SELECTION FOR LITTER SIZE IN MICE:
RESPONSES USING NOVEL CRITERIA

M.K. Nielsen, J.M. Gion and A.C. Clutter
Animal Science Department, University of Nebraska
Lincoln, Nebraska 68583-0908, USA

SUMMARY

Selection was conducted on an index of components of litter size (I = 1.21 x ovulation rate + 9.05 x ova success), on uterine capacity (measured as number of pups born to unilaterally ovariectomized dams), and on litter size concurrent with an unselected control. Selection criteria (IX = index, UT = uterine capacity, LS = litter size and LC = control) were applied in each of 3 replicates. After 13 generations, mean ovulation rate, ova success and litter size (measured as number of fetuses at 17 d gestation in intact females) were IX: 14.25, .84, 11.95; LS: 14.15, .82, 11.64; UT: 12.61, .86, 10.77; and LC: 12.27, .82, 9.98. The regression of number born (litter size in IX, LS and LC; uterine capacity with only a functional left uterine horn in UT) on cumulative selection differential was .12 $\pm$ .01, .09 $\pm$ .02 and .08 $\pm$ .02 for IX, LS and UT, respectively. The regression of breeding value for litter size on each selection criterion, estimated as response in the generation-13 evaluation divided by cumulative selection differential, was .11 $\pm$ .02, .08 $\pm$ .01 and .05 $\pm$ .03 for IX, LS and UT, respectively. Regression of response in number born on generation number was .17 $\pm$ .01, .15 $\pm$ .04 and .10 $\pm$ .02 for IX, LS and UT, respectively.

INTRODUCTION

This study was undertaken with mice to evaluate novel methods of selection for increasing litter size. Selection on an index of the components in the manner proposed by Johnson et al. (1984) and selection on number born in unilaterally ovariectomized females, designed to emphasize uterine capacity (Leymaster et al., 1986; Christenson et al., 1987; Bennett and Leymaster, 1989; Clutter et al., 1990), are being compared to direct selection on litter size. Included in this paper are results from selection through thirteen generations.

EXPERIMENTAL PROCEDURE

Selection Methods. A population of outbred, CF1 mice was used to generate lines for implementation of the following selection criteria:

IX: As suggested by Johnson et al. (1984), selection based on an index of ovulation rate (corpora lutea) and ova success (proportion of number of pups to number of ova) was practiced. The index (I= 1.21 x ovulation rate + 9.05 x ova success) was derived from the base population as the optimum linear criterion based on the nonlinear objective of ovulation rate and ova success (Clutter et al., 1990). The index weightings were scaled to these values (1.21 and 9.05) so the expected standard deviation of index value would be the same as for litter size.

UT: This criterion selects for uterine capacity, as described for swine by Christenson et al. (1987). Females had their right ovary excised at 4 wk of age. The rationale for this procedure as a method for selecting on uterine capacity in mice was given in Clutter et al. (1990).

LS: Selection in LS was on litter size.

LC: This criterion was a randomly selected control.

Each selection criterion was replicated three times, with all four selection criteria contemporary within a replicate. Replicates were propagated from the base stock so that all four criteria within a replicate had common grandparents. Line in this paper refers to a replicate-criterion population.

Litters of the 16 or occasionally 17 highest ranking dams within each selection line (IX, LS, and UT), were chosen as breeders each generation based on their dam's performance. All females and two males (if available) from each of the selected litters were assigned to matings to minimize inbreeding at approximately 9 wk of age. Approximately 70 to 100 litters were produced per selection line each generation; there were 30 to 60 litters in the contemporary control lines. In the control lines, one female that had reproduced was randomly chosen from each of the 16 families of full-sib females representing the generation.

Measurement of Selection Differentials. Realized cumulative selection differentials (CSD) for all lines were calculated by the method below:

$$CSD_n = .5 \; F_{n-1} + .25 \sum_{i=0}^{n-2} (F_i + M_i) \qquad n \geq 2$$

where n is the number of generations of selection completed, and F and M are "female" and "male" selection differentials. Differentials for females (F) were weighted by the number of her daughters that had records the next generation. Male differentials (M) were weighted by the number of granddaughters (through sons) that had records. Therefore, selection accumulated in increments of .25 x (female selection differential + male selection differential). Correlated selection differentials for number born in IX and unintentional selection in LC were measured in the same manner.

Evaluation of Thirteen Generations of Selection. Litters from approximately 20 dams (representing the average of each line and as many families as possible) were chosen in each line from those remaining after the 16 highest ranking litters had been selected to propagate the next generation. UT females were left intact. Females of all lines were sacrificed at d 17 of gestation. Left- (LOR) and right-side (ROR) ovulation rate as determined by corpora lutea, and left- (LF) and right- (RF) side fetuses were recorded for each female. Total ovulation rate (TOR) and fetuses (TF) were derived as the sum of the sides. Left- (LOS) and right-side (ROS) and total (TOS) ova success (number of fetuses/number of ova) were calculated for each female. Litter size and components data were collected on approximately 940 females.

Statistical Analyses. Data in the evaluation were analyzed using a model with the fixed effect of criterion and the random effects of replicate and the criterion x replicate interaction. Three orthogonal contrasts of the criterion means were run using criterion x replicate as the error term: IX, LS, UT versus LC, to test the general response of selection; IX, LS versus UT, to test selection for litter size to that for a component, uterine capacity; and IX versus LS to test index to usual selection for litter size.

Mean total number born in IX, LS, and UT, expressed as deviations from LC, were regressed on generation number to measure changes over time in the select lines relative to the control. The regression of breeding value for litter size on each selection criterion was estimated as the ratio of cumulative response in number of fetuses in the generation-13 evaluation to cumulative realized selection differential. The regression of response in total number born on cumulative selection differential over the generations of selection was also calculated. Response was expressed as a deviation from the control. Selection differentials in LS and LC measured selection applied for litter size. The selection differential in IX measured selection applied for index value. In UT, the selection differential measured selection applied for uterine capacity in females with only a functional left uterine horn. Standard errors for the regressions were calculated empirically from the variation among estimates of the three replicates.

RESULTS AND DISCUSSION

Evaluation at Generation 13. Least-squares means and tests of orthogonal contrasts are listed in Table 1. The average of the three selection criteria for TF was different from the unselected control after 13 generations. Differences created by selection in general and in litter size (IX, LS) versus uterine capacity (UT) were important in LF. Differences between selection criteria were more pronounced in RF; different responses were evident in litter size (IX, LS) versus uterine capacity (UT) selection and in the use of the index (IX) over simply selecting on litter size (LS). The advantage of IX, LS and UT over LC in TF was 1.97, 1.66 and .79, respectively.

No significant differences were found between criteria for ova success. The small changes that may have occurred were mainly on the right side, with ROS at generation 13 of .87, .83, .88 and .83, for IX, LS, UT and LC, respectively. Ova success on the right side seems to be more responsive to selection. The highest mean ROS was for the UT criterion where selection was actually on left-side uterine capacity. In a preliminary study, Clutter et al. 1990 found heritability of .18 for ROS versus .10 for LOS with a genetic correlation between sides of .57. Evidently there is a larger genetic covariance between left-side uterine capacity and ROS than between left-side uterine capacity and LOS.

Response in ovulation rate, as an average of the three selection criteria, was different from LC. The two criteria (IX, LS) directed toward increasing litter size showed more response in ovulation rate than selection on uterine capacity (UT). The advantage in TOR of IX, LS and UT over LC was 1.98, 1.88 and .34, respectively. Response in IX versus LS selection was not significantly different for ovulation rate.

The IX criterion showed a response of .15 pups/generation relative to the control in the evaluation data. The LS had a similar response of .13 pups/generation, whereas response in UT was only .06 pups/generation. The response in LS agrees with the response reported by Bradford (1968,1979), but was half of that reported by Eisen (1978). The increase in ovulation rate in LS was responsible for the increase in litter size, also in agreement with Falconer (1960), Bradford (1968, 1979), Joakimsen and Baker (1977), and Bakker et al. (1978). The response in IX was the result of an increase in ovulation rate, with increased ova success, especially on the right side, contributing slightly. Both a small increase in ovulation rate on the right side and a larger increase in ova success were responsible for the response in UT.

TABLE 1. SELECTION CRITERION MEANS AND SIGNIFICANCE LEVELS FOR TESTS OF LINEAR CONTRASTS: GENERATION-13 EVALUATION

	Criterion Mean				Contrast		
Characteristic[a]	IX	LS	UT	LC	IX,LS,UT vs LC	IX,LS vs UT	IX vs LS
LF	5.64	5.72	4.94	4.81	.01	.01	NS[b]
RF	6.31	5.92	5.83	5.17	.01	.17	.10
TF	11.95	11.64	10.77	9.98	.001	.01	NS
LOR	6.87	6.98	5.91	6.01	.01	.001	NS
ROR	7.38	7.18	6.70	6.26	.001	.01	NS
TOR	14.25	14.15	12.61	12.27	.001	.001	NS
LOS	.82	.82	.84	.82	NS	NS	NS
ROS	.87	.83	.88	.83	NS	NS	.20
TOS	.84	.82	.86	.82	NS	NS	NS

[a]LF, RF, TF - left, right and total fetuses, respectively;
LOR, ROR, TOR - left, right and total ovulation rate, respectively;
LOS, ROS, TOS - left, right and total ova success, respectively;
[b]NS - not significant at $P>.20$.

TABLE 2. ESTIMATED RATES OF RESPONSE THROUGH 13 GENERATIONS PER CUMULATIVE SELECTION DIFFERENTIAL

	Ratio of Response[a] in Generation-13 Evaluation to Cum. Sel. Diff.			Regression over 13 Generations of Response[a] in No. Born[b] on Cum. Sel. Diff.		
	Criterion			Criterion		
Replicate	IX	LS	UT	IX	LS	UT
1	.14	.11	.10	.14	.14	.11
2	.10	.07	.06	.10	.06	.06
3	.09	.06	-.01	.12	.09	.06
Mean	.11±.02*	.08±.01*	.05±.03	.12±.01**	.09±.02*	.08±.02*

[a]Performance deviated from LC.
[b]Litter size in IX, LS and LC; uterine capacity with only a functional left uterine horn in UT.
*$P<.05$.
**$P<.01$.

The right side had a greater ovulation rate, higher ova success, and more pups than the left side in all lines. An analysis of the left and right sides in the base population (Clutter et al., 1990) showed the right side higher in ovulation rate, higher in ova success, and therefore having a greater number of fetuses. The left side had greater variation relative to the mean for each of these traits. The continued right-side advantage for ova success in the UT was particularly interesting in light of the selection pressure on uterine capacity of the left side (right ovary excised).

Response over 13 Generations. Mean litter size in UT was initially 2.1 pups less than in LC due to surgical restriction to one functional uterine horn. The IX and LS had very similar responses, with IX slightly greater. Response over time in UT was lower than in IX or LS, but the trait measured in UT was different. Response over time as a deviation from the control was significantly different from zero for all criteria. The pooled regressions of response in number born on generation number were $.17 \pm .01$, $.15 \pm .04$ and $.10 \pm .02$ for IX, LS and UT, respectively. These responses agree with those from the evaluation data.

The IX selection can be compared to selection work by Neal et al. (1989) on an index of ovulation rate and ova success in a population of swine. After 5 generations in that study, the regression of total number born in the select line as a deviation from the control on generation number was $.19 \pm .14$. In the present study, the regression of response in number born on generation number of IX selection was slightly lower at $.17 \pm .01$, but was significant.

Breeding Value and Selection Criteria. The ratio of cumulative response in number of fetuses in the evaluation to cumulative realized selection differential is presented in Table 2 for IX, LS, and UT as deviations from LC. The regression of total number born (as a deviation from LC) on cumulative selection differential over the 13 generations of selection is also presented in Table 2.

The IX criterion had the highest value in both methods. Although no estimates of regression of breeding value for number born on an index of the components of litter size relative to direct selection of litter size are available in the literature, the .11 and .12 values for IX are on the lower end of the range of heritability reported for direct selection. The LS values of .08 and .09 are lower yet. The expectation of both values for IX and LS is the regression of breeding value for litter size on the respective selection criterion. Thus one would expect close agreement, within the level of precision. Although not significantly different, regression of breeding value for litter size on the IX criterion was about 35% higher than that on the LS criterion. Clutter et al. (1990) predicted that selection on IX would be 23% more accurate than on LS.

The expectations for the two values for the UT criterion are not equal. The expected value of the regression of response in number born on cumulative selection differential across generations is the regression of breeding value for left-side uterine capacity on the selection criterion. The ratio of response in number of fetuses at generation 13 to cumulative selection differential has expectation equal to the regression of breeding value for litter size on the selection criterion. One would expect the covariance between the uterine capacity measure used in selection and its breeding value (estimated regression = .08) to be larger than the covariance with the breeding value for litter size (estimated regression = .05) of which uterine capacity is only a part.

The regression of breeding value for the index on cumulative realized selection differential was also estimated for IX. Index values were calculated in the generation-13 evaluation and the IX mean was deviated from the LC mean. The regression values for replicate 1, 2, and 3 were .18, .15, and .11, respectively. The mean value was $.15 \pm .02$.

The inbreeding level for each line was similar across replicates. The mean inbreeding levels for IX, LS, UT, and LC criteria after 13 generations of selection were .17, .17, .16, and .12, respectively. Falconer (1960) estimated a decrease of approximately .5 pups per 10% increase in inbreeding from two experiments. In this experiment with selection for litter size, the effect of inbreeding should be even less.

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