
VOLUME 62 2002

THE EFFECT OF SELECTION FOR BODY WEIGHT AT DIFFERENT AGES ON FAT DEPOSITION IN MICE

R. L. BAKER, A. H. CARTER and E. H. COX

Ruakura Agricultural Research Centre, Hamilton

SUMMARY

Four lines of mice were formed from a common base population and selected for increased 3-week weight (weaning weight), 6-week weight and 3-6 week gain, respectively, or maintained as a randomly bred control line. Selection was terminated after 37 generations.

Body composition studies on mice sampled from all four lines were made at generation 5 (at an average age of 16 weeks) and generations 12 and 20 (6 weeks of age). At 6 weeks of age, the line selected for 3-week weight was fatter and the line selected for 6-week weight leaner than the control line. To investigate this finding more definitely, serial slaughter was carried out at generations 23, 29 and 37. These data were then pooled and analysed on a within-sex basis. There were only small differences among lines in the pattern of fat deposition in male mice. But in females, which were fatter than males, there were differences among lines in fat deposition. The line selected for 3-week weight was the leanest line at its selection age but became progressively fatter at older ages and significantly fatter than mice from the 6-week weight or control line. In contrast, the line selected for 6-week weight was the leanest line at 6 weeks of age and at older ages. The line selected for 3-6 week gain had a similar pattern of fat deposition to the line selected for 3-week weight from about 6 weeks of age and older.

These results are discussed in relation to models in the literature which postulate the genetic relationships among age at selection and growth rate, feed efficiency, appetite and body composition.

INTRODUCTION

In 1965 a selection experiment with mice was initiated to compare the efficacy, in terms of improving 6-week liveweight, of selection based on weaning (3-week) weight, post-weaning (3-6 weeks) gain and 6-week weight itself. The study was terminated after 37 generations of selection. During the course of the study the selection lines were sampled for carcass composition analysis in terms of water, fat, ash and protein.

This paper reports on the changes in body composition observed in terms of fat deposition only.

MATERIALS AND METHODS

The original base population for this study was a four-way cross of four inbred lines, namely: A_w, C57, CBA and an albino strain (called Ruakura White) of unknown origin. The population was initially split into three lines, one selected for large 6-week weight, one selected for small 6-week weight and a random-bred control line. After 12 generations of selection and then five generations of relaxed selection, these three lines were recombined in a balanced diallel crossing programme. From this foundation, four genetically similar lines were then constituted to initiate the present study.

In the selection lines the criteria for selection were increased 3-week weight, 6-week weight and 3-6 week gain, respectively. In the control line, selection was aimed at maintaining minimum selection differential for 6-week weight; that is, from each litter the male and the female chosen were those closest to the litter-sex mean. Each line comprised eight pair matings, and from each litter one male and one female were selected (*i.e.*, within-litter selection). A cyclical mating plan was used to minimize inbreeding. Litter size was *not* standardized.

Body composition of samples of mice from all lines was determined in generations 5, 12, 20, 23, 29 and 37. In generation 5 (G5), the mice sampled were those available after selection had taken place, and the average age at slaughter was about 16 weeks, although no slaughter weight is available. In G12 and 20, second litters were produced (selection having taken place in the first litter as usual), and all mice alive at 6 weeks of age from each line were slaughtered and body composition determined. Second litters were also produced for body composition analysis in G23 and 29. In G23, balanced samples (by sex and litter within lines) were serially slaughtered at 3, 6 and 9 weeks of age. and in G29 at 3, 4½, 6 and 9 weeks of age. Approximately 10 males and 10 females were slaughtered at each age from each line. In G37, additional matings were made to allow serial slaughter at 3, 6, 12 and 20 weeks of age from mice from first litters. By G37 the line selected for 6-week weight had been lost owing to poor reproduction and a severe disease outbreak in G32. In G37, litter size was standardized at birth where possible to 8 young (*i.e.*, 4 males and 4 females).

Prior to slaughter all mice were removed from access to food, but not water, for about 24 hours and an empty slaughter weight (ESW) was then recorded. Water content was determined by

TABLE 1: LEAST SQUARES MEANS (g) FOR 6-WEEK WEIGHT (6WW), EMPTY SLAUGHTER WEIGHT (ESW), FAT CORRECTED WEIGHT (FCW) AND FAT PERCENT (FP)

	Generation 5				Generation 20					Genertion 12				
Line	*n*	*6WW*	*FCW*	*FP*	*n*	*6WW*	*ESW*	*FCW*	*FP*	*n*	*6WW*	*ESW*	*FCW*	*FP*
3-6 WG	15	22.0^{a}	2.83^{a}	13.2^{a}	67	26.3^{a}	22.5^{a}	1.70^{a}	8.0^{a}	67	27.4^{a}	23.4^{a}	1.91^{a}	9.2^{a}
6WW	16	22.4^{a}	2.12^{b}	10.4^{b}	61	28.7^{b}	25.0^{b}	1.74^{a}	8.1^{a}	37	25.9^{b}	21.5^{b}	1.42^{b}	7.0^{b}
3WW	16	21.2^{ab}	2.75^{a}	12.8^{a}	58	23.1^{c}	20.9^{c}	2.08^{b}	9.9^{b}	52	23.1^{c}	19.9^{c}	1.80^{a}	9.0^{a}
Control	16	19.3^{b}	2.57^{a}	11.3^{a}	54	19.0^{d}	17.3^{d}	1.74^{a}	8.3^{a}	54	18.9^{d}	15.6^{d}	1.89^{a}	8.9^{a}
RSD		2.78	0.61	2.92		2.55	2.49	0.53	2.64		2.91	2.56	0.40	2.10
b (±s.e.)		0.19±.03				0.07±.01					0.15±.01			

[a], [b], [c], [d] Means which do not have the same superscript differ significantly from one another ($P<0.05$).

drying in an oven for at least 12 hours. For each mouse the dry residue was then washed with petroleum ether to remove most of the fat, and the residue again dried and weighed, the difference being designated crude fat. The residues were then bulked, as far as possible within ages and lines, and Soxhlet extraction of bulk samples carried out to determine the average remaining fat percentage. The total fat for each mouse was then calculated.

Statistical analysis of body composition data in G5, 12, and 20 allowed for lines, sexes and the interaction between lines and sexes. In analysing the weight of fat, an analysis of covariance was also carried out including either 6-week weight (G5) or ESW (G12 and 20) as the covariate.

For the serial slaughter data collected in G23, 29 and 37, regression analyses similar to those developed by Clarke (1969) and Hayes and McCarthy (1976) were applied. Initially the data were analysed within each generation, fitting a model which included effects for lines, sexes, the interaction of lines by sexes and the regression of fat weight on ESW partitioned by lines, sexes and lines × sexes. These analyses revealed some important interactions with sexes, but reasonably consistent results across generations. Therefore the data from G23, 29 and 37 were pooled and then analysed on a within-sex basis. The model fitted included lines, generations, lines × generations and within line × generation regression of fat weight on empty slaughter weight. Analyses were carried out on both the raw data and their logarithms.

RESULTS

Generation means for 3-week weight (3WW), 6-week weight (6WW) and 3-6 week gain (3-6WG) are shown in Fig. 1 for all three selection lines and the control line. In the case of 6WW (*i.e.*, "final" weight) the lines selected for 6WW and 3-6WG were the heaviest lines, with the 3WW line being about intermediate between these lines and the control.

Least-squares means for 6WW, ESW and fat weight adjusted for body weight (FCW) and fat percent (FP), from analysis of data from G5, 12 and 20, are given in Table 1. The interaction of line by sex was not significant in any of these analyses and was therefore deleted from the model, leaving just the two main effects (lines and sexes) and the covariate (6WW or ESW) where this was fitted. In all three generations both lines and sexes were significant sources of variations ($P < 0.05$) for all traits

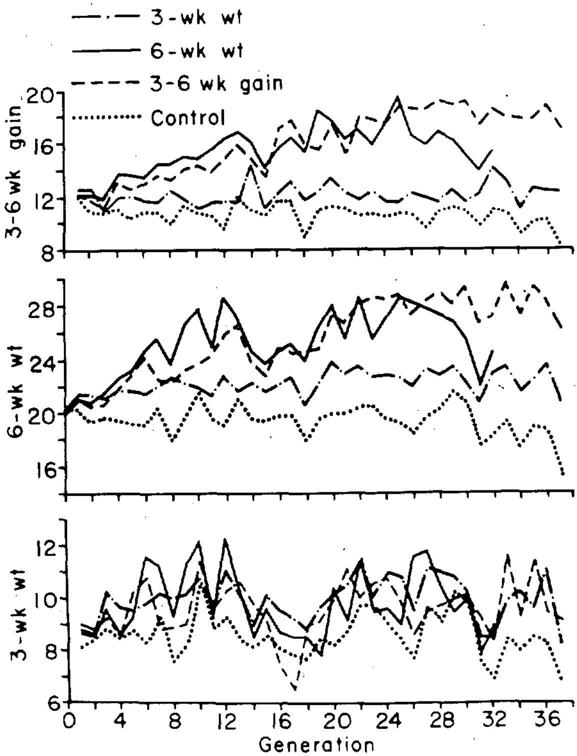

FIG. 1: *Direct and correlated responses to selection for 3-week weight, 6-week weight and 3-6 week gain.*

analysed. While males were significantly heavier than females at 6 weeks of age, the fat percentage was significantly higher in females than males (difference of about 1.5%) at this age.

Fat percentage is presented in Table 1 to facilitate comparison of the present results with other published data. Among others, Dinkell *et al.* (1965) have pointed out that ratios can be used validly to adjust a carcass component for weight only when the regression line between the component and weight passes through the origin and is linear from the origin through the region of interest. This is clearly not the case in these data, but in the data collected at a fixed age of 6 weeks (at least in G12 and 20) there was not enough variation in ESW to invalidate the use of the ratio versus the more correct covariance analysis.

In the analysis of covariance of fat weight carried out in G5, 12 and 20, tests of the differences among slopes of the regression of fat weight on empty slaughter weight were made both for lines and for sexes. The slopes were not significantly different in these data (in contrast to the results to be presented next), so the regression coefficients shown in Table 1 are those pooled within sex-line subclasses.

In interpreting the results from Table 1 more emphasis should be given to the analyses in G12 and 20 than in G5 because of the possibility of biased sampling among lines in G5. In G12 the mice from the line selected for 3WW were significantly fatter than those from the other three lines, although it was not the heaviest line. In G5 and 20 the only significant difference in FCW was that the line selected for 6WW was leaner.

These initial analyses prompted the more definitive serial slaughter approach used in G23, 29 and 37. The assessment of body composition at a single age is a very dubious procedure since body composition is known to change with age and weight, as has been discussed extensively previously (*e.g.*, Clarke, 1969; Sutherland *et al.*, 1974; Hayes and McCarthy, 1976).

The results of the analyses of the serial slaughter data are presented in Table 2 separately for male and female mice. Because of non-linearity in the relationship between fat weight and ESW, the data were converted to natural logarithms. The regression coefficients shown in Table 3 then estimate the exponent b in the allometric equation $Y = Ax^b$, where Y and X are fat

TABLE 2: ESTIMATES FOR THE INTERCEPTS (A') AND REGRESSION COEFFICIENTS (*b*) BY LINES FROM ANALYSIS OF LOG FAT ON LOG EMPTY SLAUGHTER WEIGHT FOR DATA FROM GENERATIONS 23, 29 AND 37[1]

Line	*n*	*A*	*b* ± *S.E.*
Females:			
3-6WG	98	—4.27	1.58 ± 0.06
6WW	56	—4.02	1.45 ± 0.08
3WW	127	—4.77	1.74 ± 0.07
Control	87	—3.87	1.42 ± 0.08
Males:			
3-6WG	112	—4.01	1.42 ± 0.05
6WW	52	—4.01	1.44 ± 0.08
3WW	120	—4.54	1.57 ± 0.06
Control	91	—3.62	1.31 ± 0.07

[1] For the statistical model used, see text.

weight and empty slaughter weight, respectively. The A estimates the log of the intercept of the regression equation. The A and b values presented in Table 2 were derived from a model which included lines, generations, lines × generations and the within-line regression of log fat weight on log ESW. Initial analyses established uniformity of the regression coefficients over the three generations. The smaller number of mice sampled from the line selected for 6-week weight was due to the fact that this line was not present in G37.

Interpretation of the data presented in Table 2 is facilitated by considering the regression lines in Fig. 2. The logarithmic equations have been converted back to arithmetic values for graphical presentation.

There are much smaller differences in the pattern of fat deposition among lines for males than for females, although the pattern of fat deposition among lines is fairly consistent for the two sexes with the exception of the line selected for 6WW. In females

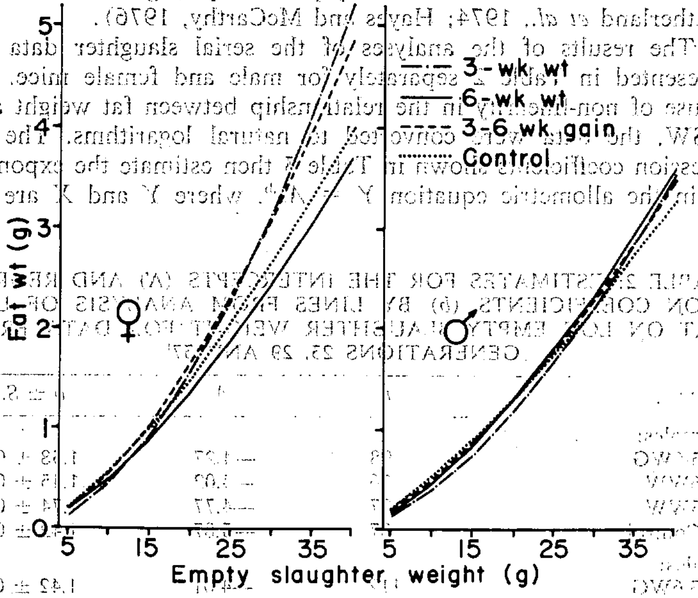

FIG. 2: *Allometric regression lines of fat weight on empty slaughter weight for selection groups and sexes from data from mice slaughtered in generations 23, 29 and 37.*

we see more clearly the effect that selection at different ages has had on the pattern of fat deposition. The line selected for 3-week weight is the leanest at this age, but subsequently mice in this line became progressively and significantly fatter than the mice from the control or 6WW line. In contrast, the line selected for 6WW is the leanest line at the age of selection (*i.e.*, an empty slaughter weight of about 20 g) and remains the leanest line at older ages, although not significantly leaner than the control line. The line selected for 3-6WG has a very similar pattern of fat deposition to that selected for 3-week weight.

DISCUSSION

Three published studies are particularly relevant to the patterns of fat deposition observed in this study. Hull (1960) found that the proportion of fat in the carcasses of the selected animals at 6 weeks of age increased markedly in the line selected for high 3-week weight, while in the other two lines selected for increased 4½- and 6-week weight the fat proportion remained the same as that in the control line. Hayes and McCarthy (1976) found that their line selected for high body weight at 5 weeks of age was slightly fatter than their line selected for high 10-week body weight when the lines were compared at 5, 10 and 21 weeks of age.

Brown *et al.* (1977) compared the body composition at 3, 6 and 8 weeks of age of *male* mice from lines selected for 3-week weight and 3-6 week gain. In spite of substantial differences in growth patterns as a result of 14 generations of selection (with the gain line being the heaviest), there were no major differences in body composition of the male mice sampled among the two groups of selected lines or the unselected controls. These results are consistent with the present finding that there were no differences in fat deposition between the lines selected for 3-week weight or 3-6 week gain in either male or female mice. But, in contrast to the results of Brown *et al.* (1977), in the present study the lines selected for 3-week weight and 3-6 week gain were fatter than unselected control mice, at least in females. Brown *et al.*, however, sampled only male mice.

Clarke (1969) carried out comprehensive carcass analyses of Falconer's (1973) replicated lines selected for high and low 6-week weight. One of his main conclusions was that when you select for increased body weight at a fixed age there is very little effect on fatness (if anything they may be relatively leaner than controls) up to the age of selection, but after the age of selection large mice become progressively fatter. This conclusion appears to hold for the present study and for that of Hull (1960) and Hayes and McCarthy (1976), where in each case mice from the line selected for increased body weight at the youngest age (3 weeks or 5 weeks) had more fat, on average, than those from other lines.

Hayes and McCarthy (1976) present a model to explain these results. The essential features of this model, as paraphrased by Roberts (1979), are as follows: "In the young growing animal genetic variation in growth is mostly due to food intake and animals selected for early growth simply eat more. At later ages, however, as fat accumulates, there is further genetic variation in the partitioning of food between fat and protein. Because — the argument goes — fat is energetically denser than lean, the leaner animals are more efficient and therefore grow more rapidly. It is these leaner animals that are selected at later ages, whereas animals selected when young are voracious and grow fat." McCarthy (1978) further elaborated on this model and reviewed data tending to support it. In addition, the review of Webster (1977) adds some further dimensions to the general problem of selection for leanness and the nutritional considerations, particularly the detailed picture of energy flow, which might be important.

It has been suggested (Frisch, 1977) that the proportion of fat in the body is associated with puberty and reproduction in the human and the rat. Puberty was not recorded in the study reported here, but clearly this is an area which warrants further investigation (Cockrem, 1979; Roberts, 1979). The discussion to date has related to animals selected under *ad libitum* feeding, but it may also be possible to modify the relationship between body weight gain and fatness through selection under different (*e.g.*, restricted) feeding regimes (Roberts, 1979).

In light of the well-documented need to produce leaner animals to meet future market requirements (*e.g.*, Kirton, 1977), the present results and the model suggested to explain them could be particularly relevant. The present study was unreplicated, and the results could have been influenced by random genetic differences in the relative rate of fat deposition (Clarke, 1969). However, the findings are reasonably consistent with those of Hull (1960) and Hayes and McCarthy (1976), giving reason for some confidence in the general conclusions. Sutherlend *et al.* (1974) also warn against extrapolating body composition results with laboratory rodents (mice or rats), often just evaluated at a specific age, to domestic farm animals, because of possible important species differences. Thus while increased growth rate in mice usually results in fatter animals (at least at 6 weeks of age and older), there is also ample evidence that large, rapidly growing breeds of cattle and sheep (*e.g.*, Charolais and Suffolk) are much leaner, not only at a given weight but also at a given age, than smaller, slower-growing breeds (*e.g.*, Angus and Southdown). Factors other than growth probably featured in the evolutionary history of these breeds, however (*e.g.*, draught use in cattle).

These results with mice should be tested with farm livestock on a within-breed basis. Selection for body weight at two quite different ages (*e.g.*, 6 and 12 months) in Suffolk and Southdown sheep is under consideration. The thesis would be that selection at 12 months of age may result in a leaner strain of sheep than selection at 6 months of age or unselected controls. There is also a selection study in progress in New Zealand selecting Angus cattle for increased weight at 15 and 20 months of age with a random-bred control (Baker and Carter, 1972). It would clearly be wise to monitor any changes in body composition in this programme.

Finally, there is a case for further work, perhaps initially with mice, to investigate further the genetic relationships among growth at different ages, appetite, feed efficiency and body composition. There appear to be only two published reports selecting for three or more of these traits simultaneously in the one experiment from a common base population. Sutherland *et al.* (1970) selected for growth rate, appetite and efficiency of feed utilization in mice and found that the line selected for appetite became very fat compared with the other lines. In a study with broiler chickens (Pym, 1971; Pym and Nicholls, 1979; Pym and Solvyns, 1979), selection was carried out for body weight gain, food consumption and feed utilization efficiency. It was found that the feed consumption line was the fattest and the feed efficiency line the leanest after five generations of selection.

Two factors of particular interest in this general syndrome may be metabolic heat production (Webster, 1977) and the general role of fat in overall metabolism (Cockrem, 1979). Selection for metabolic heat production in mice, while monitoring other traits such as body composition, appetite, feed efficiency and growth, might provide useful leads for more in-depth studies of a similar nature with sheep and cattle in the future.

ACKNOWLEDGEMENTS

To Chemical Services, particularly Miss B. Crane, for body composition analyses, and the Small Animal Colony staff for servicing.

REFERENCES

Baker, R. L.; Carter, A. H., 1972. *Beef Cattle Breeding Research Programme at Waikite North* (unpublished mimeo).

Brown, M. A.; Frahm, R. R.; Johnson, J. J., 1977. *J. Anim. Sci.*, 45: 18.

Clarke, J. N., 1969. Ph.D. thesis, University of Edinburgh.

Cockrem, F. R. M., 1979. *Proc. N.Z. Soc. Anim. Prod.*, 39: 23.

Dinkel, C. A.; Wilson, L. L.; Tuma, H. J.; Minyard, J. A., 1965. *J. Anim. Sci.*, 24: 425.

Falconer, D. S., 1973. *Genet. Res.*, 22: 291.

Frisch, R. E., 1977. *Res. in Reprod.*, 9: 1.

Hayes, J. F.; McCarthy, J. C., 1976. *Genet. Res.*, 27: 389.

Hull, P., 1960. *J. agric. Sci., Camb.*, 55: 317.

Kirton, A. H., 1977. *Proc. Nutr. Soc. N.Z.*, 2: 63.

McCarthy, J. C., 1978. In *Genetic Models of Obesity in Laboratory Animals* Symposium of the Medical Research Council Laboratory Animals Centre, Great Britain.

Pym, R. A. E., 1971. M.Sc. thesis, University of New South Wales.

Pym, R. A. E.; Nicholls, P. J., 1979. *Br. Poult. Sci.*, 20: 73.

Pym, R. A. E.; Solvyns, A. J., 1979. *Br. J. Poult. Sci.*, 20: 87.

Roberts, R. C., 1979. *Livest. Prod. Sci.*, 6: 93.

Sutherland, T. M.; Biondini, P. E.; Ward, G. M., 1974. *Genetics*, 78: 525.

Webster, A. J. F., 1977. *Proc. Nutr. Soc. G. Br.*, 36: 53.