BREEDING MICE FOR INCREASED LONGEVITY OF REPRODUCTION

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SUMMARY

To demonstrate that animal stocks with increased reproductive longevity can be developed by selective breeding, experiments using mice were conducted. A base population synthesized from mouse lines characteristic of increased lactational performance and adult body weight was used to develop two selected lines and one control line. Parents that were pair-mated at 7 weeks of age were selected mainly based on reproductive longevity. At generation 16, the two selected lines (one with litter size standardized at birth and the other not standardized) showed a significantly ($P<0.01$) longer life of reproduction than the control. Concomitant increases in lifetime performance such as total number of progeny produced per pair-breeder during lifetime were observed. Conclusions were that (1) reproductive longevity can be increased by selective breeding and (2) lifetime performance of animals improved as a correlated response to selection for reproductive longevity.

INTRODUCTION

When animals, domestic and laboratory, are maintained as breeders, efficient lifetime (herd-life) production of progeny is desired. Ease of becoming pregnant, lactation, health and other factors are involved throughout life. If animals exhibit efficient reproduction continuously, the cost of maintenance during their lifetime (until death or culling), relative to the monetary returns from production, will be lowered. Moreover, unnecessary increases in inbreeding due to a rapid turnover of parents can be avoided. Healthy, Efficient Lifetime Producers (HELP animals) are needed from the standpoints of both animal production and animal resources conservation.

In spite of the fact that HELP animals are desirable, literature on this issue has been meagre, particularly on breeding principles of developing HELP animals. The main reason is that lifetime production (performance) involves ageing processes of animals that have been characterized by a plethora of theories but not by data from well-designed experiments. Also the cost, labour and time for studying lifetime performance is prohibitively large when livestock such as cattle or swine are used.

Basic breeding principles transcend species. Mice are a useful pilot organism for studying such principles because the cost for maintaining mice is low and their generation interval is short, relative to those of livestock. Furthermore, ageing processes at the molecular, cellular, and organism levels are reasonably well documented in mice.

The objectives of the present study were to develop, by selective breeding, lines of mice with increased reproductive longevity and lifetime performance, and to examine the differences between selected and unselected lines in various lifetime performance measures.

MATERIALS AND METHODS

Mice: The breeding history of mice selected for increased length of reproductive life and unselected controls has been described by Nagai et al. (1990). Briefly, two lines of mice selected for increased postnatal maternal performance and two lines of mice selected for increased adult body weight (Nagai et al. 1978) were used to

synthesize a population for the present study. Two lines of mice selected for increased length of reproductive life that were designated as selected lines 121 and 141 (previously SA2 and SN2 lines, respectively, Nagai et al. 1990) and one unselected control line 221 (previously UA2 line) were derived from the synthetic population.

In the selected lines, pairs cohabited at 7-8 weeks of age and were maintained in the same cage continuously as long as they produced litters, usually up to 333 days after cohabitation. Progeny born to a pair were discarded at 18 days of age until the 5-9th parity. Then, progeny at a subsequent parity were used as breeders at the next generation. Thirty pair matings were made with the avoidance of full-sib mating. The procedure was repeated every generation. Litter size was adjusted to eight at birth in lines 121 and 221, but not adjusted in line 141. In line 221, the unselected control, progeny in the first litter were used as breeders for the maintenance of the line. Basically, one female and one male of each litter were chosen at random and 30 pairs were mated randomly at 7-8 weeks of age, avoiding full-sib mating. It is obvious from the above procedures that generation numbers of selected and control lines are not the same when they are compared for long-term performance contemporaneously. Actually, contemporary comparisons between selected and control lines in the present study were conducted at generations 12 and 16 of the selected lines with the corresponding generations of 34 and 41 in the control line, respectively. In these generations, parents were kept for 430 days after cohabitation.

Throughout the experiment a commercial pellet feed (Lab Chows, Ralston Purina) and tap water were supplied *ad libitum*. Mice were maintained in a specific-pathogen-free building where temperature ranged from 20 to 24°C and humidity ranged from 40 to 55%.

Measurements: Reproductive longevity was measured by days from cohabitation of a pair to the last parturition. During the reproductive life, number of parturitions and number of young born alive and dead were recorded. Ratio of reproductive longevity in selected line (line 121 or 141) to that of control line (line 221) was calculated using data collected contemporaneously. In evaluating lifetime performance of selected line 141 where all progeny born alive were left to the mother, performance of control line 221 (where litter size was adjusted at birth) was used as a reference.

In each line, the proportion of reproducing pairs (in percentage) at a particular date was calculated from the number of reproducing pairs x 100/the number (26-30) of pairs bred in the beginning to compare persistency of reproduction between selected and control lines.

Analyses of data: Differences in mean performance between selected and control lines were tested by the t-test. Inbreeding coefficients for individual breeders were calculated using Quaas' algorithm (Quaas 1976).

RESULTS

Mean reproductive days in selected line 121 at generation 12 were 48% longer than those in control line 221 (Table 1). Number of parturitions during lifetime in the selected line 121 increased by 62%, with a concomitant 41% increase in total number of young born alive during lifetime of parents. At generation 16 (Table 1), the results from selective breeding were more obvious in all traits examined. Increases in various traits in selected line 141, relative to control line 221, appeared to be larger than those in selected line 121 at both generations 12 and 16.

Standard deviations for days of reproductive life and number of parturitions were large in both selected and control lines (Table 1). Although large portions of distribution of reproductive longevity were overlapping between selected and control lines at generation 12, the distribution of the selected lines at generation 16 shifted upward (Figure not shown), indicating a tendency for producing selected and control lines with distinctly separate distributions.

Curves showing persistency of reproduction over time (Figure 1) clearly demonstrate that the two selected lines 121 and 141 are different in the pattern from control line 221. The point of time for a 50%

reproduction in control line 221 was about 110 days as compared to 250 days in selected lines 121 and 141. Selected lines showed more than twice the persistency of the control line.

Inbreeding coefficients in selected lines 121 and 141 were 9.2 ± 0.8 and 8.8 ± 1.0% at generation 12, and equal at 9.8 ± 0.2% for generation 16 while those in control line 221 were 8.1 ± 0.2 and 11.7 ± 0.2% at the contemporaneous generations 34 and 41, respectively.

TABLE 1. Means of lifetime performance in selected and control mice

Generation[a]	Trait	Selected (Line 121)		Control (Line 221)		Selected (Line 141)	
12	Reproductive life (days)	235.7** (1.48)[c]	99.7[b]	159.0	92.9	265.0** (1.67)	107.8
	No. of parturitions during lifetime	8.63** (1.62)	3.8	5.34	2.7	9.61** (1.80)	4.0
	No. of young born alive during lifetime,	78.3** (1.41)	37.8	55.5	2.64	89.1 ** (1.61)	39.2
	dead	13.3** (3.59)	13.7	3.7	4.9	6.0 (1.62)	7.9
	No. of dams (pairs)	30		29		28	
16	Reproductive life (days)	240.8** (1.79)	105.3	134.6	88.9	243.0** (1.90)	70.9
	No. of parturitions during lifetime	8.74** (1.78)	4.0	4.90	3.2	9.47** (1.93)	2.7
	No. of young born alive during lifetime,	77.2** (1.68)	36.4	45.9	28.5	82.8** (1.80)	29.7
	dead	8.4 (2.40)	11.2	3.5	9.7	7.1 (2.03)	7.7
	No. of dams (pairs)	26		29		30	

[a] : Generation # of selected lines. Contemporaneous control line was at generation 34 and 41, respectively.
[b] : Standard deviation.
[c] : Ratio of selected line mean with control line mean within contemporaneous comparison.
** : Significantly ($P<0.01$) different from line 221.

DISCUSSION

Reproductive longevity and lifetime performance are complex traits which consist of various component traits such as growth and lactational performance. The component traits have been known as the characteristics under the control of genetic and environmental factors (Nagai et al. 1978). Heritability of reproductive longevity was estimated as 0.11 (Nagai et al. 1990) and various traits were genetically associated with lifetime performance such as number of parturitions during lifetime (Nagai et al. 1986). Results obtained from the present long-term selection study support the previous conclusions: selected lines showed about an 80% increase in the traits examined after 16 generations. It would be interesting to determine whether selected and control lines can be developed with distinctly separated distributions.

In general, inbreeding causes inbreeding depression, particularly in fitness traits (Falconer 1981). Inbreeding rates in the present study were relatively low and comparable among lines. Thus, a direct

comparison of lifetime performance among lines without adjusting for inbreeding is justified. The reason for the comparable inbreeding rates among lines was due to the fact that the control line had a 50% larger population size than the selected lines at the early stage of this study (Nagai et al. 1990).

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Figure 1. Length of reproductive life of mice in two selected lines (lines 121 and 141 at generation 16) and one unselected line (line 221 at generation 41) that were compared contemporaneously.