.78	4.05	20.70	25.78
10	0.55	28.49	33.98	0.54	25.70	33.98
11	1.37	30.89	38.67	1.34	31.10	38.67
12	1.79	45.58	43.46	1.77	–	43.46
13	2.69	–	48.88	2.69	–	48.88
14	3.56	–	53.88	3.62	–	53.88
15	0.99	–	57.33	1.14	–	57.33
16	1.32	–	58.58	1.32	–	58.58
17	1.97	–	63.57	1.96	–	63.57
18	3.24	–	52.41	–	–	–

TABLE 2

Percentage of successful mating in each generation

Generation	Line 1	Line 6A	Line 6B
4	100%	100%	100%
5	95	100	100
6	95	90	100
7	100	90	100
8	100	100	100
9	100	80	90
10	90	60	90
11	90	50	90
12	85	40	90
13	100	–	100
14	95	–	70
15	100	–	100
16	100	–	80
17	85	–	60
18	85	–	71

each generation for the selected trait (which in this case is the litter-weight at nine weeks of age) and its response.

The results indicate that the only period when there was some indication of response to selection was in the earlier generations (generation 8 to 10) when there was a tendency for both Line 6A and Line 6B to increase in their total litter weight. The weight subsequently dropped below to that of Line 1.

Among the other traits, litter size at birth among the selected lines did not differ very much from that of the control line until just before the extinction of the selected lines.

The weight of litters at weaning showed a similar trend to that of the total litter weight at 9 weeks of age.

Mortality rate of mice was very high among the selected lines at the later generation when the coefficient of inbreeding was high but the relationship of the two factors was not linear.

TABLE 3
Mean adjusted total litter-weight at nine weeks in each generation in the unselected and selected lines, and the intensity of selection applied

Generation (of parents)	Line 1 (control) Total Litter wt. (grams)	Line 6A Selection intensity (*i*)	Line 6A Total litter-weight (grams)	Line 6B Selection intensity (*i*)	Line 6B Total litter-weight (grams)
4	259.64 ± 43.66	0.635	252.76 ± 76.42	1.241	285.39 ± 45.89
5	271.64 ± 51.43	1.090	283.66 ± 53.00	0.693	283.53 ± 104.45
6	285.61 ± 51.39	0.976	275.23 ± 74.81	1.015	292.03 ± 59.50
7	312.66 ± 46.36	0.914	283.90 ± 76.29	0.821	278.96 ± 97.24
8	297.56 ± 54.90	0.932	239.65 ± 73.17	1.134	280.78 ± 46.44
9	253.81 ± 63.55	1.109	303.54 ± 28.91	0.868	248.23 ± 44.56
10	285.44 ± 75.48	0.761	285.26 ± 93.46	1.042	307.84 ± 35.62
11	320.05 ± 0.49	0.553	237.96 ± 80.93	0.663	283.55 ± 86.62
12	224.93 ± 88.31	–	195.07 ± 82.00	0.748	273.56 ± 80.47
13	305.63 ± 52.51	–	–	0.896	239.83 ± 66.66
14	207.25 ± 90.29	–	–	0	147.44 ± 113.05
15	258.32 ± 59.90	–	–	1.168	189.59 ± 78.76
16	300.06 ± 56.87	–	–	0.606	197.84 ± 49.55
17	298.17 ± 58.91	–	–	0	137.09 ± 82.27
18	268.61 ± 85.76	–	–	0	168.36

TABLE 4
Average litter-size (live and dead) at birth in each generation

Generation (of parents)	Line 1	Line 6A	Line 6B
4	10.0	9.4	10.9
5	9.3	9.2	8.8
6	9.3	8.3	8.5
7	10.3	10.0	8.1
8	9.3	6.8	8.6
9	8.6	9.4	9.9
10	9.1	9.5	9.4
11	9.5	8.6	9.2
12	9.2	7.0	10.8
13	9.5	–	8.3
14	10.1	–	8.9
15	9.1	–	8.8
16	9.2	–	8.9
17	10.3	–	10.2
18	10.5	–	5.6

TABLE 5
Adjusted total litter-weight at three weeks in each generation in the various lines

Generation (of parents)	Line 1	Line 6A	Line 6B
4	77.24g.	69.93g.	76.91g.
5	99.52	105.19	98.90
6	97.41	88.64	93.43
7	100.68	97.63	88.29
8	106.37	88.19	98.60
9	71.25	87.57	69.17
10	88.29	84.62	91.99
11	97.72	83.88	69.39
12	71.68	–	82.53
13	92.51	–	68.53
14	81.55	–	46.29
15	92.04	–	53.56
16	89.90	–	59.22
17	90.23	–	32.63
18	90.48	–	40.96

TABLE 6
Percentage mortality between birth and three weeks, and between three to nine weeks of age in each generation

Generation (of parents)	% Mortality, birth to 3 weeks			% Mortality, 3 to 9 weeks		
	Line 1	Line 6A	Line 6B	Line 1	Line 6A	Line 6B
4	2.92	11.76	12.24	9.36	7.06	15.31
5	4.54	7.61	6.82	0.57	1.09	0
6	5.08	6.67	8.23	2.26	1.33	5.88
7	6.67	10.00	13.58	3.86	3.33	0
8	7.49	19.12	8.14	2.14	0	2.32
9	10.40	25.33	26.97	2.31	1.33	6.74
10	3.05	8.77	5.88	1.83	1.75	2.35
11	2.92	16.28	22.89	0	2.32	0
12	20.51	65.71	17.53	7.69	0	9.28
13	4.74	–	16.87	1.58	–	2.51
14	21.87	–	53.23	18.75	–	8.06
15	6.01	–	26.14	9.29	–	14.77
16	4.35	–	18.31	2.17	–	21.13
17	7.43	–	62.50	6.29	–	8.93
18	8.95	–	64.29	12.10	–	14.29

The mean bodyweight of the selected progeny at three weeks of age showed a decline after generation 10 when the coefficient of inbreeding exceeded 25% in both Lines 6A and 6B.

TABLE 7
Mean bodyweight at three weeks of age in each generation among males and females selected for breeding in the various lines

Generation	Line 1		Line 6A		Line 6B	
	Males	Females	Males	Females	Males	Females
4	10.1g.	10.5g.	13.4g.	13.7g.	13.3g.	13.1g.
5	8.7	8.0	9.4	9.4	7.4	7.8
6	11.3	10.9	10.7	11.0	13.3	13.0
7	11.0	11.2	8.8	9.5	10.2	9.5
8	10.5	10.7	7.8	9.6	9.3	8.6
9	12.2	12.0	14.4	13.8	10.4	11.4
10	8.8	9.0	6.8	7.6	8.2	7.4
11	10.5	10.3	8.1	9.2	8.5	9.4
12	10.7	10.9	9.7	10.1	8.1	8.1
13	10.4	10.4	–	–	7.4	7.6
14	10.6	10.5	–	–	8.6	7.7
15	10.9	10.1	–	–	7.8	6.5
16	10.4	10.3	–	–	7.4	7.3
17	10.6	10.5	–	–	7.2	7.9
18	9.5	9.5	–	–	7.9	8.7

The mean bodyweight at nine weeks of age tended to decline after generation 13 in line 6B when the inbreeding coefficient exceeded 45%. There was no marked decline in bodyweight at nine weeks of age in line 6A.

DISCUSSION

The differences in the response of the two selected lines may in part be due to some differences in the genetic constitution of the two lines although every effort had been made to give similar treatment to both lines. As described previously the control line and the selected lines were derived from the progeny of two populations A and B where some differences in feeding were imposed at generations 2 and 3. At generation 4, all the progeny from both population were mixed and treated as one population. From this base population, the various lines were developed. Because of the random distribution of mice into the various lines it was assumed that all the lines would have a similar genetic constitution. This assumption may not have been valid particularly when the size of each line was rather small (only 10 families for the selected lines) as this could result in significant variation in gene frequency between lines due to the effect of sampling (Falconer, 1960).

The assumption that mice of generation 4 were unrelated is also not correct. The effect of the assumption is to make the coefficient of inbreeding in the early generations of Table 1 lower than it actually is. However, increase in the inbreeding coefficient after generation 15 is no longer affected by this assumption.

To obtain a reasonable response from selection the intensity of selection must be high and this requires heavy culling of animals at each generation. This same procedure will also lead to reduction in population size resulting in a rapid rise in inbreeding coefficient with its consequent depressing effects on performance. The two opposing factors acted jointly in line 6A and line 6B and it was not possible to estimate the separate effects of each. Looking at the changes in the level of performance at each generation it may be inferred that the only trait to indicate some response to selection was the growth rate of the individuals in the litter when the rate of inbreeding was still low. Similar results were

TABLE 8

Mean bodyweight at nine weeks of age in each generation among males and females selected for breeding in the various lines

Generation	Line 1		Line 6A		Line 6B	
	Males	Females	Males	Females	Males	Females
4	31.9g.	28.7g.	35.2g.	29.8g.	36.1g.	30.1g.
5	29.2	24.4	34.0	28.3	32.7	26.7
6	31.6	26.5	35.6	28.4	35.9	29.3
7	34.8	27.0	31.5	30.5	37.0	29.3
8	32.9	27.0	31.2	27.8	35.5	26.4
9	33.5	27.6	37.0	32.4	34.5	29.1
10	31.7	26.7	30.2	27.5	35.2	27.2
11	33.9	27.3	34.1	29.3	34.2	28.3
12	34.0	28.9	34.9	28.4	36.8	29.6
13	35.0	28.0	–	–	30.8	26.8
14	34.0	28.4	–	–	32.4	26.0
15	32.9	27.3	–	–	31.0	23.3
16	33.6	27.7	–	–	31.6	25.8
17	35.5	28.8	–	–	32.5	26.0
18	33.1	27.3	–	–	31.6	27.3

reported in Iowa with experiments in pigs where continuous selection and inbreeding had been applied (Bereskin *et al.*, 1969, 1970). Selection was shown to be effective and inbreeding less depressing on growth while litter-size showed an erratic but generally downward trend.

Most experiments on selection for high rate of reproduction in various species of domestic mammals have been shown to be unsuccessful except in sheep (Revelle and Robinson, 1973). Dalton and Bywater (1963) obtained no response to selection for litter-size and litter-weight at weaning age after 14 generations of selection in mice maintained at high and low levels of feeding. Some workers, however, reported some indirect response through selection for bodyweight (Fowler and Edward, 1960; Rahnefeld *et al.*, 1968). Bradford (1970, 1971), however, obtained no response in litter-size either through direct selection for the trait or through indirect selection for weight gain between 21 and 42 days of age but there was a response to selection for low litter size.

The general decline in reproductive performance among the selected lines may be related to the depressing effect of inbreeding but it could also be due to the fact that the animal's overall fitness has been compromised by conflicting selection pressures as suggested by Goddard and Beilharz (1977), according to whom there are certain optimum values and combinations for the various components that constitute total fitness. Selection for one component of fitness may have caused a decline in the total fitness. This has been demonstrated in sheep where there has been a definite cost associated with selection for twins among Corriedale sheep (Baharin and Beilharz, 1977a). Baharin and Beilharz (1977b) showed that in pigs there was a high percentage of mortality at very large litter-sizes and that little is to be gained by increasing the total litter size above 13 piglets when artificial rearing is practised.

CONCLUSIONS

Selection for high litter-weight at nine weeks of age in mice failed to show any positive response. In fact, it showed a depression in performance compared to the performance in the control line. This could be due to inbreeding depression or breakdown in total fitness due to conflicting selection pressures. Fertility as measured by mortality rates of progeny between birth and three weeks of age, and between three and nine weeks of age, was unaffected by selection and depressed at high levels of inbreeding. Bodyweight showed some initial response at the beginning of the selection programme, but at very high level of inbreeding, this trait too showed depression.

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