

Long Term Selection for Body Weight in Mice

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IN 1930 H. D. Goodale began an experiment with mice in which he selected for body weight at 60 days of age. This study sought to determine the limits of change that could be produced through the utilization of individual, progeny test, and family methods of selection continuing for 84 generations. Dr. Goodale's stated objective was to breed mice as large as possible, and he felt it conceivable that by selection mice exceeding the size of rats could be produced⁶. At that time, little was known of selection limits, so his ideas concerning plateaus were not illogical.

Reports by Goodale⁶⁻⁸ on the early results of this study showed a consistent increase in body size with no evidence of a plateau. MacArthur^{9, 10}, utilizing information from the individual's phenotype plus those of relatives, reported a consistent divergence of lines of mice selected for high and low 60-day body weight. After 23 generations of selection, the males and females of the high line were approximately 3.2 and 3.6 times as heavy as the males and females in the low line, respectively. After 11 generations of within-family selection for large and small body size at 42 days, Falconer¹ reported a divergence between the two lines of 11 grams, or 50 percent of the initial weight. Heritability was about 20 percent for upward selection and 50 percent for downward. Continued selection by Falconer and King⁵ for high 6-week body weight in samples of the Goodale and MacArthur lines at (approximately) generations 43 and 26, respectively, yielded little or no additional increase in body size. Roberts¹¹, working with several populations, found that selection for large and small size produced mice with mean 6-week body weights of approximately 30 and 12 grams at cessation of response. These limits were realized after 10 to 30 generations of selection.

Considerable information is now available indicat-

ing that definite limits to selection response do exist, and that these limits are reached regardless of the selection method used. The genetic reasons for the attenuation of response are not always evident, but the exhaustion of additive genetic variation, by either chance fixation or as a result of selection, appears to be the major factor.

The data from this first long term selection experiment for body size in mice are of considerable historical interest and are presented in that light.

Procedure

The establishment of the base population at Mount Hope Farm and the procedures used in selecting potential parents of the next generation were previously described by Goodale⁶. However, for convenience, descriptions of these procedures will be repeated.

Albinos of no particular distinction were obtained from a commercial breeder as the foundation mice. Four males and eight females were received on April 3, 1930, and 12 females on May 14, 1930. On January 27, 1931, four males and eight females were added. The population was then closed. Differential numbers of offspring were produced by the foundation stock, so that offspring born after January 29, 1934, (the date of birth of male 1000), would descend from 5 of the foundation males and 11 of the foundation females. It follows then, that no more than 16 mice were represented in the ancestry of later generations.

Most body weights were taken at 60 days of age with those deviating adjusted to a 60-day equivalent. Once every week several virgin males (usually three) were each mated to several females (usually five). These mice were, in most cases, the largest available at the moment; however, when the weights of the members of a family of full sibs proved uniformly large, then its members were given preference over members of other families. Mice weighed during the preceding week were given preference over older mice. The males were held after mating until their offspring were weaned; if these offspring appeared to be exceptionally large, the sires were remated to the same females. Sires whose offspring were not conspicuously large at weaning remained out of service until their offspring were weighed. However, few

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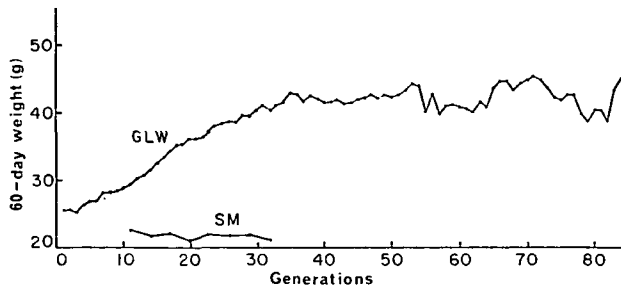


FIGURE 1—Average 60-day weights by generations for the GLW line, and by years for the SM line.

adults qualified for return to the mating cages and most were discarded.

Each pregnant female was placed in an individual cage where the young were born and remained until one month of age. At this time mice of the same sex from two or more litters were allotted to each growing cage. Sixty-day body weight (in grams) was used both as the basis of selective mating and as a measure of results. Litters were not standardized, and all mice that lived were fed to 60 days.

Dr. Goodale did not maintain discrete pedigree generations, but summarized the data by groups of 500 mice within sexes, with each of these groups containing individuals from several generations. Consequently, considerable overlapping of generations and mating of individuals from different generations created a problem in assigning individual offspring to pedigree generations. The method used assigned each offspring to the generation higher by one than the generation number of the parent belonging to the higher number generation.

To adjust the data to a male equivalent, each female weight was multiplied by a correction factor of 1.19. This sex correction factor calculated from the data was determined by the relative averages of male and female weights within generations. All analyses on adjusted data consisted of standard analysis of variance and correlation-regression techniques. Corrected sums of squares and cross products were calculated within generations. Most parameter estimates were presented on a generation by generation basis, while those needing additional precision were pooled over intervals of approximately ten generations. Symbols used are as follows:

- \bar{x} —mean
- σ —standard deviation
- σ^2_A —additive genetic variance
- σ^2_p —phenotypic variance
- cv —coefficient of variation
- h^2_s —heritability from the sire component of variance
- h^2_{os} —heritability from regression of offspring on sire
- h^2_{od} —heritability from regression of offspring on dam

- h^2_r —realized heritability
- r_{12} —correlation between 60-day weight and litter size at birth
- r_{13} —correlation between 60-day weight and litter size at 60 days
- b_{ms} —regression of male offspring on sire
- b_{fs} —regression of female offspring on sire
- s —selection differential, weighted by number of offspring at 60 days of age
- s_1 —secondary selection differential, weighted by number of offspring at 60 days of age
- i —selection intensity, $i = \frac{s}{\sigma_p}$
- wt —body weight at 60 days of age
- GLW—albino mice selected for high 60-day weight
- SM—randomly selected, randomly mated strain of agouti mice
- r —phenotypic correlation between mates

Results and Discussion

Population structure

The total number of individuals weighed at 60 days of age during the 84 generations of this experiment was 54,535. There was considerable fluctuation in numbers over generations with lows of about 100, and highs exceeding 1000; however, only 15 generations had fewer than 300 offspring (Table I). The number of sires and dams per generation averaged approximately 37 and 100 respectively. Because of the length of the experiment and a finite population size, inbreeding built up to levels that had considerable effect on reproductive efficiency. From the approximate formula of $\Delta F = 1/8M + 1/8F$, (where M and F are the average numbers of sires and dams per generation) ΔF was estimated to be .0045 per generation, and F was 38 percent at generation 84. Falconer⁴ reported a reduction in 42-day body weight of female mice of .58 grams per 10 percent increase in inbreeding. Information is not available regarding the effect of inbreeding on 60-day body weight, but a small reduction would probably result. On the one hand, selection would favor those individuals that by chance maintained more than the average amount of heterozygosis, while on the other hand, related individuals from superior families would be favored. These two forces would tend to cancel each other and probably would not drastically affect heterozygosis one way or the other.

No formal control population was maintained throughout the course of this study, although a randomly selected and mated line of agouti mice (SM) was maintained from 1935 through 1942. Data from this population have not been separated into discrete generations, but are presented as mean 60-day weights, with an average of 236 individuals per year for each of the above mentioned years (Figure 1). This time period would coincide approximately with generations 11 through 32 of the selection study. The yearly means from the SM population ranged from 21.0 to 22.4 grams, strongly indicating that there was no consistent environmental trend during

this period when the selected population was consistently increasing in 60-day weight.

Selection response

Generation means (Table I) indicate that 60-day weight at the initiation of this work was approximately 25 grams, increasing steadily to approximately 43 grams at generation 35. Although selection was continued for an additional 49 generations, appar-

ently little or no further increase in body weight occurred. There were considerable generation to generation fluctuations as well as periods when additional progress was evident (generation 65-73), but regression did occur and apparent progress was not maintained. This population, which sustained response to selection for increased 60-day weight somewhat longer than did Roberts'¹¹ populations selected for 42-day weight, also yielded seven phenotypic

Table I. Generation parameters

| Gen. | No. indiv. | No. born | No. 60d | \bar{x} wt. | σ wt. | s wt. | i wt. | s_1 no. born | s_1 no. 60d | r mates | % males |
|------|------------|----------|---------|---------------|--------------|---------|---------|----------------|---------------|-----------|---------|
| 1 | 75 | 4.59 | 4.41 | 25.38 | 2.62 | 1.89 | .72 | .69 | .49 | .00 | 52.0 |
| 2 | 100 | 3.79 | 3.38 | 25.46 | 2.55 | .76 | .30 | .86 | 1.12 | .30 | 42.0 |
| 3 | 245 | 5.14 | 4.75 | 25.02 | 2.60 | .87 | .33 | -.09 | -.04 | .11 | 49.8 |
| 4 | 287 | 4.56 | 4.10 | 26.23 | 2.54 | 1.73 | .68 | -.25 | .01 | .07 | 47.0 |
| 5 | 390 | 3.69 | 3.12 | 26.81 | 2.54 | 1.24 | .49 | .19 | .96 | .00 | 46.2 |
| 6 | 270 | 4.92 | 2.87 | 26.85 | 2.96 | 1.41 | .48 | -.73 | .33 | .05 | 44.1 |
| 7 | 185 | 5.99 | 2.73 | 28.03 | 2.72 | .37 | .14 | .54 | 1.47 | .27 | 39.5 |
| 8 | 203 | 7.30 | 3.43 | 28.19 | 2.93 | 1.30 | .44 | -.30 | .90 | .28 | 37.9 |
| 9 | 456 | 6.72 | 3.81 | 28.30 | 2.55 | 1.14 | .45 | -.01 | .32 | .01 | 43.4 |
| 10 | 1028 | 6.85 | 4.30 | 28.77 | 3.48 | 3.17 | .91 | .83 | .124 | .00 | 45.1 |
| 11 | 1685 | 6.76 | 4.83 | 29.18 | 2.50 | 3.32 | 1.33 | -.68 | .03 | .36 | 47.1 |
| 12 | 1573 | 6.66 | 5.02 | 30.11 | 2.67 | 3.58 | 1.34 | -.80 | -.20 | .26 | 43.3 |
| 13 | 1611 | 6.83 | 5.10 | 30.66 | 2.99 | 4.17 | 1.39 | -1.02 | -.28 | .34 | 46.7 |
| 14 | 1388 | 6.69 | 4.82 | 31.35 | 3.12 | 4.13 | 1.32 | -1.30 | -.40 | .28 | 47.3 |
| 15 | 1045 | 7.03 | 4.82 | 32.51 | 3.14 | 4.12 | 1.31 | -.94 | .17 | .21 | 45.1 |
| 16 | 974 | 6.83 | 4.73 | 33.41 | 3.39 | 3.82 | 1.13 | -.75 | -.08 | .05 | 44.9 |
| 17 | 742 | 6.36 | 4.46 | 34.28 | 3.69 | 3.82 | 1.04 | -.21 | .46 | .04 | 43.3 |
| 18 | 794 | 6.34 | 4.94 | 35.05 | 3.52 | 4.56 | 1.30 | -.04 | 1.27 | .14 | 48.5 |
| 19 | 946 | 6.74 | 5.27 | 35.41 | 3.77 | 4.54 | 1.20 | -.38 | .10 | .13 | 45.6 |
| 20 | 985 | 6.23 | 5.16 | 36.15 | 3.55 | 4.39 | 1.24 | -.34 | -.43 | .02 | 46.8 |
| 21 | 1094 | 6.62 | 5.17 | 36.26 | 3.50 | 4.88 | 1.39 | -.70 | -.22 | .14 | 47.7 |
| 22 | 861 | 6.44 | 4.89 | 36.37 | 3.62 | 4.69 | 1.30 | .04 | .40 | .08 | 48.3 |
| 23 | 758 | 6.31 | 4.57 | 37.14 | 4.17 | 4.32 | 1.04 | .31 | .00 | .27 | 47.9 |
| 24 | 793 | 6.27 | 4.53 | 38.11 | 3.71 | 4.30 | 1.16 | -.25 | .26 | .02 | 50.8 |
| 25 | 804 | 5.92 | 4.42 | 38.49 | 4.06 | 4.02 | .99 | -.50 | .11 | .04 | 46.8 |
| 26 | 919 | 5.83 | 4.58 | 38.78 | 4.01 | 4.41 | 1.10 | .02 | .37 | .14 | 48.5 |
| 27 | 870 | 6.03 | 4.66 | 38.68 | 4.25 | 5.10 | 1.20 | -.28 | .04 | .22 | 47.4 |
| 28 | 983 | 6.05 | 5.00 | 39.84 | 4.37 | 3.91 | .89 | -.19 | .06 | .23 | 51.1 |
| 29 | 1061 | 6.47 | 5.33 | 39.55 | 4.08 | 4.69 | 1.15 | -.32 | -1.02 | .04 | 48.9 |
| 30 | 877 | 5.94 | 4.97 | 40.51 | 3.76 | 4.30 | 1.14 | -.52 | -.06 | .06 | 51.4 |
| 31 | 708 | 5.58 | 4.30 | 41.21 | 4.24 | 4.57 | 1.08 | -.40 | .07 | .26 | 47.9 |
| 32 | 762 | 5.87 | 4.66 | 40.49 | 4.09 | 4.52 | 1.11 | -.70 | -.20 | .06 | 50.1 |
| 33 | 1038 | 5.91 | 4.85 | 41.30 | 4.88 | 4.34 | .89 | .38 | .92 | .09 | 49.2 |
| 34 | 1081 | 6.00 | 4.90 | 41.70 | 4.74 | 4.74 | 1.00 | .17 | .17 | .30 | 48.9 |
| 35 | 1094 | 5.51 | 4.47 | 43.10 | 4.77 | 5.37 | 1.13 | .36 | .52 | .01 | 50.0 |
| 36 | 888 | 5.66 | 4.60 | 42.82 | 4.99 | 4.85 | .97 | .34 | .57 | .17 | 49.4 |
| 37 | 543 | 5.95 | 4.61 | 41.86 | 5.14 | 5.47 | 1.06 | .04 | .25 | .00 | 48.6 |
| 38 | 409 | 5.49 | 4.45 | 42.66 | 4.77 | 4.30 | .90 | .34 | .55 | .24 | 48.7 |
| 39 | 494 | 5.76 | 4.70 | 42.24 | 4.81 | 4.28 | .89 | .46 | .60 | .17 | 52.0 |
| 40 | 593 | 6.21 | 5.45 | 41.70 | 5.30 | 4.95 | .93 | -.24 | -.03 | .01 | 48.6 |
| 41 | 910 | 6.55 | 5.95 | 41.85 | 5.03 | 5.31 | 1.06 | .38 | .46 | .18 | 52.0 |
| 42 | 796 | 5.55 | 4.90 | 42.05 | 4.83 | 4.60 | .95 | .60 | .58 | .16 | 54.3 |
| 43 | 757 | 6.14 | 5.69 | 41.61 | 4.61 | 5.34 | 1.16 | .67 | .89 | -.08 | 54.4 |
| 44 | 586 | 5.65 | 5.19 | 41.15 | 4.99 | 5.39 | 1.08 | .33 | .60 | -.26 | 50.2 |
| 45 | 553 | 5.79 | 5.22 | 42.08 | 5.19 | 4.71 | .91 | .50 | .69 | .32 | 48.6 |



standard deviations of response that exceeded the amount of response reported by Roberts¹¹. From the long and continuous plateau that occurred, it is evident that the use of progeny test and family selection did not lead to unlimited change; instead, it led to a very definite selection limit.

When considering the reasons for response to selection, or attenuation of response, there is concern about the amount of selection imposed, characterized by the selection differential and the amount of additive genetic variance relative to the total phenotypic variance (heritability). The within-generation selection differentials in Table I are adjusted for differen-

tial reproduction and mortality; therefore, they include the effects of any natural selection that might have occurred. Selection differentials in the first nine generations were rather small, which is probably attributable to excessive mortality occurring early in the experiment, and to a high percentage of offspring maintained as potential parents in order to increase the size of the population. Estimates of the amount of selection practiced, in terms of standard deviation units (*i*), indicate that selection differentials after nine generations generally equaled or exceeded one phenotypic standard deviation (except for the period from generations 47 through 56). The evidence in-

Table I (Continued)

| Gen. | No. indiv. | No. born | No. 60d | \bar{x} wt. | σ wt. | <i>s</i> wt. | <i>i</i> wt. | s_1 no. born | s_1 no. 60d | <i>r</i> mates | % males |
|------|------------|----------|---------|---------------|--------------|--------------|--------------|----------------|---------------|----------------|---------|
| 46 | 598 | 6.34 | 5.28 | 42.38 | 5.17 | 4.72 | .91 | .19 | .42 | .07 | 48.5 |
| 47 | 845 | 6.31 | 5.32 | 42.82 | 4.71 | 3.11 | .66 | 1.07 | .87 | -.03 | 49.9 |
| 48 | 713 | 6.34 | 5.36 | 42.50 | 4.90 | 3.96 | .81 | .79 | .97 | .15 | 51.1 |
| 49 | 869 | 6.57 | 5.33 | 42.77 | 4.59 | 2.82 | .61 | 1.48 | 1.74 | -.11 | 47.4 |
| 50 | 770 | 6.86 | 5.54 | 42.45 | 3.52 | 2.37 | .67 | .36 | .30 | .11 | 49.4 |
| 51 | 583 | 7.53 | 5.95 | 42.82 | 3.53 | 1.32 | .37 | .30 | 1.04 | .21 | 49.9 |
| 52 | 357 | 7.91 | 6.26 | 43.51 | 2.57 | .89 | .35 | .50 | .64 | .28 | 48.2 |
| 53 | 195 | 6.97 | 4.88 | 44.62 | 3.68 | 1.36 | .37 | 1.67 | 1.33 | .19 | 40.5 |
| 54 | 318 | 7.19 | 6.00 | 44.18 | 3.47 | .59 | .17 | 1.00 | 1.13 | -.51 | 51.3 |
| 55 | 270 | 6.94 | 5.51 | 40.29 | 5.57 | 3.99 | .72 | .58 | 1.09 | .13 | 48.9 |
| 56 | 169 | 7.72 | 5.83 | 43.03 | 4.38 | 2.06 | .47 | .40 | 1.86 | -.20 | 52.7 |
| 57 | 186 | 8.08 | 7.15 | 40.12 | 5.10 | 4.71 | .92 | -.68 | -.20 | -.10 | 52.2 |
| 58 | 231 | 7.32 | 6.24 | 41.26 | 5.81 | 4.05 | .70 | -.09 | .67 | -.36 | 57.6 |
| 59 | 689 | 7.96 | 7.13 | 41.42 | 4.77 | 4.91 | 1.03 | -.49 | .10 | .10 | 53.6 |
| 60 | 720 | 7.59 | 6.14 | 40.96 | 5.11 | 4.94 | .97 | -.57 | .20 | -.36 | 54.9 |
| 61 | 775 | 7.49 | 6.11 | 40.92 | 5.84 | 3.85 | .66 | -.63 | .20 | .10 | 54.8 |
| 62 | 1245 | 8.00 | 7.07 | 40.30 | 5.82 | 6.81 | 1.17 | -.18 | -.19 | .09 | 53.0 |
| 63 | 622 | 7.35 | 6.55 | 41.76 | 5.13 | 6.38 | 1.24 | .03 | .19 | .06 | 49.8 |
| 64 | 439 | 7.03 | 6.20 | 41.07 | 5.78 | 6.88 | 1.19 | -1.20 | -.60 | .18 | 57.4 |
| 65 | 615 | 7.19 | 6.44 | 43.94 | 5.20 | 5.55 | 1.07 | -.32 | -.17 | .20 | 52.2 |
| 66 | 612 | 7.15 | 6.38 | 44.85 | 5.32 | 5.93 | 1.11 | -.25 | .07 | -.01 | 51.1 |
| 67 | 465 | 6.16 | 5.68 | 44.99 | 5.80 | 6.84 | 1.18 | -.17 | .11 | -.09 | 57.4 |
| 68 | 427 | 6.17 | 5.55 | 43.72 | 5.93 | 4.85 | .82 | 1.26 | 1.42 | .32 | 52.2 |
| 69 | 390 | 6.00 | 5.65 | 44.71 | 4.95 | 4.47 | .90 | .68 | .78 | .10 | 52.3 |
| 70 | 321 | 5.35 | 5.08 | 45.33 | 5.37 | 3.39 | .63 | 1.57 | 1.56 | .10 | 52.3 |
| 71 | 397 | 5.46 | 5.08 | 45.83 | 6.44 | 4.32 | .67 | .72 | .86 | -.13 | 50.1 |
| 72 | 467 | 5.85 | 5.31 | 45.31 | 5.09 | 5.15 | 1.01 | 1.62 | 1.50 | .02 | 50.7 |
| 73 | 470 | 6.08 | 5.16 | 44.24 | 6.06 | 5.70 | .94 | .25 | .45 | -.17 | 53.8 |
| 74 | 631 | 6.73 | 5.95 | 42.60 | 5.84 | 2.40 | .41 | .07 | .43 | .06 | 51.2 |
| 75 | 664 | 6.52 | 6.04 | 42.34 | 5.58 | 6.55 | 1.17 | -.06 | -.02 | .07 | 48.8 |
| 76 | 665 | 7.09 | 6.26 | 43.00 | 5.15 | 4.80 | .93 | .29 | .62 | .05 | 50.2 |
| 77 | 509 | 6.87 | 5.92 | 42.96 | 5.79 | 5.97 | 1.03 | -.18 | -.14 | .03 | 53.4 |
| 78 | 472 | 6.45 | 5.38 | 40.14 | 5.35 | 4.71 | .88 | .24 | .50 | -.01 | 54.2 |
| 79 | 441 | 5.69 | 4.50 | 39.13 | 6.11 | 5.68 | .93 | -.20 | .50 | .08 | 54.0 |
| 80 | 331 | 5.09 | 4.19 | 40.92 | 6.94 | 5.52 | .80 | -.03 | .47 | .19 | 55.9 |
| 81 | 358 | 5.63 | 4.45 | 40.83 | 6.74 | 5.72 | .85 | .46 | 1.09 | -.19 | 54.5 |
| 82 | 265 | 5.02 | 3.66 | 39.15 | 7.32 | 8.26 | 1.13 | -.09 | .35 | .19 | 58.1 |
| 83 | 124 | 5.65 | 3.65 | 43.71 | 6.52 | 5.51 | .85 | -.05 | .91 | -.40 | 56.5 |
| 84 | 103 | 6.91 | 4.48 | 45.46 | 5.38 | — | — | — | — | — | 57.6 |

icates that considerable selection pressure was diverted to litter size during this period⁸, and the reason for termination of selection response was not attributable to a failure to obtain adequate selection differentials.

Additive genetic variance (σ^2_A), estimated from the sire component of an analysis of variance, changed very little from generation 1 through 50. In the interval of generations 51 through 60, when selection was somewhat relaxed for body weight, σ^2_A appeared to decrease. However, in the last 24 generations when selection pressure was strong and selection progress was not attained, σ^2_A was quite large. The high estimates of σ^2_A contributed to similarly high estimates of h^2_s (Table II). Because of the experimental procedure, sire offspring groups were from a rather wide time interval, with considerable time-related environmental effects confounded with variation among sire groups. Phenotypic variance (σ^2_p) increased in the early and late stages of the experiment. This was particularly true in the last 24 generations, and remained so when the variance was presented as a coefficient of variation (*cv*), thus removing the effect of increased body size. Obviously environmental contributions to total variance were large in the late generations, and this fact, combined with the obvious confounding of time effects with differences among sire groups, accounted for a portion of the estimates of σ^2_A , when no additive variance was available to selection. The dam component of variance, which was almost completely confounded with time-related environmental effects, was greatly inflated and was not used. Selection would be expected to reduce the variance among parental groups; however, this effect was overwhelmed by the strong upward bias of the confounded environmental effects. The progressive inbreeding that occurred in this population decreased σ^2_A and probably increased σ^2_p , with the effects being greater in later generations.

Heritability of 60-day weight, estimated by regression of offspring on sire (h^2_{os}) and dam (h^2_{od}), was quite low in the first 10 generations (Table II). However, h^2_{os} and h^2_{od} averaged about 20 percent during the remaining generations, except for genera-

tions 51 through 60 when these estimates were small and negative. There seemed to be little association between selection response, or lack of it, and the magnitude of h^2_{os} and h^2_{od} . (Unlike h^2_s estimates, these calculations should not be confounded with environmental fluctuations.) The low estimates in the early generations might be related to the disease problems that existed in the laboratory at that time. However, it is interesting to note the persistence of covariation among parents and offspring except for the one interval that included the previously mentioned period when selection intensity for body weight was reduced. While there is no adequate explanation for this situation, it seems possible that nonallelic gene interactions, maintained by selection and correlated between parent and offspring somewhat less than .25, could be responsible. Nevertheless, this explanation would be more logical if selection for 60-day weight during generations 51 through 60 had been reduced more than the approximately 50 percent that actually did occur. A more plausible explanation for the situation involving these generations may be that it occurred entirely by chance. Also, there was a slight reduction in mean 60-day weight during this interval (generations 51 through 60), followed by a small increase in the next interval when normal selection pressure was resumed. A probable explanation for this situation, since litter size does affect 60-day weight (Table II), is the larger litters, born and reared during generations 51 through 60, plus the subsequent reduction in litter size in the following period, when selection for 60-day weight again increased.

Realized heritability (h^2_r), determined by dividing the accumulated response by the accumulated selection differential for a given increment of generations, was very high in the first 10 generations (Table II). Although genetic progress was being made, some of the increase in h^2_r was probably due to improving environmental conditions during the early generations of study. There was a consistent reduction in response relative to the accumulated selection differential until plateau at, or about, generation 35. From generations 35 through 50 and 71 through 84, h^2_r

Table II. Parameters calculated from information pooled over 10-generation intervals

| Item | Generations | | | | | | | |
|--------------------|-------------|-----------|-----------|-----------|-----------|------------|-----------|-----------|
| | 1-10 | 11-20 | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 | 71-84 |
| No. indiv. | 3239 | 11743 | 9020 | 7610 | 7397 | 3718 | 5911 | 5897 |
| σ^2_A , wt. | 3.40 | 5.00 | 5.04 | 4.04 | 5.41 | 2.99 | 8.40 | 9.88 |
| σ^2_p , wt. | 8.68 | 9.96 | 15.67 | 22.77 | 22.56 | 20.11 | 30.98 | 35.32 |
| <i>cv</i> , wt. | .09 | .09 | .10 | .11 | .11 | .11 | .13 | .14 |
| h^2_s , wt. | .39 ± .09 | .48 ± .06 | .32 ± .07 | .18 ± .07 | .24 ± .07 | .15 ± .10 | .27 ± .08 | .28 ± .09 |
| h^2_{os} , wt. | .05 ± .03 | .16 ± .02 | .16 ± .04 | .14 ± .04 | .22 ± .04 | -.06 ± .06 | .22 ± .06 | .14 ± .05 |
| h^2_{od} , wt. | .10 ± .03 | .30 ± .02 | .30 ± .02 | .24 ± .03 | .16 ± .03 | -.02 ± .03 | .24 ± .04 | .04 ± .02 |
| h^2_r , wt. | .32 | .19 | .10 | .03 | .02 | -.06 | .08 | .00 |
| r_{1s} | -.21 | -.46 | -.46 | -.47 | -.36 | -.33 | -.47 | -.37 |
| r_{1d} | -.05 | -.35 | -.47 | -.38 | -.31 | -.26 | -.37 | -.27 |
| b_m , wt. | .02 | .10 | .10 | .06 | .10 | -.11 | .03 | .08 |
| b_{fs} , wt. | .02 | .06 | .07 | .07 | .12 | .05 | .19 | .04 |

deviated little from zero. There was a reduction in mean 60-day body weight of 6 percent of the accumulated selection differential in generations 51 through 60; in generations 61 through 70 there was an increase of 8 percent.

The results of this experiment reiterate the findings reported by Roberts¹¹—that response to selection for body weight in mice does not continue indefinitely, but does indeed reach a definite limit. The length of time to reach such a limit varies considerably and is affected by the intensity of selection, the amount of variation in the population, and the population size. However, the utilization of a progeny test or family selection apparently does not result in a higher limit. These authors also agree with Robert's statement that more experimental work is needed to elucidate the genetic nature of the limits of artificial selection.

Other information

There were consistently negative correlations between body weight at 60 days and litter size at birth (r_{12}), and body weight at 60 days and litter size at 60 days (r_{13}), (Table II). These correlations were of sufficient magnitude to be statistically significant ($P < .05$), indicating that the heavier individuals at 60 days tended to be from smaller litters. In selecting potential parents, there would have been a tendency to select individuals from small litters; however, this would have been offset by the fact that larger litters produce more individuals.

Secondary selection differentials (s_1) (Table I) for average number born per litter were mostly negative for generations 1 through 32. However, from generation 33 to generation 57, secondary selection differentials for number of offspring per litter were generally positive, indicating a selection pressure for increased litter size at birth. From generations 56 to 84, there were periods of consistently negative and positive secondary selection differentials for number of offspring born per litter. Little or no attention was paid to litter size when selections were made during the earlier years of the experiment, while later on some selection pressure was diverted to this trait⁸. However, the negative secondary selection differentials in the early generations suggests that selection for 60-day weight alone resulted in some selection for smaller litters at birth. The secondary selection differentials were largely positive for number of offspring per litter at 60 days. This fact plus the previously mentioned negative secondary selection differentials for litter size at birth indicate that litters with more offspring at birth had a considerably higher mortality rate, i.e., in many generations, the litters producing the selected, potential parents had fewer offspring at birth than the average, but more offspring at 60 days than the average.

The correlation between mates (r), although not large, was consistently positive for the first 42 generations, causing a small upward bias in estimates of heritability. After generation 42, r had much less tendency to be positive.

The sex ratio, presented as the percentage of males surviving to 60 days, shows the rather interesting trend of a steady progression from percentages in the mid forties in early generations to the mid fifties toward the end. The mice were sexed at weaning, but since little mortality occurred between weaning and 60 days, the sex ratio at these times should be nearly the same. Conversely, there was considerable mortality prior to weaning. It is somewhat difficult to visualize environmental conditions that would initially favor viability in females, and then progressively change to favor males. However, if it is true that female mice can withstand more environmental adversity, and that environmental conditions gradually improved along with there being a predominance of male zygotes, then a sex by environment interaction for mortality could be held accountable.

Since progeny test or family selection for body weight would favor individuals that were parents of, or came from, families with a predominance of males, it is conceivable that the change in the sex ratio was an indirect result of selection for increased body weight. However, Falconer² was not successful in changing the sex ratio of mice by direct selection, and Weir¹³⁻¹⁵ was able to affect sex ratio only as a correlated response to selection for blood-pH.

Individual regressions of male (b_{ms}) and female (b_{fs}) offspring 60-day weight on sire 60-day weight were approximately equal (Table II). This indicates that sex-linked genes were not a major factor in determining 60-day body weight in this population of mice.

Assuming that selection for small body size at 60 days would have reached a limit at a given level, (e.g., 15 grams, based on Roberts¹¹ results of 12 grams for 42-day weight) then a rough estimate of the number of body weight loci segregating in the base population could be made. Although the assumptions are quite restrictive, by utilizing Wright's¹⁶ well-known formula

$$n = \frac{R^2}{8\sigma_A^2}$$

where n = number of loci, R = total range, and σ_A^2 = additive genetic variance, the number of loci segregating for 60-day body weight was estimated to be approximately 30, which is slightly higher than that reported by Roberts¹¹.

Summary

Data were analyzed from H. D. Goodale's 84-generation selection experiment for body weight in mice. The average number of mice per generation was 649 with a total number of 54,535 animals surviving to 60 days. Female weights were corrected to a male equivalent; the initial generation mean was 25.38 grams. An undefined combination of individual, family, and progeny test selection resulted in a progression of 60-day weight to a high of approximately 43 grams at generation 35. Selection was continued to generation 84, with no additional increases

in body size, but with considerable fluctuations of the generation means.

Estimates of heritability indicated that genetic variance was not exhausted, and reproduction was such that the selection intensity was generally one phenotypic standard deviation. However, the long plateau also indicated that the estimates of genetic variability were probably biased and that no genetic variation for increased body weight was available to selection.

A progressive change in sex ratio occurred during the experiment from an excess of females to an excess of males. However, it could not be determined whether the cause was due to a change in the pattern of mortality, or to selection for body weight favoring those families producing an excess of males.

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